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A SELECTED COMPENDIUM
OF SEASN MEMBERS’ RESEARCH
PUBLICATIONS ON WEHAB+3:
HEALTH

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The establishment of South East Asia Sustainability Network (SEASN) has provided a platform to support higher education institutions and other related sustainability organisations in South East Asian countries for exchanging ideas, findings, information, and good practices in teaching, research, community engagement and institutional arrangement that relate to their work. In order to expedite this process the SEASN Secretariat at Universiti Sains Malaysia has taken the initiative to publish a compendium entitled ‘A Selected Compendium of SEASN Members’ Research Publications on WEHAB+3’, in order to share information and best practices in sustainability studies.

This publication will be a medium to exchange research findings in sustainability and to promote sustainability at the global level for the benefit of the wider community of higher educational institutions.

The focus of this book is on the sectors, Water, Energy, Health, Agriculture, Biodiversity (WEHAB); and cross-sectors, Climate Change and Disaster Risk Management, Consumption and Production, and Population and Poverty; collectively represented as WEHAB+3. The Water (W) and Energy (E) have been successfully published and in this third compendium is focus on Health (H).

Incidentally, WEHAB was launched at the World Summit on Sustainable Development by Kofi Annan in 2002 as a priority set of sectors for sustainability implementation. When we add the three cross sectoral issues, the approach becomes very comprehensive and a broad treatment WEHAB+3 would cover almost all major sustainability challenges.

In this sense, the current compendium will help promote better understanding of sustainable management of Health and create knowledge societies that ensure improved quality of life for the present and future generations.

I would like to extend my deepest appreciation and gratitude to all the contributors, authors and editors for their hard work in materializing this compendium. The dedication and tireless efforts of the CGSS staff for the success of the compendium is fully recognized and acknowledged.

Professor Dato’ Dr. Omar Osman
Chairman
South East Asia Sustainability Network (SEASN)
The South East Asia Sustainability Network (SEASN) is an alliance of higher education institutions and other related sustainability institution in South East Asian countries committed to promote, engage and integrate sustainability in their mission areas in a systematic way. In this regards, ‘A Selected Compendium of SEASN Members’ Research Publications on WEHAB+3’ and is in line with the vision and objectives of SEASN.

This book is seen mainly as a means to build a platform for the sharing of research findings in the form of abstracts of published papers. Our survey has revealed that there is enough scope for eight volumes of valuable information that has already been published in the eight areas of WEHAB+3. We have selected the abstract, including reference details, in the hope that it will make life easier for prospective researchers to focus on critical sustainability issues that matter most to their respective countries or the global community at large.

In compiling the abstracts we are mindful of the Intellectual Property Rights of original authors, and in properly acknowledging them CGSS declares that we do not make any claim on IP issues whatsoever.

We do hope that this effort will provide a tangible and inspiring example of publication to address sustainability challenges quickly and more cost effectively. It is also hoped that this book will contribute towards development and progress that is best for the environment, individuals and the economy without compromising the ability of future generations to meet their needs and ultimately ensuring a sustainable future for all.

Professor Dr. Kamarulazizi Ibrahim

Secretary
South East Asia Sustainability Network (SEASN)
Introduction

This book entitled A Selected Compendium of SEASN Research Publication on Health consists of compilation of abstract of SEASN’s sustainability research output and the resulting publications related to Health from member of South East Asia Sustainability Network (SEASN) which includes of South East Asia higher education institutions, other related sustainability organisations, agencies, NGOs and industries in South East Asia countries with an interest in sustainability.

The link between the environment and human health is very powerful. Toxic chemicals and other hazardous materials are basic elements of development. Yet more than one billion people breathe unhealthy air, and three million people die each year from air pollution — two thirds of them poor people, mostly women and children, who die from indoor pollution caused by burning wood and dung. Tropical diseases such as malaria and African guinea worm are closely linked with polluted water sources and poor sanitation. Conventions and other steps aimed at reducing waste and eliminating the use of certain chemicals and substances can go a long way to creating a healthier environment.

This book aims to share information and best practices in sustainability studies focused in the 8 known areas of sustainability (WEHAB+3), to exchange ideas, concepts and research findings in sustainability and to promote sustainability at the global level for the benefit of the wider higher educational community. The first and second book have been published which focus on sustainability research on Water (W) and Energy (E). Meanwhile, this third book will focus on sustainability research on Health (H). In addition to this, there will be a following book on sustainability research on Agriculture (A), Biodiversity (B) as well as three major cross-sectoral areas, which include Climate Change and Disaster Risk Management (CC+DRM), Production and Consumption (PC) and Population and Poverty (PP) which will be published soon.

This book comprises of compendium which combines knowledge on Health from many primary sources of member of SEASN into a single publication. Some of the primary sources were given by the organization and some of them were extracted from Sciencedirect, Scopus and Thomson Reuters ISI. It is hoped that this book will provide a quick and relatively understand to overview regarding sustainability research output on Health. Thus, it will hopefully provide a foundation for further studies, and catalyse for new research in South East Asia region.
A prospective survey and analysis of nosocomial infections in a tertiary care teaching hospital in South India

Aaseer Thamby S.

The scope of the present study is to identify the type and incidence rate of nosocomial infections in the intensive care units, the organisms that cause them and their susceptibility pattern to commonly used antimicrobial agents. Patients hospitalized in the intensive care units are 5 to 10 times more likely to acquire nosocomial infections than other hospital patients. Use of mechanical ventilation, urinary catheters and intravenous catheters are major contributing factors to this disparity. The Center for Disease Control reported that 5.7% of all hospitalized patients acquire nosocomial infections. The Joint Commission on Accreditation of Health care Organization (JCAHO) recommends surveillance of nosocomial infections in the United States as an important criterion for hospital accreditation. There are no figures to assess the incidence of nosocomial infections in India. Most of the hospitals in India have not implemented infection control measures and there are no proper surveillance systems. The present study was undertaken in order to understand the etiology of ICU-acquired infections. We prospectively examined the sites of infections, causative agents and their susceptibility pattern to commonly used drugs. The study was carried out over a period of 6 months. Of the 37 specimens processed, 8 grew normal flora. The isolated pathogens were *Escherichia coli* (18.9%), *Klebsiella* (18.9%), *Staphylococcus aureus* (18.9%) and *Pseudomonas aeruginosa* (5.4%). The most commonly reported infections were Thrombophlebitis (40.5%), Urinary tract infection (16.2%) and Pneumonia (8.1%). Susceptibility testing of the organisms to the most commonly used antibiotics showed that all the isolated *E.coli* were resistant to ampicillin, amoxicillin and erythromycin; *Klebsiella* showed resistance to cefotaxime and ceferoperazone; *Staphylococcus aureus* to ampicillin, amoxicillin, cloxacillin, erythromycin and amikacin. Various parameters employed to describe the incidence of nosocomial infections in the intensive care units include Crude Infection Rate, Incidence
Rate, Device-Associated Infection Rate and Device-Day Utilization. Inadequate infection control is of particular concern because studies have shown that 1/3rd of all nosocomial infections are preventable. A prospective study was conducted in 2 ICUs (Medical Intensive Care Unit and Intensive Pulmonary Care Unit) of a 350- bedded multispecialty hospital in South India for a period of 6 months. Clinical, demographic and microbiological data were collected in customized data entry sheets from patients who developed symptoms of hospital-acquired infections, and were later analysed. The crude infection rate, device-associated infection rate, device day utilization and incidence rate were calculated. The ultimate goal was to improve awareness and understanding of risks of infection and encourage consistent application of infection control in all intensive care units to promote more favorable outcomes for patients.

Keywords

E.coli; Hospital-acquired infections; Klebsiella; Nosocomial; P. aeruginosa
Medical education is facing challenges created by rapid changes in socio economic scenario world over. The focus of treatment has shifted from cure to comfort and safety. Due to work pressure and changing management strategies, contact time with patients has become shorter. Patients are not too happy to allow students to practice on them. All these have affected the skill development capabilities of students of anaesthesia. Traditional methods of teaching are unable to meet the needs of the students. Many methods are used to bridge the gap. Anaesthesiologists came forward with the concept of simulation training not only in the field of anaesthesia but in other areas of health care. Simulation offers teaching in a safe environment where deliberate practice is possible without causing harm to the patient. Students get immediate feedback and can go back to the problems any time they want. Several studies have shown positive effect of simulation in the field of anaesthesiology in the form of improved competency, especially in learning non technical skills. Simulation training is yet to achieve universal acceptance, mainly due to lack of trained teachers and initial cost. But, the situation is rapidly changing and may soon be incorporated in simulation anesthesia curriculum.

Keywords
Teaching technologies; Simulation training in anesthesia
Antioxidant and Antibacterial Activity of Different Parts of Leucas aspera

Ai Lan Chew, Jeyanthi James Antony Jessica, Sreenivasan Sasidharan

Objective
To evaluate antioxidant, antimicrobial and cytotoxic activity of different parts (root, flower, leaf and stem) of Leucas aspera (L. aspera) (Labiatae).

Methods
Different parts of L. aspera were extracted with 80% (v/v) methanol. The methanol extracts were subjected to antioxidant, antimicrobial and brine shrimp lethality assay.

Results
All the extracts showed moderate to potent antioxidant activity, among which the root extract demonstrated the strongest antioxidant activity with the IC$_{50}$ value of 6.552μg/mL. Methanol extract of root possessed antioxidant activity near the range of vitamin E and thus could be a potential rich source of natural antioxidant. In case of antimicrobial screening, crude extracts of root, flower, leaf and stem showed notable antibacterial activity against tested microorganisms. The root extract showed the highest mean zone of inhibition ranging from 9.0–11.0 mm against tested microorganisms, at a concentration of 100 mg/mL. In the brine shrimp lethality bioassay, it was evident that the methanol root extract did not show significant toxicity. The LC$_{50}$ value for 12 h and 24 h observation was 2.890 mg/mL and 1.417 mg/mL, respectively.

Conclusions
The present finding suggests that the methanol root extract of L. aspera could be developed as pharmaceutical products.

Keywords
Leucas aspera; Antioxidant activity; Antimicrobial activity; Cytotoxic activity; Inhibition of zone; Natural antioxidant; Labiatae
Methicillin-resistant *Staphylococcus aureus* nasal carriage among patients and healthcare workers in a hospital in Kelantan, Malaysia

Al-Talib, H., Yean, C.Y., Hasan, H., Nmn, N.Z., Ravichandran, M.

*Staphylococcus aureus* nasal carriage is a common source of nosocomial infection and colonization. The aim of the present study was to assess the burden of methicillin-resistant *S. aureus* nasal carriage, its association with factors of interest including its genetic relationships. The prevalence of *S. aureus* nasal carriage was found to be 28.7%. This study showed that patients with a history of previous antibiotic intake, nasogastric tube, and longer hospitalization had a significantly high risk of being MRSA nasal carriers. The genetic relationship of all 34 nasal MRSA isolates revealed four major clusters of isolates, and there was a relationship between MRSA isolated from inpatients and healthcare workers.

**Keywords**

MRSA; Nasal carriage; Nosocomial infection
Treating patients with infectious diseases relies heavily on rapid and proper diagnosis. Molecular detection such as PCR has become increasingly important and efforts have been made to simplify these detection methods. This study reports the development of a glass fibre-based lateral flow DNA biosensor that uses capture reagents coupled to carrier beads and detector reagent bioconjugated to gold nanoparticles, for the detection of foodborne pathogen, *Vibrio cholerae*. The DNA biosensor contains a test line which captures target PCR amplicons, an internal amplification control (IC) line which captures IC amplicons and a control line which acts as membrane control to validate the functionality of this device. The test line captures biotin labelled DNA, while the IC line captures digoxigenin labelled DNA. The detector reagent recognizes the fluorescein haptens of the amplified DNA and produces visual red lines. Scanning electron microscopy (SEM) studies performed indicated that the capture reagents remained relatively immobile within the matrix of the membrane even after binding of the detector reagent. The DNA biosensor recorded a limit of detection (LoD) of 5 ng of target DNA. A clinical evaluation was carried out with 174 strains of *V. cholerae* and non *V. cholerae* bacteria and the DNA biosensor recorded 100% for both sensitivity and specificity when compared to conventional agarose gel detection of DNA. Thus it is a viable alternative to agarose gel analysis and is easy-to-use, disposable and do not require any specialized equipment and use of carcinogenic chemicals.

**Keywords**

DNA biosensor; *Vibrio cholerae*; Microspheres; Lateral flow
In vitro antioxidant and anticancer activity studies on Drosera indica L. (droseraceae)

Asirvatham, R., Christina, A.J.M., Murali, A.

**Purpose:** The aim of present in vitro studies was performed to examine the antioxidant and anticancer activities of ethanol and aqueous extracts of *Drosera indica* L.

**Methods:** Different concentrations (5 - 640mcg/ml) of the ethanol (EEDI) and aqueous (AEDI) extracts of *D.indica* L were used in various antioxidant assay methods such as hydroxyl radicals, DPPH, super oxide radical scavenging activity, chelating ability of ferrous ion, nitric oxide radical inhibition, ABTS and reducing power. Ascorbic acid (AA) was used as the standard antioxidant for the free radical scavenging assays. Dalton’s Ascitic Lymphoma (DAL) and Ehrlich Ascitic Carcinoma (EAC) cell lines were used as the in vitro cancer models for the tryphan blue dye and LDH leakage assays, where 5 to 250mcg /ml of both EEDI and AEDI were tested.

**Results:** EEDI showed antioxidant activities with the minimum IC\(_{50}\) values of 34.8±0.43 mcg/ml in scavenging of hydroxyl radical and moreover AEDI showed minimum IC\(_{50}\) values of 94.51±0.84 mcg/ml in Fe\(^{2+}\) chelating assay. EEDI on the reducing power assay and ABTS showed higher IC\(_{50}\) than standard AA. IC\(_{50}\) values of AEDI on Fe\(^{2+}\) chelating assay and super oxide radical assay was lesser than IC\(_{50}\) value of AA. Both extracts at 250mcg/ml dose showed remarkable increase in the percentage of dead cancer cells (90% by EEDI and 86% by AEDI in DAL model and 89% by EEDI and 80% by AEDI in EAC model).

**Conclusion:** It is concluded from this study that *D.indica* L exhibited excellent antioxidant activity against the different in vitro antioxidant models and anticancer activity against the two different cell lines tested.

**Keywords**
Anticancer activity; Dalton’s Ascitic Lymphoma (DAL); Drosera indica L; Ehrlich Ascitic Carcinoma (EAC); In vitro antioxidant activity
Preliminary studies on antimicrobial activity of *Swietenia macrophylla* leaf extract

Ayyappadhas, R., Jestin, C., Kenneth, N., Dayana, N., Dhanalekshmi, U.M.

The plant *Swietenia macrophylla* belonging to the family Meliaceae is a traditionally important plant with more medicinal properties. Phytochemical investigation of crude extracts of *Swietenia macrophylla* resulted in the identification of various chemical constituents. The crude extracts were also tested against human pathogenic bacteria and fungal strains. Based on minimum inhibitory concentration (MIC) of the present study, the plant extract has antibacterial activity as well as good antifungal activity. This study supports the traditional claim and usefulness of the plant.

**Keywords**

Antibacterial; Antifungal; Extract; *Swietenia macrophylla*
In vivo toxicity study of Lantana camara

Badakhshan Mahdi Pour, Sreenivasan Sasidharan

Objective
To investigate the toxicity of methanol extract of various parts (Root, Stem, Leaf, Flower and Fruit) of Lantana camara (L. Camara) in Artemia salina.

Methods
The methanol extracts of L. camara were tested for in vivo brine shrimp lethality assay.

Results
All the tested extract exhibited very low toxicity on brine shrimp larva. The results showed that the root extract was the most toxic part of L. camara and may have potential as anticancer agent.

Conclusions
Methanolic extract of L. camara is relatively safe on short-term exposure.

Keywords
Lantana camara; Artemia salina; Toxicity
Cardiovascular Pleiotropic Actions of DPP-4 Inhibitors: A Step at the Cutting Edge in Understanding their Additional Therapeutic Potentials

Balakumar P., Dhanaraj S.A.

Dipeptidyl peptidase 4 (DPP-4) is a serine protease enzyme expressed widely in many tissues, including the cardiovascular system. The incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are released from the small intestine into the vasculature during a meal, and these incretins have a potential to release insulin from pancreatic beta cells of islets of Langerhans, affording a glucose-lowering action. However, both incretins are hurriedly degraded by the DPP-4. Inhibitors of DPP-4, therefore, enhance the bioavailability of GLP-1 and GIP, and thus have been approved for better glycemic management in patients afflicted with type 2 diabetes mellitus (T2DM). Five different DPP-4 inhibitors, often called as ‘gliptins’, namely sitagliptin, vildagliptin, saxagliptin, linagliptin and alogliptin have been approved hitherto for clinical use. These drugs are used along with diet and exercise to lower blood sugar in diabetic subjects. T2DM is intricately related with an increased risk of cardiovascular disease. Growing body of evidence suggests that gliptins, in addition to their persuasive anti-diabetic action, have a beneficial pleiotropic action on the heart and vessels. In view of the fact of cardiovascular disease susceptibility of patients afflicted with T2DM, gliptins might offer additional therapeutic benefits in treating diabetic cardiovascular complications. Exploring further the cardiovascular pleiotropic potentials of gliptins might open a panorama in impeccably employing these agents for the dual management of T2DM and T2DM-associated perilous cardiovascular complications. This review will shed lights on the newly identified beneficial pleiotropic actions of gliptins on the cardiovascular system.

Keywords
Gliptins; DPP-4 inhibition; Diabetes mellitus; Cardiovascular protection
Voluntary body donation has become an important source of cadavers for anatomical study and education. The objective of this study was to assess knowledge, attitude, and practice (KAP) regarding whole body donation among medical professionals in a medical institute in India. A cross-sectional study was conducted at Kasturba Hospital, Manipal, India, among medical doctors. Data was collected from consenting individuals in the age group of 25-65 years by convenience sampling method. A semi-structured, pretested, questionnaire designed to assess KAP regarding whole body donation was provided to the study population (n = 106); 97 individuals returned the completed questionnaire. Results showed that 8% of the medical professionals were unaware of the term body donation and 85% believed that donated bodies were misused. A large proportion of the respondents did not know about the authority that oversaw body donation, or its criteria for accepting donated bodies and diseases for which bodies were screened before acceptance. Only 22% of polled physicians were willing to donate their bodies for medical education, but 68% expected the public to do the same. While only 7% had already registered their own names for body donation, 64% were not aware of any known person having registered and 72% indicated that their decision would not be influenced even if they knew of friends who had registered. These results suggest that educating medical students and professionals regarding the altruistic act of body donation is as important as educating the general public.

Keywords

Attitude to body donation; Medical bequest program; Medical professionals; Whole body donation
Types of endophytic bacteria associated with traditional medicinal plant *Lantana camara* Linn.

*Bhore Subhash Janardhan, Komathi Vijayan*

**Background:** Traditionally, *Lantana camara* plant (Family: Verbenaceae) is used in herbal medicine as an antiseptic for wounds, in the treatment of skin itches, and externally for leprosy and scabies. The leaves of this plant possess adulticidal activity against different mosquito species. Endophytic bacteria (EB) can produce bioactive compounds found in their host; hence, investigation to find out what types of EB are associated with *L. camara* is necessary.

**Objectives:** The main objective of this study was to isolate and identify EB associated with *L. camara*.

**Materials and Methods:** *Lantana camara* twigs along with the leaves and fruits samples were collected; and EB were isolated from surface-sterilized tissue samples. The 16S rRNA gene fragments were amplified using PCR method; and endophytic bacterial isolates (EBIs) were identified based on 16S rRNA gene sequence similarity method.

**Results:** Cultivable, 50 EBIs were analyzed; and analysis of their 16S rRNA gene sequences suggests that varied 40 types of EB are associated with *L. camara*. Majority (24%) of EBIs were from *Bacillus* genus.

**Conclusion:** Thus, we conclude that *Lantana camara* plants harbour a wide array of cultivable endophytic bacteria.

**Keywords**
16S rRNA; Diversity; Endophytes; Herbal medicine; Malaysia; Natural products
**Isolation and identification of bacterial endophytes from pharmaceutical agarwood-producing *Aquilaria* species**

*Bhore S., Preveena J., Kandasamy K.*

**Background:** Resins and gums are used in traditional medicine and do have potential applications in pharmacy and medicine. Agarwood is the fragrant resinous wood, which is an important commodity from *Aquilaria* species and has been used as a sedative, analgesic, and digestive in traditional medicine. Endophytic bacteria are potentially important in producing pharmaceutical compounds found in the plants. Hence, it was important to understand which types of endophytic bacteria are associated with pharmaceutical agarwood-producing *Aquilaria* species.

**Objective:** This study was undertaken to isolate and identify endophytic bacteria associated with agarwood-producing seven (7) *Aquilaria* species from Malaysia.

**Materials and Methods:** Botanical samples of seven *Aquilaria* species were collected, and endophytic bacteria were isolated from surface-sterilized-tissue samples. The 16S rRNA gene fragments were amplified using PCR method, and endophytic bacterial isolates (EBIs) were identified based on 16S rRNA gene sequence similarity based method.

**Results:** Culturable, 77 EBIs were analyzed, and results of 16S rRNA gene sequences analysis suggest that 18 different types of endophytic bacteria are associated with (seven) *Aquilaria* species. From 77 EBIs, majority (36.4%) of the isolates were of *Bacillus pumilus*.

**Conclusion:** These findings indicate that agarwood-producing *Aquilaria* species are harboring 18 different types of culturable endophytic bacteria.

**Keywords**

16S rRNA; Malaysia; Biodiversity; Endophytes; Medicine; Natural products; Ribosomal DNA; Traditional medicine
Endophytic bacteria as a source of novel antibiotics: An overview

Christina A., Christapher V., Bhore S.

World human population is increasing with an alarming rate; and a variety of new types of health issues are popping up. For instance, increase in number of drug-resistant bacteria is a cause of concern. Research on antibiotics and other microbial natural products is pivotal in the global fight against the growing problem of antibiotic resistance. It is necessary to find new antibiotics to tackle this problem. The use of therapeutic plant species in traditional medicine is as old as mankind; and currently, it is strongly believed that all types of plant species across the plant kingdom do harbour endophytic bacteria (EB). The natural therapeutic compounds produced by EB do have several potential applications in pharmaceutical industry. The EB derived natural products such as Ecomycins, Pseudomycins, Munumbicins and Xiamycins are antibacterial, antifungal and antiplasmodial. Some of these natural products have been reported to possess even antiviral (including Human Immunodeficiency Virus (HIV)) properties. Therefore, to deal with increasing number of drug-resistant pathogens EB could serve as a potential source of novel antibiotics.

Keywords

Bioprospecting; Ecomycins; Human immunodeficiency virus; Kakadumycins; Medicinal plants; Munumbicins; Natural products; Pseudomycins; Traditional medicine; Xiamycins
Diversity of endophytic bacteria in Malaysian plants as revealed by 16S rRNA encoding gene sequence based method of bacterial identification

Chye Ying Loh, Yin Yin Tan, Rahim Rohani, Jean-Frédéric F. Weber, Subhash Janardhan Bhore

Bacterial endophytes do have several potential applications in pharmacy, medicine and agricultural biotech industry. The main objective of this study was to understand types of bacterial endophytes associated with dicotyledonous (dicot) and monocotyledonous (monocot) plant species. Isolation of the endophytic bacteria was performed using surface-sterilized various tissue samples, and identification of the endophytic bacterial isolates (EBIs) was completed using 16S rRNA encoding gene sequence similarity based method. In total, 996 EBIs were isolated and identified from 1055 samples of 31 monocot and 65 dicot plant species from Peninsular Malaysia. The 996 EBIs represented 71 different types of bacterial species. Twelve (12) out of 71 species are reported as endophytes for the first time. We conclude that diverse types of bacterial endophytes are associated with dicot and monocot plants, and could be useful in pharmacy, medicine and agricultural biotechnology for various potential applications.

Keywords

Dicots; Endophytes; Monocots; Natural compounds; Bioprospecting
Nutritional labeling and health claims on infant food products marketed in India and Malaysia: Implications on infant oral health

Cugati N., Peethambar P., Sudhakaran S., Anand P., Amanna E.S., Dewi F.D.

This article validates the adherence of infant food products marketed in India and Malaysia to their national regulation and its implications on oral health of infants from dental perspective. For the assessment purpose, Infant milk substitutes and infant formulae that are marketed in both the countries were analyzed for: a) Nutrition Labeling b) Health Claims c) Additional required labels. d) Special Instructions. A qualitative and quantitative evaluation of 15 Indian and 19 Malaysian infant food products marketed were evaluated using non-experimental cross-sectional descriptive design. It was found that infant food products were considerably far in its proximity to the regulations of their country and lacked vital instructions/labeling required to maintain Infant oral hygiene and health. It was concluded that inspite of the timely amendments made in the regulations for marketing infant formula foods, there was stretching of rules from the manufacturing companies. Regulatory rigidity in marketing infant food products to safeguard oral as well as general health of infants is required. Infant dental health and hygiene was not given considerable importance by the governing bodies in both the developing nation. This emphasizes dental professionals to create awareness and educate the parents regarding Infant oral health.

Keywords: Breastfeeding; Codex committee; Health claims; Infant formula; Infant oral Health; Labeling; Nutrition claims
Factors associated with infections in diabetic population

Gillani S.W., Sulaiman S.A.S., Sundram S., Sari Y.O., Baig M., Iqbal M.S.

Increase in the prevalence of diabetes worldwide and it becoming an epidemic has resulted in a clinical research shift to the management of diabetes mellitus globally. The study aimed to investigate the socio-demographic differences among diabetes patients with infection incidence. The study was conducted in an urban, governmental hospital in Penang Malaysia. The records of patients, more than and equal to age 18 years, who were admitted with diabetes mellitus between January 1, 2008 and December 31, 2010 were reviewed. Statistical analyses were performed using SPSS version 17®. This study was approved by the hospitals “Clinical Research Committee (CRC)” as well as “Ministry of Health Malaysia (MOH)”. During the time period of January 2008 through December 2010, there were total 2174 diabetes patients admitted; 2174 (100%) patients’ charts were reviewed. Of the total, 1063 (48.9%) were males and the rest, 1111 (51.1%), females. Mean and standard distribution (SD) showed females have less mean age distribution (35.2 ±4.187 years) as compared to males (37.9±5.724 years). A total of 798 (36.7%) had infection exposure before and/or during hospital admission; statistical significance (p<0.001) was found in association of diabetes ketoacidosis (DKA) and infection exposure. Though the rate of hospitalization increased among females, OR showed that males were more likely to get the infection severely as compared to females (1.81 (95%CI 1.1-2.40) p <0.021). Profound ethnic difference is three times more prone to severity rate of infection among Malay diabetic patients as compared to other non-Malays (OR 3.44 (95%CI 1.60-5.68) p<0.001). Further analysis showed that with the age of ≥ 65 years and history of diabetes (mean ± SD: 27.13 ± 2.782) average patient utilizes 135.7 days (average) of antibiotic course. Increased and recurrent use of antibiotic was found among Malays; also Malays predominantly experience clinical manifestations (poor glycaemic control) as compared to other ethnics. Every third patient with diabetes mellitus had infectious exposure.

Keywords
Clinical management; Diabetes mellitus; Endocrinology; Factors association; Infections; Metabolic disorder
Serological prediction of infections in diabetic patients with diabetes ketoacidosis in Penang, Malaysia

Gillani S.W., Syed Sulaiman S.A., Sundram S., (...), Baig M., Shahid Iqbal M.M.

Purpose: To determine the prevalence and predictors of infection in diabetic patients with diabetes ketoacidosis (DKA) who were ≥18 years.

Methods: A retrospective cohort design was adopted for this study. A total of 967 diabetes ketoacidosis patients from Hospital Pulau Pinang for the 3-year period, Jan 2008 - Dec 2010, were identified and enrolled. The data were analysed, as appropriate, by Student t-test and ANOVA for the normally distributed data, Mann-Whitney U rank sum and Kruskall-Wallis tests for continuous, non-nominal data and Chi-square for dichotomous variables. Odd Ratios with 95% confidence interval (CI) were also presented where applicable.

Results: Of the total diabetes ketoacidosis patients, 112 (11.6 %) were cases without infection, 679 (70.2 %) bacterial infection cases and 176 (18.2 %) presumed viral infection cases. The mean white blood count (WBC) for all the patients was 18,177 ± 9,431 while 721 (74.6 %) had leukocytosis, defined by WBC ≥ 15,000/mm 3. WBC differential, leukocytosis, as well as sex and body temperature were not significant predictors (p >.05) of bacterial infection. There was, however, a significant difference (p <.05) in terms of age within groups, as those > 57 years showed a higher rate of infection.

Conclusion: The infection rate in elderly patients with DKA is high and a majority of them lack clinical evidence. Age has a significant effect on the rate and prediction of infection. Leukocytosis is commonly found but severe ketoacidosis was more likely than the presence of infection.

Keywords: Diabetes mellitus; Diabetes ketoacidosis; Infections; Predictors; White blood cells
Histone deacetylase inhibitors have been actively explored as a new generation of chemotherapeutics for cancers, generally known as epigenetic therapeutics. Two novel series of N-(2-amino-phenyl)-4-[[2/3/4-substituted-phenylcarbamoyl]-methyl]-amino)-butyramide and N-(2-amino-phenyl)-4-[[2/3/4-substituted-phenylcarbamoyl]-methyl]-amino)benzamide were designed and synthesized as novel histone deacetylase inhibitors. The anticancer potential of the compounds were determined in-vitro using MTT assay against HCT-116 and U251 (glioma) cell lines and histone deacetylase inhibitory assay. The synthesized compounds were investigated for anti-tumor activity against Ehrlich ascites carcinoma (EAC) cells in Swiss albino mice. The efforts were also made to ascertain structure–activity relationships among test compounds. The results of the present studying represents appraisal of γ-aminobutyric acid (GABA) and para-aminobenzoic acid (PABA) as linker moiety for development of newer benzamide based histone deacetylase inhibitor.

Keywords
GABA; PABA; Anticancer activity; Histone deacetylase inhibitors
Understanding, perceptions and self-use of complementary and alternative medicine (CAM) among Malaysian pharmacy students


Background: In recent times the basic understanding, perceptions and CAM use among undergraduate health sciences students have become a topic of interest. This study was aimed to investigate the understanding, perceptions and self-use of CAM among pharmacy students in Malaysia.

Methods: This cross-sectional study was conducted on 500 systematically sampled pharmacy students from two private and one public university. A validated, self-administered questionnaire comprised of seven sections was used to gather the data. A systematic sampling was applied to recruit the students. Both descriptive and inferential statistics were applied using SPSS ® version 18.

Results: Overall, the students tend to disagree that complementary therapies (CM) are a threat to public health (mean score = 3.6) and agreed that CMs include ideas and methods from which conventional medicine could benefit (mean score = 4.7). More than half (57.8%) of the participants were currently using CAM while 77.6% had used it previously. Among the current CAM modalities used by the students, CM (21.9%) was found to be the most frequently used CAM followed by Traditional Chinese Medicine (TCM) (21%). Most of the students (74.8%) believed that lack of scientific evidence is one of the most important barriers obstructing them to use CAM. More than half of the students perceived TCM (62.8%) and music therapy (53.8%) to be effective. Majority of them (69.3%) asserted that CAM knowledge is necessary to be a well-rounded professional.

Conclusions: This study reveals a high-percentage of pharmacy students who were using or had previously used at least one type of CAM. Students of higher professional years tend to agree that CMs include ideas and methods from which conventional medicine could benefit.
Keywords

Adolescent; Adult; Alternative medicine; Article; Comprehension; Cross-sectional study; Education; Female; Health personnel attitude; Human; Knowledge; Malaysia; Male; Perception; Pharmacy student; Psychological aspect; Questionnaire; Utilization review; Chinese medicine; Health behavior; Health belief; Homeopathy; Music therapy; Professional competence; Public health; Risk benefit analysis; Self care; Self concept; Traditional medicine; University student
Epidemiological analysis of typhoid fever in Kelantan from a retrieved registry

Ja’afar Nuhu Ja’afar, Yuan Xin Goay, Nur Fatihah Mohammed Zaidi, Heng Chin Low, Hani Mat Hussin, Wan Mansor Hamzah, Subhash Janardhan Bhore, Prabha Balaram, Asma Ismail, and Kia Kien Phua

Aim: Despite the endemicity of typhoid in Kelantan, epidemiological data showing typhoid association to age, sex, ethnicity and district of patients is limited. This retrospective study investigated the statistical association of these variables from a retrieved registry.

Methodology and Results: Cross-tabulation using SPSS was used to analyze 1394 cases of confirmed typhoid patients admitted to various hospitals in Kelantan state over a six-year period. Fourteen age groups with a five-year range interval were generated. There was a significant association between typhoid infection and sex of subjects, whereby females were generally more susceptible than males. Ethnicity and district of typhoid patients did not show significant association.

Conclusion, Significance and Impact of Study: The observation of an increased number of typhoid cases with a male predominance in the age group 5-14 and female predominance in the 20-60 age group calls for improved hygiene, continued public health education, together with better laboratory diagnostics to identify carriers, are some measures to control this disease.

Keywords: Salmonella Typhi; Kelantan; Malaysia; Retrospective study; Typhoid
Overexpression of anti-apoptotic Bcl-2 is often observed in a wide variety of human cancers. It prevents the induction of apoptosis in neoplastic cells and contributes to resistance to chemotherapy. RNA interference has emerged as an efficient and selective technique for gene silencing. The potential to use small interfering RNA (siRNA) as a therapeutic agent for the treatment of cancer has elicited a great deal of interest. However, insufficient cellular uptake and poor stability have limited its therapeutic applications. The purpose of this study was to prepare chitosan nanoparticles via ionic gelation of chitosan by tripolyphosphate for effective delivery of siRNA to silence the anti-apoptotic Bcl-2 gene in neoplastic cells. Chitosan nanoparticles loaded with siRNA were in the size range 190 to 340 nm with a polydispersive index ranging from 0.04 to 0.2. They were able to completely bind with siRNA, provide protection against nuclease degradation, and enhance the transfection. Cell culture studies revealed that nanoparticles with entrapped siRNA could efficiently silence the antiapoptotic Bcl-2 gene. Studies on Swiss albino mice showed that siRNA could be effectively delivered through nanoparticles. There was significant decrease in the tumor volume. Blocking the expression of anti-apoptotic Bcl-2 can enhance the sensitivity of cancerous cells to anti-cancer drugs and the apoptosis rate. Therefore, nanoformulations with siRNA can be promoted as an adjuvant therapy in combination with anti-cancer drugs.

Keywords
Chitosan; RNA interference; siRNA; Bcl-2; Apoptosis; Cancer; Nanoformulation
Polyalthia longifolia Sonn: an ancient remedy to explore for novel therapeutic agents

Jothy S.L., Choong Y.S., Saravanan D., Deivanai S., Latha L.Y., Vijayarathna S. Sasidharan S.

Polyalthia longifolia (Sonn.) Thwaites (PL) (Family: Annonaceae) is a tall handsome evergreen tree and it is cultivated all over India. The plant has been commonly used in traditional system of medicine for the treatment of fever, skin diseases, diabetes, hypertension and helminthiasis. In view of the immense medicinal importance of P. longifolia, this review was aimed at compiling all currently available botanical, phytochemical, pharmacological, and toxicological and ethnomedical information on P. longifolia’s including its mechanisms of action. Information in the biomedical literature has indicated the presence of a variety of medicinally-important chemical constituents in P. longifolia. Pharmacological studies by various groups of investigators have shown that P. longifolia possesses significant biological and pharmacological activities, such as antibacterial, antifungal, antitumor, anti-ulcer and antioxidant properties. Beside this, toxicity studies of this plant have revealed no toxic effect on mice. P. longifolia can be considered as an ancient remedy to be explored for the development of various novel therapeutic agents.

Keywords

Ethnomedicinal uses; Pharmacological properties; Phytochemistry; Polyalthia longifolia
The genus Cassia, comprising about 600 species widely distributed worldwide is well known for its diverse biological and pharmacological properties. Cassia spectabilis (sin Senna spectabilis)(DC) Irwin et Barn (Fabaceae) is widely grown as an ornamental plant in tropical and subtropical areas. C. spectabilis has been commonly used in traditional medicine for many years. Information in the biomedical literature has indicated the presence of a variety of medicinally-important chemical constituents in C. spectabilis. Pharmacological studies by various groups of investigators have shown that C. spectabilis possesses significant biological activity, such as antibacterial, antibiofilm, antifungal and antioxidant properties. Beside this, toxicity studies of this plant have revealed no toxic effect on mice. In view of the immense medicinal importance of C. spectabilis, this review aimed at compiling all currently available information on C. spectabilis’s botany, phytochemistry, pharmacology, and mechanism of actions, toxicology and its ethnomedicinal uses.

Keywords
Cassia spectabilis; Pharmacological properties; Ethnomedicinal uses; Phytochemistry
Researchers throughout the world are focusing intensively on the methods for the development of new drug delivery systems to enhance patient’s compliance. The oral route however still remained as the best administration route of therapeutic agents for its ease of ingestion, pain avoidance and versatility. Hence, fast dissolving tablets become an emerging trend in the pharmaceutical industry. Fast dissolving tablets are ideal for all types of people, including for people who have swallowing difficulties, paediatric, geriatric, and bedridden patients. It is also for active patients who are busy, travelling and may not have access to water. Fast dissolving tablets are also known as orodispersible tablets, mouth-dissolving tablets, orally disintegrating tablets, melt-in mouth tablets, rapimelts, porous tablets, quick dissolving etc. This type of tablets disintegrates quickly once introduced into the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. Many drugs have the potentials to be made into orodispersible tablets. They vary from analgesics to neuroleptics and anti-psychotic drugs. However only a small percentage of them are researched on and some have been manufactured and marketed. In this review article, drug candidates suitable for fast dissolving drug delivery and the available marketed products have been listed.

Keywords

Fast dissolving tablet (FDT); Marketed fast dissolving tablets; Potential candidates
Objectives

The study attempts to delineate the clinical correlates (suicidal risk, manic, depressive and psychotic symptom severity) and course characteristics (age of onset and details of past affective episodes) of bipolar mixed state and compare with bipolar manic and bipolar depressed state diagnosed according to ICD-10 Diagnostic Criteria for Research (ICD-10 DCR).

Methodology

The study was carried out in inpatient psychiatry setting of Kasturba Hospital, Manipal, India over a period of 10 months. It was an Open, Non-randomised, Naturalistic study with sequential sampling. The rating scales used were Hamilton Depression Rating Scale (HDRS), Young Mania Rating Scale (YMRS), Positive and Negative Symptom Scale for Schizophrenia (PANSS) and Beck Scale for suicidal ideation.

Results

A total of 70 subjects were included in the study meeting the criteria of bipolar disorder currently manic, depressed and mixed state according to ICD-10 DCR. Manic group constituted the majority (n1 = 47) followed by depressed (n2 = 17) and mixed groups (n3 = 6). Mixed group was characterized by preponderance of females, high suicidal intent, high frequency of mood-incongruent psychotic symptoms, illness severity and significant family history.

Conclusion

The study was able to establish some core features that were specific to mixed states. A larger sample size and a prospective follow up study would throw light on the existence of this group as an independent entity.
Prevalence and clinical characteristics of oral tori among outpatients in northern Malaysia

K Sathya, Sham Kishor Kanneppady, T Arishiya

Objectives

The objectives of this study were to determine the prevalence and clinical characteristics of torus palatinus (TP) and torus mandibularis (TM) in Malaysian dental patients.

Methods

 Thousand five hundred and thirty-two dental patients were examined for the presence of oral tori at the Faculty of Dentistry outpatient clinic, AIMST University. Factors such as race, age, sex, size, and shape of tori were studied.

Results

The prevalence rates were 12% for TP and 2.8% for TM. A variation in the presence of tori among the three races in Malaysia–Chinese, Malays, and Indians–was noted, where the Chinese significantly had a higher prevalence of TP (17.9%) and TM (4.6%). Predominantly, tori were observed >40 years and older age group, and further both TP and TM were seen more commonly in women. Most TP were of smooth type (52.2%) and >2 cm (67.4%), while all TM were bilateral and nodular, plus most were <2 cm (67.4%).

Conclusion

Presence of tori (TP and TM) was detected in 12.5% of the participants. The variations noted in the prevalence and clinical characteristics of tori among people of different races living in the same country reflect its multifactorial etiology. Both genetic and environmental factors are responsible for its occurrence, and particular races are more prone genetically where its expression is enhanced by environmental factors.

Keywords

Tori; Torus mandibularis; Torus palatinus
A novel drug delivery systems of colon targeted: A review

Kumar J.R., Muralidharan S., Dhanaraj S.A., Umadevi S.K.

In the current year colonic drug delivery has gained significance for delivery of drug for the treatment of local diseases related with colon and systemic delivery of therapeutic peptides and proteins. Management could be more effective if it is possible for drug to be directly delivered to colon. This article gives an overview on different approaches utilized for colon specific drug delivery.

Keywords
Novel drug delivery systems of colon targeted
Evaluation of hepatoprotective effect of methanolic extract of *Clitoria ternatea* (Linn.) flower against acetaminophen-induced liver damage

Kuppan Nithianantham, Kwan Yuet Ping, Lachimanan Yoga Latha, Subramanion L Jothy, Ibrahim Darah, Yeng Chen, Ai-Lan Chew, Sreenivasan Sasidharan

**Objective**

To evaluate the hepatoprotective and antioxidant activity of *Clitoria ternatea* (*C. ternatea*) flower extract against acetaminophen-induced liver toxicity.

**Methods**

The antioxidant property of *C. ternatea* flower extract was investigated by employing established in vitro antioxidant assay. The *C. ternatea* flower extract was studied in this work for its hepatoprotective effect against acetaminophen-induced liver toxicity in mice. Activity was measured by monitoring the levels of aspartate aminotransferase, alanine aminotransferase, bilirubin and glutathione with histopathological analysis.

**Results**

The amount of total phenolics and flavonoids were estimated to be 105.40±2.47 mg/g gallic acid equivalent and 72.21±0.05 mg/g catechin equivalent respectively. The antioxidant activity of *C. ternatea* flower extract was 68.9% at a concentration of 1 mg/mL and was also concentration dependant, with an IC$_{50}$ value of 327.00 μg/mL. The results of acetaminophen-induced liver toxicity experiment showed that mice treated with the extract (200 mg/kg) showed a significant decrease in alanine aminotransferase, aspartate aminotransferase, and bilirubin levels, which were all elevated in the paracetamol group (*P*<0.05). Meanwhile, the level of glutathione was found to be restored in extract treated animals compared to the groups treated with acetaminophen alone (*P*<0.05). Therapy of extract also showed its protective effect on histopathological alterations and supported the biochemical finding.
Conclusions
The present work confirmed the hepatoprotective effect of *C. ternatea* flower against model hepatotoxicant acetaminophen.

Keywords
*Clitoria ternatea* flower; acetaminophen; hepatoprotective; antioxidant activity
Beliefs and practices surrounding postpartum period among Myanmar women

Kyi Kyi Sein

Objective
To examine the postpartum beliefs and practices among young women (15–24 years)

Design
Both quantitative and qualitative approaches were used: a cross-sectional comparative study using a semi-structured questionnaire and focus group discussions (FGDs).

Setting
Kyimyindaing Township in the western district of Yangon, Myanmar.

Participants
Young women (15–24 years) who had experience of at least one live birth were included. A total of 196 women for a quantitative survey and 31 women for FGDs were recruited.

Measurement and Findings
Postpartum beliefs and practices at the last childbirth were explored by a pretested semi-structured questionnaire and four FGDs (two in urban and two in rural areas). The survey questionnaire covered socio-demographic data, food and behavioural restrictions and observances during the last postpartum period and underlying reasons for those practices. Majority of participants followed the traditional postpartum practices regardless of the area of residence and education level. Notion of ‘dirty lochia’ was identified.
Key Conclusions

Traditional beliefs and practices surrounding postpartum were highly prevalent among young women. Variation in degree and duration of adherence to postpartum taboos was noted. These beliefs and practices were imparted and perpetuated by women’s close social network.

Implications for Practice

The findings point out the importance of awareness of postpartum beliefs and practices among health staff for providing culturally sensitive health care and gaining better co-operation and mutual understanding in giving health care.

Keywords

Postpartum beliefs and practices; Traditional beliefs and practices; Postnatal period; Myanmar
Plants play important roles in human life not only as suppliers of oxygen but also as a fundamental resource to sustain the human race on this earthly plane. Plants also play a major role in our nutrition by converting energy from the sun during photosynthesis. In addition, plants have been used extensively in traditional medicine since time immemorial. Information in the biomedical literature has indicated that many natural herbs have been investigated for their efficacy against lethal irradiation. Pharmacological studies by various groups of investigators have shown that natural herbs possess significant radioprotective activity. In view of the immense medicinal importance of natural product based radioprotective agents, this review aims at compiling all currently available information on radioprotective agents from medicinal plants and herbs, especially the evaluation methods and mechanisms of action. In this review we particularly emphasize on ethnomedicinal uses, botany, phytochemistry, mechanisms of action and toxicology. We also describe modern techniques for evaluating herbal samples as radioprotective agents. The usage of herbal remedies for combating lethal irradiation is a green antiirradiation approach for the betterment of human beings without high cost, side effects and toxicity.

Keywords
Green approach; Ionizing radiation; Medicinal plant; Radioprotective
Effectiveness of direct vs indirect technique myofascial release in the management of tension-type headache

M.S. Ajimsha

Background
Tension-type headache (TTH) is essentially defined as bilateral headache of a pressing or tightening quality without a known medical cause. Myofascial release (MFR) is currently being applied for patients with TTH but its efficacy has not been evaluated formally.

Objective
To investigate whether direct technique myofascial release (DT-MFR) reduces the frequency of headache more effectively than the indirect technique myofascial release (IDT-MFR) in comparison to a Control Group receiving slow soft stroking.

Design
Randomized, controlled, single blinded trial.

Setting
The clinical wing of Myofascial Therapy and Research Foundation, Kerala, India.

Participants
63 patients with episodic or chronic tension-type headache.

Interventions
DT-MFR, IDT-MFR or Control. The techniques were administered by certified myofascial release practitioners and consisted of 24 sessions per patient over 12 weeks.
Main outcome measure

Difference in numbers of days with headache between Weeks 1–4 (i.e. 4 weeks prior to start of Intervention) and Weeks 17–20, following 12 weeks of Intervention between Weeks 5–16 as recorded by participants in headache diaries.

Results

The number of days with headache per 4 weeks decreased by 7.1 (2.6) [mean (SD)] days in the DT-MFR group compared with 6.7 (1.8) days in the IDT-MFR group and 1.6 (0.5) days in the control group, (P < 0.001). Patients in the DT-MFR Group, IDT-MFR Group and Control Group reported a 59.2%, 54% and 13.3% reduction in their headache frequency in Weeks 17–20 compared to that in Weeks 1–4.

Conclusions

This study provides evidence that Direct Technique or Indirect Technique Myofascial Release is more effective than the Control Intervention for tension headache.

Keywords

Myofascial release; Myofascial trigger points; Tension headache
Cost-effectiveness analysis for the use of serum antiepileptic drug level monitoring in children diagnosed with structural-metabolic epilepsy


Treatment with antiepileptic drugs is commonly guided by serum level monitoring. Such monitoring requires expensive laboratory equipment and products. However, well-conducted studies on the cost-effectiveness of therapeutic drug monitoring for antiepileptic drugs are lacking particularly in patients with structural-metabolic epilepsy. The study aims to assess the cost-effectiveness of serum level monitoring services in the management of children with structural-metabolic epilepsy during the first year of diagnosis. A retrospective cost-effectiveness analysis was conducted from the provider perspective. It included patients attended a paediatric neurology clinic. The effectiveness measures used in this analysis were the number of patients that achieved ≥50% reduction in seizure frequency, and the number of patients with 3-month seizure free. Medical records of the patients were reviewed for the required information. Medical chart/billing data obtained from the hospital were collected to estimate the resources used (One Malaysian Ringgit MYR is equivalent to 0.31 USD). The recruited children were followed for one year following their first visit. The average cost effectiveness ratio for the monitored patients (MYR 2735 per patient that achieved a ≥50% reduction in seizure frequency) was lower than that for non-monitored patients (MYR 2921 per patients that achieved a ≥50% reduction in seizure frequency), with incremental cost-effectiveness ratio of MYR 2357 per one additional patient that achieved a ≥50% reduction in seizure frequency. The average cost effectiveness ratios for monitored and non-monitored group were MYR 8279 and MYR 6433 per patient with a 3-month seizure-free period, respectively, with incremental cost-effectiveness ratio of MYR 29,666 per one additional patient with a 3-month seizure-free period.

In terms of the effectiveness measures used, serum level monitoring of antiepileptic drugs was found to be cost-effective. However, the incremental cost-effectiveness ratio was found to be sensitive to the cost of management.

**Keywords**

Cost-effectiveness analysis; Structural-metabolic epilepsy; Paediatrics; Malaysia
Method development and validation of a liquid chromatographic - Mass spectrometric method for clarithromycin in human plasma

Muralidharan, S., Dhanaraj, S.A.

A simple, fast and sensitive High-Performance Liquid Chromatography (HPLC)-Mass Spectrometric (MS) method has been developed for the validation of Clarithromycin in human plasma using alprazolam as internal standard. After protein precipitation, chromatographic separation of Clarithromycin in plasma was achieved at 40°C with a C18 reversed-phase column with 10 mM Ammonium acetate and acetonitrile (10:90% v/v) and detected using Electrospray Ionization (ESI) mass spectrometry in positive Selected Ion Monitoring (SIM) mode. The validated method was accurate, precise, selective, and sensitive. It’s applicable in pharmacokinetic, bioavailability or bioequivalence studies.

Keywords

Clarithromycin; Human plasma; LC-MS; Validation
Antimicrobial activity of different tissues of snakehead fish *Channa striatus* (Bloch)

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**Objective**

The aim of this study was to identify the presence of antimicrobial activity in different organs/tissues (gills, blood, skin, liver, intestine, kidney, tissue and ovary) extract of snakehead fish *Channa striatus*.

**Methods**

A total of 48 fractions from the organs and tissue extracts were obtained by solid-phase extraction and the fractions were assayed for antimicrobial activity. The screening of antimicrobial activity for all the fractions were tested against 8 human pathogens including Gram positive (Methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus aureus*, *Bacillus cereus*) and Gram negative bacteria (*Salmonella enteritidis*, *Shigella flexneri*, *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*) using the British Society for Antimicrobial Chemotherapy (BSAC) standardized disc susceptibility test method. The activity was measured in terms of zone of inhibition in mm.

**Results**

The results indicated that, among the 8 organs/tissues tested only blood and gills extract fractions (40 and 60 % ACN fraction) showed inhibition against *Escherichia coli* and 60 % ACN fraction of gill extract showed inhibition against *Salmonella enteritidis*. Protein profile analysis by SDS-PAGE showed that antimicrobial activity of the partially purified blood and gill tissue extracts might be due to low molecular weight peptides.
Conclusions

The present study showed that, gill and blood extracts of *Channa striatus* can be a potential source of an antimicrobial protein for specific human pathogens.

**Keywords**

Snakehead fish; *Channa striatus*; Tissue; Organ; Antibacterial activity
Chemical characterisation and antifungal activity of methanolic extract of Cinnamomum verum J. Presl bark against Malassezia spp.

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Context
Malassezia spp. are the organisms causing skin infections like dandruff, pityriasis versicolor, seborrhoeic dermatitis etc. in human and in animals. Using natural ingredients for treating these diseases could be a better task.

Aim
To investigate the phytochemical constituents and antifungal efficacy of Cinnamomum verum (CV) bark methanolic extract against dandruff, pityriasis versicolor, seborrhoeic dermatitis causing dimorphic fungi belonging to the genus Malassezia.

Materials and methods
Cultures of Malassezia globosa, Malassezia sympodialis, and Malassezia furfur of clinical origin were prepared by adjusting inoculum size to $10^8$ cfu/ml. Minimum inhibitory concentration (MIC) and zone of inhibition (ZOI) for methanolic extract of CV bark were done to find out the lowest concentration of extract required to inhibit the growth of Malassezia spp. and the preliminary phytochemical and GC–MS analysis was carried out to identify the phytoconstituents.

Results
Methanolic extract of bark of CV showed MIC value ranging from 0.5 to 2 mg/ml against Malassezia spp. The major chemical constituents were identified as trans-Cinnamaldehyde (20.28%), (E)-3-(2-Methoxyphenyl)-2-propenoic acid (40.41%), 4-Vinyl benzoic acid (10.54%) and coumarin (8.47%) by GC–MS.
Conclusions

C. verum bark methanolic extract has potential antifungal activity and can be exploited against skin infections caused by *M. globosa*, *M. sympodialis*, and *M. furfur*.

Keywords

Anti-malassezial; Antifungal; *Cinnamomum verum*; Cinnamon; Bark; Cinnamaaldehyde
Evaluation of in vitro and in vivo anti-inflammatory activity of Garcinia Combogia L.

Prasanth N.V., Rasheed S.P., Thomas T., Joseph S., Varghese C.P.

Objective

Garcinia combogia is plant grows throught India and southeast Asia. The fruit of the plant is a commonly used diet ingredient in India. The major objective of the study was to evaluate the in vitro and in vivo anti-inflammatory activity of the ethanolic extract of Garcinia combogia.

Methods

In vitro anti-inflammatory activity was evaluated using hRBC membrane stabilization method. The extract possessed moderate membrane stabilization activity for all the concentrations tested. Diclofenac was used as the standard. To study the anti-inflammatory activity carrageenan induced paw oedema model was used. Ibuprofen 100mg/kg was used as the standard. Doses of 200 mg/kg and 400 mg/kg were tested.

Results

In hRBC membrane stabilization method the extract showed moderate in vitro anti-inflammatory activity. Significant (P <0.05) reduction in the paw volume of the standard and test treated group compared to the control was observed when measured at the third hour.

Conclusion

It can conclude that the ethanolic extract of Garcinia combogia posses significant in vivo anti-inflammatory activity, and moderate in vitro anti-inflammatory activity as per the present study.
Catechin is a known hepatoprotective and anticancer agent but has limited bioavailability. Its apoptotic signaling pathway in human hepatocellular carcinoma is vaguely explored. Thus, this study was designed to explore cytotoxicity by MTT assay, induction of apoptosis via DNA fragmentation, nuclear staining, bivariate flow cytometric analysis using annexin V- FITC and propidium iodide, cell cycle analysis and apoptotic markers by RT-PCR and western blotting in HepG2 cells. To increase the bioavailability and selectivity to cancer cells, various liposomes of catechin viz., conventional, charged and PEGylated forms were prepared by film hydration method and evaluated for cytotoxicity in vitro in HepG2 cells and in in vivo in EAC-induced liquid tumor model. Catechin and catechin liposomes inhibited the growth of HepG2 cell lines at concentrations 100–200 μg mL\(^{-1}\) depending on the length of exposure. It induced apoptosis and inhibited G\(_2\)/M phase in cell cycle analysis. Catechin down regulated Bcl-2, initiated the release of cytochrome c into the cytosol and upregulated Bax, caspase-3,-9 and p53 in the HepG2 cells. Catechin and its liposomal formulation, at a dose of 200 mg/kg body weight was found to be significantly \((p < 0.05)\) effective in inhibiting percentage increase in body weight and enhancing the mean survival time. Deviated hematological parameters, antioxidant parameters (superoxide dismutase, catalase and lipid peroxidation) and LFT in tumor bearing mice were found to be significantly \((p < 0.05)\) restored towards normal after treatment with catechin and its liposomes.

**Keywords**

HepG2 cells; Catechin; Liposomes; Gene expression; Cell cycle and Ehrlich ascites carcinoma
Tuberculosis (TB), an epidemic disease, affects the world with death rate of two million people every year. The bacterium Mycobacterium tuberculosis was found to be a more potent and disease-prolonged bacterium among the world due to multi-drug resistance. Emergence of new drug targets is needed to overcome the bacterial resistance that leads to control epidemic tuberculosis. The pathway thiamine biosynthesis was targeting M. tuberculosis due to its role in intracellular growth of the bacterium. The screening of enzymes involved in thiamin biosynthesis showed novel target thiazole synthase (ThiG) involved in catalysis of rearrangement of 1-deoxy-D-xylulose 5-phosphate (DXP) to produce the thiazole phosphate moiety of thiamine. We carried out homology modeling for ThiG to understand the structure-function relationship, and the model was refined with MD simulations. The results showed that the model predicted with ($\alpha + \beta$)8-fold of synthase family proteins. Molecular docking of ThiG model with substrate DXP showed binding mode and key residues ARG46, ASN69, THR41, and LYS96 involved in the catalysis. First-line anti-tuberculosis drugs were docked with ThiG to identify the inhibition. The report showed the anti-tuberculosis drugs interact well with ThiG which may lead to block thiamin biosynthesis pathway.

Keywords

DXP; Homology modeling; MD simulations; Mycobacterium tuberculosis; Tuberculosis
In *silico* approach of anticancer activity of phytochemical coumarins against cancer target JNKs

Rohini K., Srikumar P.S.

**Objective**: Phytochemicals are the secondary metabolites of medicinal plants and are considerably used in traditional cancer research. *Homo sapiens*-Jun NH2-terminal kinases (JNKs) are enzymes critical in chronic diseases. JNKs are proteins best known for its role in the activation of the c-Jun/activator protein-1 (AP-1) transcription-factor complex. Targeting JNKs inhibition might initiate the clinical benefits in chronic disease like cancer.

**Methods**: In silico approach is an attempt at identifying the anticancer activity of phytochemical coumarins from medicinal plants against the cancer target *Homo sapiens* JNKs. The dataset comprising of coumarins compounds obtained from medicinal plants like *Psoraleacorylifolia* and *Selinummonnierae* were used for virtual screening in AutoDock Vina and molecular docking in AutoDock.

**Results & discussion**: The results of virtual screening of coumarins showed the predicted binding affinity towards JNKs binding site. Among the phytochemicals screened, hit compounds imperatorin and osthol was further docked to confirm the binding mode and confirmed the effective inhibition of JNKs and anticancer activity. Conclusion: Our study suggests that the potential use of phytochemicals imperatorin and osthol from *Selinummonnierae* may act as better leads and in turn prevent cancer.

**Keywords**

Phytochemicals; JNKs; Coumarins; Virtual screening; Molecular docking
Characteristics of seizure frequency among Malaysian children diagnosed with structural-metabolic epilepsy


Introduction: Seizure-free patients or substantial reduction in seizure frequency are the most important outcome measures in the management of epilepsy. The study aimed to evaluate the patterns of seizure frequency and its relationship with demographics, clinical characteristics, and outcomes.

Materials and Methods: A retrospective cohort study was conducted at the Pediatric Neurology Clinic, Hospital Pulau Pinang. Over a period of 6 months, the required data were extracted from the medical records using a pre-designed data collection form.

Results: Seizure frequency showed no significant association with patient’s demographics and clinical characteristic. However, significant reduction in seizure frequency from the baseline to the last follow-up visit was only seen in certain subgroups of patients including Malays, females, patients <4 years of age, patients with global developmental delay/intellectual disability, and patients with focal seizure. There was no significant association between seizure frequency and rate of adverse events. Polytherapy visits were associated with higher seizure frequency than monotherapy visits (27.97 ± 56.66, 10.94 ± 30.96 attack per month, respectively) (P < 0.001). There was a clear tendency to get antiepileptic drugs used at doses above the recommended range in polytherapy (8.4%) rather than in monotherapy (1.4%) visits (P < 0.001). A significant correlation was found between seizure frequency and number of visits per patient per year (r = 0.450, P < 0.001).

Conclusion: Among children with structural-metabolic epilepsy, Malays, females, patients <4 years of age, patients with global developmental delay/intellectual disability and patients manifested with focal seizure are more responsive antiepileptic drug therapy than the other subgroups of patients.

Keywords

Pediatrics; Seizure frequency; Structural-metabolic epilepsy
Extraction, isolation and characterization of bioactive compounds from plants’ extracts

Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K.M., Yoga Latha, L.

Natural products from medicinal plants, either as pure compounds or as standardized extracts, provide unlimited opportunities for new drug leads because of the unmatched availability of chemical diversity. Due to an increasing demand for chemical diversity in screening programs, seeking therapeutic drugs from natural products, interest particularly in edible plants has grown throughout the world. Botanicals and herbal preparations for medicinal usage contain various types of bioactive compounds. The focus of this paper is on the analytical methodologies, which include the extraction, isolation and characterization of active ingredients in botanicals and herbal preparations. The common problems and key challenges in the extraction, isolation and characterization of active ingredients in botanicals and herbal preparations are discussed. As extraction is the most important step in the analysis of constituents present in botanicals and herbal preparations, the strengths and weaknesses of different extraction techniques are discussed. The analysis of bioactive compounds present in the plant extracts involving the applications of common phytochemical screening assays, chromatographic techniques such as HPLC and, TLC as well as nonchromatographic techniques such as immunoassay and Fourier Transform Infra Red (FTIR) are discussed.

**Keywords**

Bioactive compound; Herbal preparations; Isolation; Natural products; Plant extraction
Autonomic status and pain profile in patients of chronic low back pain and following electro acupuncture therapy: A randomized control trial

Shankar N., Thakur M., Tandon O.P., Saxena A.K., Arora S., Bhattacharya N.

Pain is a syndrome characterized by several neurophysiological changes including that of the autonomic nervous system. Chronic low back pain (LBP) is a major health problem and is a frequent reason for using unconventional therapies especially acupuncture. This study was conducted to evaluate the autonomic status and pain profile in chronic LBP patients and to observe the effect of electro acupuncture therapy. Chronic LBP patients (n=60) were recruited from the Department of Orthopaedics, GTB Hospital, Delhi. Age and sex matched healthy volunteers were selected as controls (n=30). Following a written consent, LBP patients were randomly allocated into two study groups - Group A received 10 sittings of electro acupuncture, on alternate days, at GB and UB points selected for back pain, while the Group B received a conventional drug therapy in the form of oral Valdecoxib together with supervised physiotherapy. Controls were assessed once while the patients were assessed twice, before and after completion of the treatment program (3 weeks). The autonomic status was studied with non-invasive cardiovascular autonomic function tests which included E: I ratio, 30:15 ratio, postural challenge test and sustained handgrip test. Pain intensity was measured with the visual analogue scale (VAS) and the global perceived effect (GPE). Statistical analysis was performed using repeated measure’s ANOVA with Tukey’s test. Pain patients showed a significantly reduced vagal tone and increased sympathetic activity as compared to the controls (P<0.05 to P<0.001 in different variables). Following treatment, both the study groups showed a reduction in vagal tone together with a decrease in the sympathetic activity. There was also a considerable relief of pain in both groups, however, the acupuncture group showed a better response (P<0.01). We conclude that there is autonomic dysfunction in chronic LBP patients. Acupuncture effectively relieves the pain and improves the autonomic status and hence can be used as an alternative/additive treatment modality in these cases.
Influenza A H5N1 and pH1N1 viruses have broadly emerged and become widespread in various countries around the world. Oseltamivir, the most commonly used antiviral drug against the seasonal and pandemic influenza viruses, is targeted at the viral neuraminidase (NA), but some isolates of this virus have become highly resistant to this drug. The novel long-acting drug, laninamivir, was recently developed to inhibit influenza A and B viruses of either the wild-type (WT) or the oseltamivir resistant mutant of NA. To understand the high efficiency of laninamivir, all-atom molecular dynamics simulations were performed on the WT and H274Y mutant of H5N1 and pH1N1 NAs with laninamivir bound. As a result, the novel drug was found to directly interact with 11 binding residues mainly through salt bridge and hydrogen bond formation (as also seen by electrostatic contribution). These are comprised of 7 of the catalytic residues (R118, D151, R152, R224, E276, R292 and R371), and 4 of the framework residues (E119, W178, E227 and E277). Laninamivir showed a similar binding pattern to all four NAs, but strong hydrogen bonding interactions were only found in the WT strain, with a slightly lowered contribution at some drug contact residues being observed in the H274Y mutation. This is in good agreement with the experimental data that the H274Y mutant has a small increase (1.3–7.5-fold, which was not statistically significant) in the IC\textsubscript{50} value of laninamivir.

Keywords
Laninamivir; Neuraminidase; H5N1; Pandemic H1N1; Molecular dynamics simulation
Pharmacogenetic screening of carbamazepine-induced severe cutaneous allergic reactions

Chaichon Locharernkul, Vorasuk Shotelersuk, Nattiya Hirankarn

Recent studies associated the HLA-B*1502 allele with carbamazepine (CBZ)-induced Stevens–Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) in patients from China, Thailand and Malaysia. No association has been found in patients from Europe or Japan. Linkage summary reports from East and Southeast Asia predict a highly significant odds ratio (OR) of 84.75 (95% confidence interval [CI] = 42.53–168.91; \( p = 8.96 \times 10^{-15} \)) with sensitivity and negative predictive values of 92% and 98%, respectively. The higher prevalence of HLA-B*1502 allele among certain Asian populations (10–15%) compared to Caucasians (1–2%) may explain a 10-fold to 25-fold higher incidence of CBZ-SJS/TEN in patients from Asia. Screening for HLA-B*1502 before using CBZ can prevent SJS/TEN in certain populations, but screening may be less beneficial in populations with low HLA-B*1502 allele frequency and in patients exposed to CBZ for more than 2 months. A retrospective study demonstrated that the costs of HLA-B*1502 screening were less than those of SJS treatment. This article reviews possible benefits and concerns of HLA-B*1502 screening in clinical practice.

Keywords
Antiepileptic drug; Clinical practice; Cost-effectiveness; HLA-B*1502; Stevens–Johnson syndrome; Toxic epidermal necrolysis
The immunogenicity and safety of pneumococcal conjugate vaccine in human immunodeficiency virus-infected Thai children

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Background

HIV-infected children have high risk of invasive pneumococcal disease (IPD) despite receiving highly active antiretroviral therapy (HAART). This study aimed to determine the immunogenicity and safety of a 7-valent pneumococcal conjugate vaccine (PCV-7) in Thai HIV-infected children compared to HIV-exposed uninfected children.

Methods

A prospective study was conducted among children 2 months to 9 years. The number of PCV-7 doses depended upon age and HIV status; 2–6 months of age: 3 doses; 7–23 months of age: 2 doses; HIV-infected child ≥24 months: 2 doses and HIV-exposed child ≥24 months: 1 dose. Serotype-specific pneumococcal IgG antibody concentrations were measured at baseline and 28 days after complete vaccination. The primary end point was the proportion of children who achieved serotype-specific IgG antibody concentration at a cut off level ≥0.35 μg/mL. Secondary end points were a 4-fold increase in serotype-specific IgG antibody, rates of adverse events and predictors for seroconversion among HIV-infected children.

Results

Fifty-nine HIV-infected and 30 HIV-exposed children were enrolled. The median (IQR) age was 97 (67–111) and 61 months (51–73), respectively (p < 0.001). Among HIV-infected children, current and nadir CD4 counts were 1079 cell/mm³ and 461 cell/mm³, respectively. The proportion of children who achieved pneumococcal IgG ≥0.35 μg/mL was in the range of 85–98% in HIV-infected and 83–100% in HIV-exposed children depending on serotype. The lowest response was to serotype 6B in both groups. The 4-fold increase in serotype-specific IgG concentrations was similar between HIV-infected and HIV-exposed groups, except for serotype 9V (p = 0.027). HIV-infected children who had a history of AIDS had a lower antibody response to serotype 23F (p = 0.025). Seven (12%) HIV-infected children had a grade 3 local reaction.
Conclusion

PCV-7 is highly immunogenic and safe among HIV-infected children treated with HAART. The use of the pneumococcal conjugate vaccine among HIV-infected children is encouraged in order to prevent IPD.

Abbreviations

HIV, human immunodeficiency virus;
HAART, highly active antiretroviral therapy;
IPD, invasive pneumococcal disease;
PCV, pneumococcal conjugate vaccine;
PPV, pneumococcal polysaccharide vaccine

Keywords

HIV-infected children; Pneumococcal conjugate vaccine; Thailand
Cytokine levels in patients with chikungunya virus infection

Chintana Chirathaworn, Yong Poovorawan, Somrat Lertmaharit, Norra Wuttirattanakowit

Objective
To investigate cytokine profile in patients with chikungunya virus (CHIKV) infection.

Methods
Twenty eight pairs of serum samples collected from CHIKV infected patients during the outbreak of chikungunya fever in South Thailand in 2008 were obtained. A multiple cytokine assay for detection of 17 cytokines was performed.

Results
In the acute stage of CHIKV infection, the patients had significantly higher levels of interleukin-6, granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor, monocyte chemotactic protein 1 and tumor necrosis factor alpha than the control ($P<0.001$, $P=0.023$, $P=0.015$, $P<0.001$ and $P=0.024$, respectively). When the disease developed to the recovery stage, the patients had significantly lower levels of interleukin-6, granulocyte-macrophage colony-stimulating factor, monocyte chemotactic protein 1 and macrophage inflammatory protein beta than in the acute stage ($P<0.001$).

Conclusions
This study provides additional information that these cytokines could play roles in pathogenesis of CHIKV infection and could be used as disease biomarkers or drug targets.

Keywords
Chikungunya virus; Cytokine; Interleukin-6; Granulocyte-macrophage colony-stimulating factor; Monocyte chemotactic protein 1
Many cost-benefit/effective rabies research projects need to be carried out in less-developed canine-endemic regions. Among these are educational approaches directed at the public and governments. They would address effective primary wound care, availability, and proper use of vaccines and immunoglobulins, better reporting of rabies, final elimination of dangerous nerve tissue-derived vaccines, and the recognition that rabies is still expanding its geographic range. Such efforts could also reduce deaths in victims who had received no or less than adequate postexposure prophylaxis. There is a need for new technology in canine population control and sustainable vaccination. We have virtually no workable plans on how to control bat rabies, particularly that from hematophagous bats. Preexposure vaccination of villagers in vampire rabies-endemic regions may be one temporary solution. Current efforts to reduce further the time required and vaccine dose required for effective postexposure vaccination need to be encouraged. We still have incomplete understanding of the transport channels from inoculation site to rabies virus antibody generating cells. The minimum antigen dose required to achieve a consistently protective and lasting immune response has been established for intramuscular vaccine administration, but is only estimated for intradermal use. Greater knowledge may have clinical benefits, particularly in the application of intradermal reduced dose vaccination methods. Curing human rabies is still an unattained goal that challenges new innovative researchers.

**Keywords**

Intradermal; Postexposure; Preexposure; Rabies; Vaccine
The potential for pneumococcal vaccination in Hajj pilgrims: Expert opinion


Hajj is the annual pilgrimage to Mecca in the Kingdom of Saudi Arabia, and is one of the largest mass gathering events in the world. Acute respiratory tract infections are very common during Hajj, primarily as a result of close contact among pilgrims, intense congestion, shared accommodation and air pollution. A number of vaccines are (or have been) recommended for Hajj pilgrims in recent years. Several additional vaccines could significantly reduce the morbidity and mortality at Hajj and should be considered in health recommendations for pilgrims. Pneumococcal vaccines (particularly for those aged >65 years) are widely available, and have been shown to reduce the burden of disease associated with *Streptococcus pneumoniae* infection. Importantly, a considerable percentage of Hajj pilgrims have pre-existing illnesses or are elderly, both important risk factors for pneumococcal infection. While there are substantial gaps that need to be addressed regarding our knowledge of the exact burden of disease in Hajj pilgrims and the effectiveness of pneumococcal vaccination in this population, *S. pneumoniae* may be an important cause of illness among this group of travelers. It can be assumed that the majority of pneumococcal serotypes circulating during Hajj are included in the existing pneumococcal vaccines.

**Keywords**

Hajj; Pneumococcal; Polysaccharide vaccine; Conjugate vaccine
Evidences of oseltamivir resistant influenza patients raised the need of novel neuraminidase inhibitors. In this study, five oseltamivir analogs PMC-31–PMC-36, synthesised according to the outcomes of a rational design analysis aimed to investigate the effects of substitution at the 5-amino and 4-amido groups of oseltamivir on its antiviral activity, were screened for their inhibition against neuraminidase N1 and N3. The enzymes used as models were from the avian influenza A H7N1 and H7N3 viruses. The neuraminidase inhibition assay was carried out by using recombinant species obtained from a baculovirus expression system and the fluorogenic substrate MUNANA. The assay was validated by using oseltamivir carboxylate as a reference inhibitor. Among the tested compounds, PMC-36 showed the highest inhibition on N1 with an IC$_{50}$ of 14.6 ± 3.0 nM (oseltamivir 25 ± 4 nM), while PMC-35 showed a significant inhibitory effect on N3 with an IC$_{50}$ of 0.1 ± 0.03 nM (oseltamivir 0.2 ± 0.02 nM). The analysis of the inhibitory properties of this panel of compounds allowed a preliminary assessment of a structure–activity relationship for the modification of the 4-amido and 5-amino groups of oseltamivir carboxylate. The substitution of the acetamido group in the oseltamivir structure with a 2-butenylamido moiety reduced the observed activity, while the introduction of a propenylamido group was well tolerated. Substitution of the free 5-amino group of oseltamivir carboxylate with an azide, decreased the activity against both N1 and N3. When these structural changes were both introduced, a dramatic reduction of activity was observed for both N1 and N3. The alkylation of the free 5-amino group in oseltamivir carboxylate introducing an isopropyl group seemed to increase the inhibitory effect for both N1 and N3 neuraminidases, displaying a more pronounced effect against N1.
Rabies remains a virtually incurable disease once symptoms develop. Neuroimaging studies demonstrate lesions in the different parts of the neuroaxis, even before brain symptoms are evident. These abnormalities have been detailed in both rabies virus-infected humans and dogs with magnetic resonance imaging (MRI). MRI disturbances were similar in both forms (furious or paralytic) in human rabies; however, they were more pronounced in paralytic than in furious rabies virus-infected dogs in which examination was done early in the disease course. Abnormalities were not confined only to neuronal structures of hippocampus, hypothalamus, basal ganglia, and brain stem but also extended to white matter. The blood–brain barrier (BBB) has been clearly shown to be intact during the time rabies virus-infected patients and dogs remained conscious, whereas leakage was demonstrated as soon as they became comatose. Although the location of MRI abnormalities can help diagnosing rabies, the intensities of signals are usually not very distinct and sometimes not recognizable. Newer techniques and protocols have been developed and utilized, such as diffusion-weighted imaging and diffusion tensor imaging, and the latter provides both qualitative and quantitative data. These techniques have been applied to normal and rabies virus-infected dogs to construct fractional anisotropy and mean diffusivity maps. Results showed clear-cut evidence of BBB intactness with absence of vasogenic brain edema and preservation of most neuronal structures and tracts except at the level of brainstem in paralytic rabies-infected dogs. Neuroimaging is one of the most useful tools for the in vivo study of central nervous system infections.

Keywords
- Rabies
- Central nervous system
- Magnetic resonance imaging
- Blood–brain barrier
- Fractional anisotropy
- Mean diffusivity
- DTI
Enhancement of immune response to a DNA vaccine against *Mycobacterium tuberculosis* Ag85B by incorporation of an autophagy inducing system

Jomkhwan Meerak, Supason P. Wanichwecharungruang, Tanapat Palaga

DNA vaccines are a promising new generation of vaccines that can elicit an immune response using DNA encoding the antigen of interest. The efficacy of these vaccines, however, still needs to be improved. In this study, we investigated the effect of autophagy on increasing the efficacy of a candidate DNA vaccine against *Mycobacterium tuberculosis* (MTB), a causative agent of tuberculosis. Low molecular weight chitosan was used to encapsulate plasmid DNA containing a gene encoding MTB Antigen 85B (Ag85B), a secreted fibronectin-binding protein. To induce autophagy upon DNA vaccination, the kinase defective mTOR (mTOR-KD) was transfected into cells, and autophagy was detected based on the presence of LC3II. To investigate whether autophagy enhances an immune response upon DNA vaccination, we coencapsulated the Ag85B-containing plasmid with a plasmid encoding mTOR-KD. Plasmids encapsulated by chitosan particles were used for primary subcutaneous immunization and for intranasal boost in mice. After the boost vaccination, sera from the mice were measured for humoral immune response. The DNA vaccine with the autophagy-inducing construct elicited significantly higher Ag85B-specific antibody levels than the control group treated with the Ag85B plasmid alone or with the Ag85B plasmid plus the wild type mTOR construct. Upon *in vitro* stimulation of splenocytes from mice immunized with recombinant Ag85B, the highest levels of secreted IFN-γ and IL-2 were detected in mice immunized with the autophagy-inducing plasmid, while no differences in IL-4 levels were detected between the groups, suggesting that the DNA vaccine regimen with autophagy induction induced primarily a Th1 immune response. Furthermore, the enhanced proliferation of CD4+ T cells from mice receiving the autophagy-inducing vaccine was observed *in vitro*. Based on the evidence presented, we conclude that incorporating an autophagy-inducing element into a DNA vaccine may help to improve immune response.

**Keywords**

DNA vaccine; mTOR; Autophagy; *Mycobacterium tuberculosis*; Chitosan
Molecular genome tracking of East, Central and South African genotype of Chikungunya virus in South–east Asia between 2006 and 2009

Kamol Suwannakarn, Apiradee Theamboonlers, Yong Poovorawan

Objective
To understand the epidemiology of the East, Central and South African (ECSA) genotype of Chikungunya virus (CHIKV) in terms of emerging and re-emerging infections, this study has been aimed at investigating the evolutionary parameters, genomic signatures and molecular tracking of the CHIKV ECSA genotype in South-east Asia and coastal areas of the Indian Ocean between 2006 and 2009 by using phylogenetic analysis and the Bayesian Markov Chain Monte Carlo (BMCMC) evolutionary estimation.

Methods
Nearly complete genome sequences of 53 CHIKV isolates from all genotypes were subjected to phylogenetic analysis and evolutionary parameter estimation. The amino acids of 67 of ECSA genotype during 2006 to 2009 were compared for finding molecular signature tracking. The ECSA genotype signatures were visualized to find the possible transmission root was projected onto a geographic map.

Results
Phylogenetic analysis showed the ECSA genotype was divided into 2 groups. The first group comprises viruses from India and Southeast Asian countries. The second group consists of strains typically circulating in Sri Lanka in 2008. The evolutionary parameters of these groups depicted the time of the most recent common ancestor at approximately 7.5 years ago. The genomic signatures revealed the positions of amino acid variation in each group.
Conclusions

The molecular evolution projected onto a geographical map showed the routes of CHIKV transmission from 2006 to 2009. Molecular tracking will assist in understanding transmission routes, epidemiology and molecular evolution of CHIKV.

Keywords

Chikungunya virus; East Central and South African genotype; Genomic signature; Evolutionary parameter
To reduce the health risk to pedestrians, urban ventilation has become increasingly important to reduce the concentrations of car exhaust emissions. In this study, the ventilation performance of a street in Bangkok, Thailand, was investigated by performing measurements therein. As a result, the influence of elevated structures was shown. It was also observed that the density of exhaust gas is a simple function of the wind speed and traffic volume when the wind is blowing parallel to the street. However, the ventilation efficiency varied drastically depending on the angle between the street and the wind direction when the wind direction was not stable.

**Keywords**

Urban ventilation; Field measurement; Bangkok; Thailand; NO2; Elevated structure
Malaria in the Greater Mekong Subregion: Heterogeneity and complexity

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The Greater Mekong Subregion (GMS), comprised of six countries including Cambodia, China’s Yunnan Province, Lao PDR, Myanmar (Burma), Thailand and Vietnam, is one of the most threatening foci of malaria. Since the initiation of the WHO’s Mekong Malaria Program a decade ago, malaria situation in the GMS has greatly improved, reflected in the continuous decline in annual malaria incidence and deaths. However, as many nations are moving towards malaria elimination, the GMS nations still face great challenges. Malaria epidemiology in this region exhibits enormous geographical heterogeneity with Myanmar and Cambodia remaining high-burden countries. Within each country, malaria distribution is also patchy, exemplified by ‘border malaria’ and ‘forest malaria’ with high transmission occurring along international borders and in forests or forest fringes, respectively. ‘Border malaria’ is extremely difficult to monitor, and frequent malaria introductions by migratory human populations constitute a major threat to neighboring, malaria-eliminating countries. Therefore, coordination between neighboring countries is essential for malaria elimination from the entire region. In addition to these operational difficulties, malaria control in the GMS also encounters several technological challenges. Contemporary malaria control measures rely heavily on effective chemotherapy and insecticide control of vector mosquitoes. However, the spread of multidrug resistance and potential emergence of artemisinin resistance in *Plasmodium falciparum* make resistance management a high priority in the GMS. This situation is further worsened by the circulation of counterfeit and substandard artemisinin-related drugs. In most endemic areas of the GMS, *P. falciparum* and *Plasmodium vivax* coexist, and in recent malaria control history, *P. vivax* has demonstrated remarkable resilience to control measures. Deployment of the only registered drug (primaquine) for the radical cure of vivax malaria is severely undermined due to high prevalence of glucose-6-phosphate dehydrogenase deficiency in target human populations. In the GMS, the dramatically different ecologies, diverse vector systems, and insecticide resistance render traditional mosquito control less efficient. Here we attempt to review the changing malaria epidemiology in the GMS, analyze the vector systems and patterns of malaria...
transmission, and identify the major challenges the malaria control community faces on its way to malaria elimination.

**Keywords**

Malaria; The Greater Mekong Subregion; Epidemiology; Anopheles vectors; Drug resistance; Border malaria; Elimination
Lifestyles and consumption in cities and the links with health and well-being: the case of obesity

Louis Lebel, Chayanis Krittasudthacheewa, Albert Salamanca, Patcharawalai Sriyasak

The urban environment has a profound influence on how people live, work and play; conversely, that environment is continually being re-shaped by shifts in lifestyles and patterns of consumption. Human well-being and health, in turn, are both outcomes of urban environments and drivers of further urban change. This paper reviews the evidence for links between urban environments, physical activity and food consumption, and obesity. It finds that there is modest, but far from universal, support for an emerging set of propositions that a sustainable and healthy urban environment is one which has: well connected, walkable and cyclable streets; public green spaces; compact and modular organization with mixed land-uses; and a healthy food environment. Although a lot of research has been carried out on some pathways, the evidence-base for many other relationships is weak and transferability of findings across countries or cultural contexts is unclear. Fortunately, many on-going urban initiatives are underway providing a good base for future studies of the effects on the ground.
Genetic variation in the matrix metalloproteinase genes and diabetic nephropathy in type 1 diabetes

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Genetic data support the notion that polymorphisms in members of the matrix metalloproteinase (MMP) family of genes play an important role in extracellular matrix remodeling and contribute to the pathogenesis of vascular disease. To identify novel genetic markers for diabetic nephropathy (DN), we examined the relationship between MMP gene polymorphisms and DN in the Genetics of Kidneys in Diabetes (GoKinD) population. Genotypic data from the Genetic Association Information Network (GAIN) type 1 DN project were analyzed for associations across 21 MMP genes in 1705 individual with type 1 diabetes, including 885 normoalbuminuric control subjects and 820 advanced DN case subjects. In total, we investigated the role of 1283 SNPs (198 genotyped SNPs and 1085 imputed SNPs) mapping to the MMP genes. We identified associations at several correlated SNPs across a 29.2 kb interval on chromosome 11q at the MMP-3/MMP-12 locus. The strongest associations occurred at 2 highly-correlated SNPs, rs610950 (OR = 0.50, \( P = 1.6 \times 10^{-5} \)) and rs1277718 (OR = 0.50, \( P = 2.1 \times 10^{-5} \)). Further examination of this locus identified 17 SNPs (2 genotyped SNPs and 15 imputed SNPs) in complete linkage disequilibrium associated with DN (P-values < 2.5 \( \times 10^{-4} \)), including a non-synonymous SNP (rs652438, Asn357Ser) located in exon 8 of MMP-12 that significantly reduced the risk of DN among carriers of the serine substitution relative to homozygous carriers of asparagine (OR = 0.51; 95% CI = 0.37–0.71, \( P = 6.2 \times 10^{-5} \)). Taken together, our study suggests that genetic variations within the MMP-3/MMP-12 locus influence susceptibility of DN in type 1 diabetes.

Keywords

Diabetic nephropathy; Type 1 diabetes; End-stage renal disease; Matrix metalloproteinase; Genetic association
Effect of flexibility exercise on lumbar angle: A study among non-specific low back pain patients

Nithima Purepong, Anusorn Jitvimonrat, Sujitra Boonyong, Premtip Thaveeratitham, Praneet Pensri

The study investigated the influence of lumbar flexibility exercise on the lumbar angle among patients with non-specific low back pain (LBP). Pre–experimental one-group pretest-posttest design trial was conducted at Health Service Center, Chulalongkorn University, Thailand. Thirty-five non-specific LBP patients with limitation in lower back range of motion and without neurological deficits were recruited (based on the LBP guidelines by ). Lumbar flexibility exercise program developed based on McKenzie therapy was performed individually each day for 2 weeks. Patients attended an exercise program daily in the first week under the supervision of a physiotherapist. The exercise program consisted of 7 sets a day (3-2-2 in the morning-afternoon-evening) in series of 10 repetitions for each set for 2 weeks. Lumbar angle was measured at the beginning and at the end of 2 weeks in order to determine the range of motion improved. The results indicated that the low back pain symptom improved as well as the angle.

Keywords
Flexibility exercise; McKenzie therapy; Lumbar angle; Low back pain
Factors associated with the use of irreversible contraception and continuous use of reversible contraception in a cohort of HIV-positive women

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Background

Effective contraception can be lifesaving by reducing maternal mortality linked to childbirth and unsafe abortion and by reducing vertical and horizontal transmission of HIV, in the case of an HIV-positive woman.

Study design

This study is a secondary analysis of a prospective cohort study. We assessed factors associated with the use of irreversible contraception and the continuous use of reversible contraception in HIV-positive Thai women. We used descriptive statistics to present baseline characteristics and logistic regression to assess the association between contraceptive use and factors in the study.

Results

Of 196 women included in the analysis, 87% self-reported always using male condoms and 56% continuously using another effective contraceptive method during the period of the study (12–18 months). The choice of effective contraceptive methods was suboptimal — 42% were sterilized, 14% used hormonal contraception and no participant reported the use of an intrauterine device. Sexual activity and past contraceptive use were factors associated positively with current continuous contraceptive use. Live births and lower levels of education were additional factors associated positively with sterilization.
Conclusions

Despite high contraceptive use, there are still uncovered contraceptive needs among HIV-positive women in Thailand. HIV-positive women need established specialized family planning services, offering an optimal variety of contraceptive choices and tailored to their individual needs. As sterilization is an irreversible choice, it cannot be a viable alternative for every woman. Due to the positive trend between current and past contraceptive use, we consider that it may be possible to improve family planning programs if they start as early as possible in a woman’s life and are continued throughout her sexually active and reproductive years.

Keywords

Family planning; Continuous contraception; HIV; Women
Immunologic monitoring in kidney transplant recipients

Natavudh Townamchai, Kassem Safa, Anil Chandraker

Transplant biopsy has always been the gold standard for assessing the immune response to a kidney allograft (Chandraker A: Diagnostic techniques in the work-up of renal allograft dysfunction—an update. Curr Opin Nephrol Hypertens 8:723–728, 1999). A biopsy is not without risk and is unable to predict rejection and is only diagnostic once rejection has already occurred. However, in the past two decades, we have seen an expansion in assays that can potentially put an end to the “drug level” era, which until now has been one of the few tools available to clinicians for monitoring the immune response. A better understanding of the mechanisms of rejection and tolerance, and technological advances has led to the development of new noninvasive methods to monitor the immune response. In this article, we discuss these new methods and their potential uses in renal transplant recipients.

Keywords
Immunology; Kidney transplant; Monitoring; Recipient
Preparation and characterization of asiaticoside-loaded alginate films and their potential for use as effectual wound dressings

Panprung Sikareepaisan, Uracha Ruktanonchai, Pitt Supaphol

A wound dressing material was successfully prepared from alginate, a natural polymer capable of forming into hydrogels, and asiaticoside (PAC), a substance from the plant Centella asiatica which has commonly been used in traditional medicine to heal wounds. Various amounts of PAC (i.e., at 2.5, 5 and 10%, based on the weight of alginate) were mixed with alginate in distilled water. The mixtures were later cast into films. The formation into solid films was achieved with the two-step cross-linking procedure with Ca$^{2+}$. First, a dilute CaCl$_2$ aqueous solution (at 0.05% (w/v), 200 mL) was added slowly into an alginate aqueous solution (at 2% (w/v), 100 mL). This step imparted the dimensional stability of the obtained “mixed” films. Secondly, the “mixed” films were cross-linked further in either 2.5 or 5% CaCl$_2$ aqueous solution to obtain “immersed” films. This step caused the “immersed” films to be more stable in environment that requires exposure to a high humidity or contact with an aqueous medium. Due to its insolubility in water, PAC existed in the films as discrete entities. The release of PAC from the PAC-loaded alginate “immersed” films was achieved by both the swelling and the erosion of the alginate matrix in the phosphate buffer solution (PBS) that contained methanol at about 10% (v/v). The potential for use of both the neat and the PAC-loaded alginate “immersed” films as wound dressings was assessed by indirect cytotoxicity evaluation and direct cell culture, using normal human dermal fibroblasts (NHDF). The results showed that these materials were non-toxic to the skin cells.

Keywords
Alginate; Asiaticoside; Hydrogel; Wound dressing
Determinants of pre-exposure rabies vaccination among foreign backpackers in Bangkok, Thailand

Philippe Gautret, Terapong Tantawichien, Vinh Vu Hai, Watcharapong Piyaphanee

Important variations were observed regarding the proportion of backpackers seeking information about travel-associated diseases before departing for Thailand. The main determinants were nationality, reason for travel and age. Sources of information used by travelers varied substantially according to nationality. Moreover, significant differences were recorded regarding pre-exposure vaccination rates against rabies. Having British or Irish citizenship and seeking advice from travel clinic specialists or friends were the strongest and most significant determinants of rabies vaccination history. A significant relationship between vaccine cost and vaccination coverage was also evidenced.

Keywords
Thailand; Rabies; Pre-travel advice; Vaccination coverage; Vaccine cost
Optimization of a Der p 2-based prophylactic DNA vaccine against house dust mite allergy

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DNA vaccines encoding allergens are promising immunotherapeutics to prevent or to treat allergy through induction of allergen-specific Th1 responses. Despite anti-allergy effects observed in small rodents, DNA-based vaccines are weak immunogens in primates and humans and particularly when administered by conventional injection. The goal of the present study was to improve the immunogenicity of a prophylactic vaccine encoding the major house dust mite allergen Der p 2. In this context, we evaluated the influence of different DNA backbones including notably intron and CpG enriched sequence, the DNA dose, the in vivo delivery by electroporation as well as the heterologous prime boost regimen on the vaccine efficiency.

We found that a minimal allergen expression level threshold must be reached to induce the production of specific antibodies but beyond this limit, the intensity of the immune response was independent on the DNA dose and allergen expression. The in vivo DNA delivery by electroporation drastically enhanced the production of specific antibodies but not the IFNg secretion. Vaccination of naïve mice with DNA encoding Der p 2 delivered by electroporation even at very low dose (2 μg) prevented the development of house dust mite allergy through Th1-skewed immune response characterized by the drastic reduction of allergen-specific IgE, IL-5 and lung inflammation together with the induction of strong specific IgG2a titers and IFNg secretion. CpG cassette in the DNA backbone does not play a critical role in the efficient prophylaxis. Finally, comparable protective immune responses were observed when using heterologous DNA prime/protein boost or homologous DNA prime/boost. Taken together, these data suggest that the potent Th1 response induced by DNA-based vaccine encoding allergens through electroporation provides the rationale for the evaluation of DNA encoding Der p 2 into HDM allergy clinical trials.

Keywords

HDM allergy; Der p 2; DNA vaccine; Electroporation; Mice model
Multiplex real–time RT–PCR for detecting chikungunya virus and dengue virus

Piyathida Pongsiri, Kesmanee Praianantathavorn, Apiradee Theamboonlers, Sunchai Payungporn, Yong Poovorawan

Objective
To develop diagnostic test for detection chikungunya virus (CHIKV and Dengue virus (DENV) infection.

Methods
We have performed a rapid, accurate laboratory confirmative method to simultaneously detect, quantify and differentiate CHIKV and DENV infection by single-step multiplex real-time RT-PCR.

Results
The assay’s sensitivity was 97.65%, specificity was 92.59% and accuracy was 95.82% when compared to conventional RT-PCR. Additionally, there was no cross-reaction between CHIKV, DENV, Japanese encephalitis virus, hepatitis C, hepatitis A or hepatitis E virus.

Conclusions
This rapid and reliable assay provides a means for simultaneous early diagnosis of CHIKV and DENV in a single-step reaction.

Keywords
Multiplex; Real-time RT-PCR; Chikungunya virus; Dengue virus
Serological evidence of pig-to-human influenza virus transmission on Thai swine farms

Pravina Kitikoon, Donruethai Sreta, Ranida Tuanudom, Alongkorn Amonsin, Sanipa Suradhat, Kanisak Oraveerakul, Yong Poovorawan, Roongroje Thanawongnuwech

We investigated influenza interspecies transmission in two commercial swine farms in Thailand. Sera from swine-exposed workers (n = 78), age-matched non-swine-exposed healthy people (n = 60) and swine populations in both farms (n = 85) were studied. Hemagglutination-inhibition (HI) assay was performed on Thai swine H1 viruses (swH1N1 and swH1N2) isolated from both farms. Thai human H1N1 (huH1N1) and pandemic H1N1 2009 (pH1N1) were also used as test antigens. The hemagglutinin (HA) 1 genes of swH1N1 and swH1N2 viruses were sequenced and shown to be genetically distinct from the Thai huH1N1 and pH1N1 viruses. Evidence of pig-to-human influenza virus transmission was found in farm workers with increased odds of elevated antibody titers to both swH1N1 (OR 42.63, 95% CI, 14.65–124) and swH1N2 (OR 58, 95% CI, 13.12–256.3) viruses. No evidence of human-to-pig influenza virus transmission was detected in this study.

Keywords
Influenza; Interspecies transmission; Hemagglutination inhibition; Antibody
Objective
To describe mammographic characterization of breast cancer associated with axillary lymph node metastasis at King Chulalongkorn Memorial Hospital.

Methods
The data were collected retrospectively from female patients with breast cancers who underwent breast surgery and axillary node dissection at King Chulalongkorn Memorial Hospital during January 1, 2004 and July 31, 2011. One hundred and ninety histopathologically proven cases of invasive ductal carcinoma (IDC) were randomly recruited; consisted of ninety-five patients with axillary lymph node metastasis and the rest of patients without axillary lymph node metastasis. All patients were reviewed their mammograms with additional ultrasounds and correlation between each mammographic characteristic and ipsilateral node involvement was analyzed, using P-value (P), Odd ratio (OR) and 95% confidence interval (CI).

Results
Mammographic characterization associated with the highest risk of axillary node metastasis was malignant pattern of ipsilateral axillary node (P < 0.001; OR = 44.53; 95% CI = 13.10 – 151.37) with following by intermediate pattern of ipsilateral axillary node (P = 0.002; OR=5.18; 95% CI = 1.79 – 15.04). The other characteristics in descending orders for associated with axillary node involvement are upper outer quadrant tumors associated risk of ipsilateral axillary node involvement (P = 0.02; OR = 3.36; 95% CI = 1.23 – 9.14) and size of breast cancer by additional ultrasound (P = 0.04; OR = 1.48; 95% CI = 1.02-2.17). There was no association between risk of axillary node involvement and the rest of mammographic findings, including microcalcification of the tumor, vascularity of the tumor and size of axillary node.
Conclusion

The highest predictive risk of axillary node metastasis in breast cancer was malignant axillary node pattern. The moderate risk was intermediate axillary node pattern and the lower risks were the tumor located in upper outer quadrant and increased tumor size. These results will be helpful for diagnostic mammogram to imply prognosis of breast cancer before patient undergo biopsy or surgical procedure.

Keywords

Mammographic characterization; Breast cancer; Axillary node metastasis; Axillary node pattern
Health behaviors among short- and long-term ex-smokers: Results from the Thai National Health Examination Survey IV, 2009

Rassamee Sangthong, Wit Wichaidit, Edward McNeil, Virasakdi Chongsuvivathong, Suwat Charialertsak, Pattapon Kessomboon, Surasak Taneepanichskul, Panwadee Putwatana, Wichai Aekplakorn, the Thai National Health Examination Survey IV Study Group

Background

Although numerous studies have shown the health behaviors of ex-smokers to be better than those in regular smokers, the differences in health behaviors among ex-smokers at varying durations of cessation have not been investigated. This study aims to examine the relationship between different durations of smoking cessation and health behaviors.

Methods

Data on dietary intake, alcohol consumption, physical activity, and smoking behavior from the Thai National Health Examination Survey IV for subjects aged 15–98 years (n = 19,371) were included in the analysis. Trends between health behaviors among regular smokers, ex-smokers with different durations of smoking (< 1 year, 1–10 years, > 10 years), and never smokers were tested. Logistic regression models adjusted for sex, age, and economic status were used.

Results

The prevalences of regular smoking, ex-smoking, and never smoking were 22.3%, 12%, and 65.7%, respectively. A trend was found for consumption of fruit, beans and meats, dairy and soy milk, whole-grain products, nutritional supplements, and eating habits. Average daily alcohol consumption (g) was lowest among ex-smokers who had quit for > 10 years ex-smokers (16.4) followed by 1–10 years ex-smokers (27.2), and < 1 year ex-smokers (33.7).
Conclusion

A longer duration of smoking cessation correlated with better health behaviors.

Keywords

Smoking cessation; National Health Survey; Health behaviors; Thailand
Prevalence and diagnostic challenge of dystonia in Thailand: A service-based study in a tertiary university referral centre

Roongroj Bhidayasiri, Lalita Kaewwilai, Natnipa Wannachai, Neil Brenden, Daniel D. Truong, Ratanaruedee Devahastin

Although the subspeciality of movement disorders was established in neurology more than 20 years ago, it is relatively new in Thailand, and while most physicians are generally aware of Parkinson’s disease, they often are not familiar with dystonia. As one of the common movement disorders seen in general practice, a number of family and population studies have suggested that as many as two-thirds of patients with dystonia may be underdiagnosed and it is likely that misdiagnosis occurs frequently. Moreover, there is little information on the prevalence of dystonia in Thailand.

The purpose of this study was to determine the prevalence and clinical profile of dystonia among Thai patients who came from the southern part of Bangkok, which is in the catchment area of Chulalongkorn University Hospital. In addition, the diagnostic accuracy of dystonia among referred patients was assessed. The medical records of 207 patients were reviewed and it was determined that a large proportion of them (71.9%) had focal dystonia with cervical dystonia being the most common form. Primary dystonia (68.1%) accounted for the majority of the cases. The prevalence of all forms of dystonia, primary dystonia and focal dystonia was 19.9, 13.6 and 14.3 per 100 000 persons, respectively.

The diagnostic accuracy of dystonia among referred patients was 85.5%. The most common misdiagnosis was cervical spondylosis, followed by myofascial pain syndrome. Most patients had an average disease duration of 4 years before dystonia was finally diagnosed. Most patients with focal dystonia responded well to botulinum toxin therapy, with 13.3% suffering only mild transient adverse events. In spite of the limitations of this study, this data will initiate a process of increasing both patient and professional awareness of dystonia in Thailand.

Keywords

Dystonia; Prevalence; Thailand; Cervical dystonia; Misdiagnosis; Botulinum toxin; Diagnostic challenge
A census of movement disorders at a Thai university hospital

Roongroj Bhidayasiri, Karn Saksornchai, Lalita Kaewwilai, Kammant Phanthumchinda

There is little information available on the number of patients with movement disorders seen by physicians in Thailand. The authors reviewed the medical records of all movement disorders patients seen at the Chulalongkorn Comprehensive Movement Disorders Center (CUMDS) in Bangkok, Thailand over a 4.5-year period to determine the number of patients with movement disorders and disease characteristics. A total of 1993 patients were assessed at CUMDS. Most of these patients had a diagnosis of parkinsonism (72%), including Parkinson’s disease (PD) (60.9%), followed by tremor (9.6%), and dystonia (8.4%). The diagnostic accuracy of PD according to United Kingdom Parkinson’s Disease Society Brain Bank clinical diagnostic criteria was 90.3%. The average referral period waiting for the consultation was more than 2 years. In spite of the limited availability of medical resources in Thailand, patients with movement disorders tend to seek specialist care and most often it is indicated. This finding documents the need for awareness of PD and other movement disorders by health professionals in Thailand, including the need for specialized training in movement disorders for physicians, including neurologists.

Keywords

Movement disorders; Parkinson’s disease; Thailand
Therapeutic strategies for nonmotor symptoms in early Parkinson’s disease: the case for a higher priority and stronger evidence

Roongroj Bhidayasiri, Daniel D. Truong

It is now recognized that the neuropathology of early Parkinson’s disease (PD) is not limited to the nigrostriatal dopaminergic system, but also involves various brainstem nuclei, the hypothalamus, the olfactory system, and the peripheral autonomic nervous system. Given the disseminated neuropathology of early PD, the earliest clinical signs include a myriad of non-motor manifestations including sleep-wake cycle regulation, cognition, mood and motivation, olfactory and gustatory functions, autonomic functions, and sensory and pain processing.

Despite this realization, there is clearly a paucity of trials that have systematically evaluated the treatment of non-motor symptoms of PD in the early stages. For example, only one large-scale, placebo-controlled randomized trial has been conducted on the treatment of depression in PD patients. There are no reports of randomized controlled trials of therapeutic agents looking at the frequently reported anxiety and fatigue in early PD patients. Based on this lack of evidence, therapy for early non-motor manifestations is often ignored and the focus remains on dopamine replacement strategies with main outcomes being restricted to motor measurements, such as the Unified Parkinson’s Disease Rating Scale. This article presents the case for prioritizing well-designed, controlled clinical trials of therapeutic interventions focusing on non-motor symptoms in early PD patients.

Keywords
Parkinson’s disease; Nonmotor symptoms; Therapeutic strategies; Anxiety; Depression; Constipation
Immunogenicity and safety of a pediatric dose virosomal hepatitis A vaccine in Thai HIV-infected children

Rachanee Saksawad, Sasithorn Likitnukul, Boonyarat Warachit, Orrawadee Hanlivatvong, Yong Poovorawan, Panitchaya Puripokai

The immunogenicity and safety of a pediatric dose of a virosomal hepatitis A vaccine (Epaxal®) was evaluated in a group of 45 Thai children with human immunodeficiency virus (HIV) infection, age 2–16 years. Vaccines were administered at 0 and 6 months. Anti-HAV antibody titers were measured at baseline (before injection) 1 and 7 months after primary vaccination. The prevalence of HAV protective antibody in 45 Thai HIV-infected children was 13.6%. The seroprotection rate was 71% at 1 month and 100% at 7 months. The booster dose increased geometric mean concentration (GMC) from 106.5 mIU/ml to 3486.1 mIU/ml. Higher CD4 lymphocyte counts at enrollment was a predictive factor for HAV antibody response. Both doses of Epaxal® were well tolerated. These preliminary data suggest that a pediatric dose of Epaxal® is an effective hepatitis A vaccine for HIV-infected children and should be considered for implementation on a larger scale in the pediatric HIV population.

Keywords
Hepatitis A vaccine; Pediatric dose; Virosome; HIV-infected children; Immunogenicity; Safety
A brief, peer-led HIV prevention program for college students in Bangkok, Thailand

Ratsiri Thato, Joyce Penrose

Study Objective
To test the effectiveness of a brief theory-based HIV prevention program led by peers among college students.

Design
A quasi-experimental research using a pretest-posttest nonequivalent control group design with 2-mo follow-up.

Setting
A university in Bangkok.

Participants
For peer leaders, 70 undergrad students taking health sexuality course were invited to participate in the study. Then, a convenience sample of undergraduate students was recruited through peer leaders, 226 for experimental group and 209 for control group.

Main Outcome Measures
Information, motivation, behavioral skills, and AIDS/STIs preventive behaviors.

Results
The study revealed that a Brief, Peer-Led HIV Prevention Program significantly increased knowledge of preventive behaviors ($\beta = 2.67, P < .000$), motivated participants to have a better attitude toward preventive behaviors ($\beta = -5.26, P < .000$), better subjective norms ($\beta = -1.54, P < .000$), and greater intentions to practice preventive behavior ($\beta = -1.38, P < .000$). The program also significantly decreased perceived difficulty of AIDS/STIs preventive behaviors ($\beta = 2.38, P < .000$) and increased perceived effectiveness at AIDS/STIs preventive behavior ($\beta = -3.03, P < .000$). However, it did not significantly increase AIDS/STIs preventive behaviors ($\beta = 2.13, P > .05$).
Conclusion

Findings of this study provide initial evidence as to how theoretical variables were operated to effectively increase knowledge, change motivation, and behavioral skills of AIDS/STIs preventive behavior among Thai college students. More research is needed to further test the effectiveness of the program on AIDS/STIs preventive behaviors among college students.

Keywords

HIV prevention; Peer leaders; Adolescents; IMB model; College students
Objective
To assess the effect of slouched sitting on shoulder range of motion (ROM).

Method
30 asymptomatic males aged between 18 and 35 years with no history of shoulder problems within the last 6 months. Shoulder ROMs in flexion and abduction as well as external rotation and internal rotation in 90° of shoulder abduction were measured while the subjects sat in 3 different sitting postures.

Results
There were statistically significant mean differences among the 3 sitting postures regarding thoracic kyphosis and shoulder ROMs ($p < 0.001$). Post hoc analyzes demonstrated significant differences in all comparisons ($p < 0.001$).

Conclusion
Changes in sitting posture affect shoulder ROMs in all directions tested. Greater changes in shoulder ROMs were associated with greater increase in thoracic kyphosis. These findings suggest that even subtle changes in thoracic kyphosis need to be considered during shoulder evaluation.

Keywords
Thoracic kyphosis; Shoulder range of motion; Slouched posture
Healthy life expectancy changes in Thailand, 2002–2007

Rukchanok Karcharnubarn, Philip Rees, Myles Gould

We investigate links between increasing longevity and health status in Thailand. Using data from 2002 and 2007 national surveys of the elderly, healthy life expectancies at older ages were estimated. Change depended on health indicator, gender and age. Self-reported health and self-care disability showed expansion of morbidity. Mobility disability change indicated compression but a wording change means this may be an artefact. We compare these findings with the 1990 and 2010 results of the Global Burden of Disease study. Using HLE based on disease prevalence, the GBD found that Thailand experienced small longevity gains and morbidity compression. Our findings suggest these results should be treated with caution, as, since 2000, Thailand has introduced universal health care.

Keywords
Healthy life expectancy; Disability; Elderly population; Thailand
Sonographic-pathologic correlation of complex cystic breast lesions

Saravech Pongrattanaman, Jenjeera Prueksadee

Abstract
Objective: To understand the pathologic basis for sonographic features of complex cystic lesions.

Methods
From 2646 female patients underwent breast sonography at King Chulalongkorn Memorial Hospital from January 2005 through December 2010, 103 cystic lesions were included. Pathologic confirmation was performed by fine-needle aspiration (n=42), core needle biopsy (n=6), excision (n=54) and mastectomy (n=1). Complex cystic breast masses were classified into 3 types as followings; thick outer wall and/or thick internal septa (type I); thick septation and thick wall were defined as equal or more than 0.5 cm, masses containing mixed cystic and solid components (at least 50% of cystic component) (type II), predominantly solid with eccentric cystic foci (at least 50% of solid component) (type III).

Results
In 103 complex cystic masses, there are 27 lesions (26%) classified as type I cystic breast masses, 37 lesions (36%) as type II cystic breast masses and 39 lesions (38%) type III cystic breast masses, 26 lesions (25.2%) are proved to be malignant. All of type I cystic breast masses in our study are benign, and 14 (38%) of type II cystic breast masses and 12 lesions (31%) of type III cystic breast lesions are proved to be malignant.

Conclusions
Type II and III lesions should suggest possibility of malignancy and biopsy should be performed in all lesions. All type I lesion in this study are benign. None of other parameters we included in this study (size or margin) can effectively differentiate between benign or malignant cystic breast lesions. Also, grading of the malignant lesions by using type of cystic breast mass cannot be applied.

Keywords
Complex cystic breast lesion; Breast sonography
Objectives

To study pandemic (H1N1) 2009 virological outcomes after Oseltamivir treatment in confirmed cases of pandemic (H1N1) 2009 virus infections. A hospital-based cohort study was conducted in south Thailand, between June and September 2009.

Methods

Throat/swab specimens were tested by real-time reverse transcriptase polymerase chain reaction (rRT-PCR) for pandemic (H1N1) 2009. All 357 confirmed cases (122 inpatients, 235 outpatients), whose received a 5-day Oseltamivir treatment. Post-treatment virological follow-up was performed in 91 eligible cases. The NA gene was screened for the H275Y mutation responsible for Oseltamivir resistance.

Results

Thirty-three of 91 patients (36%) had underlying diseases. The duration from the onset of illness to the detection of virus ranged 1–14 days (median 3 days). The rRT-PCR was positive on day 5 of treatment in 24 of 91 patients (26%). Patients with underlying diseases had a higher proportion of post-treatment positive test than those without underlying diseases (15/33 vs 9/58). The rRT-PCR-confirmed viruses detected in all 125 throat swab specimens did not show evidence suggesting Oseltamivir resistance.

Conclusions

Prolonged presence of pandemic (H1N1) 2009 detected by rRT-PCR was found. An extended course of antiviral treatment should be considered in patients with underlying diseases and severe clinical symptoms.
Choice of providers for treating a neglected tropical disease: an empirical analysis of kala azar in Nepal

Shiva Raj Adhikari, Siripen Supakankunti, M Mahmud Khan

Objective
To examine the choice of healthcare providers for treating kala azar (KA) in Nepal.

Methods
Information was collected from clinically diagnosed KA patients seeking care from public hospitals located in KA endemic districts. The survey collected information from more than 25 percent of total KA cases in the country. For empirical estimation of probability of choosing a provider-type as a first contact healthcare provider, a multinomial logit model was defined with five alternative options with self care as the reference category.

Results
The empirical model found that price of medical care services, income of households, knowledge of patients on KA and KA treatment, borrowing money, age of patient, perceived quality of provider types, etc. determine the likelihood of seeking care from the alternative options considered in the analysis. All variables have expected signs and are consistent with earlier studies. The price and income elasticity were found to be very high indicating that poorer households are very sensitive to price and income changes, even for a severe disease like KA. Using the empirical models, we have analyzed two policy instruments: demand side financing and interventions to improve the knowledge index about KA.

Conclusions
Due to high price elasticity of KA care and high spillover effects of KA on the society, policy makers may consider demand side financing as an instrument to encourage utilization of public hospitals.

Keywords
Neglected tropical disease; Kala azar; Nepal
Malaria parasite carbonic anhydrase: inhibition of aromatic/heterocyclic sulfonamides and its therapeutic potential

Sudaratana R Krungkrai, Jerapan Krungkrai

Plasmodium falciparum (P. falciparum) is responsible for the majority of life-threatening cases of human malaria, causing 1.5–2.7 million annual deaths. The global emergence of drug-resistant malaria parasites necessitates identification and characterization of novel drug targets and their potential inhibitors. We identified the carbonic anhydrase (CA) genes in P. falciparum. The pfCA gene encodes an α-carbonic anhydrase, a Zn^{2+}-metalloenzyme, possessing catalytic properties distinct from that of the human host CA enzyme. The amino acid sequence of the pfCA enzyme is different from the analogous protozoan and human enzymes. A library of aromatic/heterocyclic sulfonamides possessing a large diversity of scaffolds were found to be very good inhibitors for the malarial enzyme at moderate-low micromolar and submicromolar inhibitions. The structure of the groups substituting the aromatic-ureido- or aromatic-azomethine fragment of the molecule and the length of the parent sulfonamide were critical parameters for the inhibitory properties of the sulfonamides. One derivative, that is, 4-(3, 4-dichlorophenylureido)thioureido-benzensulfonamide (compound 10) was the most effective in vitro P. falciparum CA inhibitor, and was also the most effective antimalarial compound on the in vitro P. falciparum growth inhibition. The compound 10 was also effective in vivo antimalarial agent in mice infected with Plasmodium berghei, an animal model of drug testing for human malaria infection. It is therefore concluded that the sulphonamide inhibitors targeting the parasite CA may have potential for the development of novel therapies against human malaria.

Keywords
Malaria; Plasmodium falciparum; Carbonic anhydrase; Carbonic anhydrase inhibitor; Aromatic/heterocyclic sulfonamides; Antimalarial agents; Drug target; Biological medicine; Tropical disease; Infectious disease; Parasitic disease
Detection of oseltamivir sensitive/resistant strains of pandemic influenza A virus (H1N1) from patients admitted to hospitals in Thailand

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Oseltamivir has been used widely for prophylaxis or treatment during outbreaks of the pandemic influenza virus (H1N1) in several countries. The aim of this study was to develop a real-time RT-PCR (reverse transcription-polymerase chain reaction) to be applied for detection and monitoring of the oseltamivir resistant strains of this virus during three outbreaks (May 2009 to October 2010) in Thailand. The real-time RT-PCR assay for detecting H275Y proved highly specific for the pandemic influenza virus (H1N1) as no cross-amplification was detected with other respiratory viruses or human total RNA. The assay was also highly sensitive with a detection limit as low as 100 copies/μL for both wild-type and resistant strains. The performance of the assay was evaluated in terms of amplification efficiency (100%). The results obtained by real-time RT-PCR were in complete agreement with direct nucleotide sequencing. However, real-time RT-PCR provided more detail on the relative quantities of ratios between resistant and sensitive strains in each individual. The results revealed that four of 1288 (0.31%) patients were infected with the oseltamivir resistant strain. The number of patients infected by resistant strains was higher during the third (0.61%) and second (0.24%) waves than during the first (0%) outbreak. In conclusion, the real-time RT-PCR assay for H275Y detection is advantageous because it is specific, sensitive, and provides quantitative data. And it would be useful for large-scale testing and monitoring of oseltamivir resistant strains of the pandemic influenza A virus (H1N1).

Keywords
Oseltamivir, Pandemic influenza, H1N1, Detection
Immunogenicity assay validation for an HIV vaccine trial: High IFNγ+/IL-2+ CD8+ T cells background in healthy Thais

Sunee Sirivichayakul, Pattarawat Thantiworasit, Pornsupa Chatkulkawin, Supranee Buranapraditkun, Mee Ling Munier, Anthony D. Kelleher, Kiat Ruxrungtham

In a vaccine trial, assays for vaccine immunogenicity if performed locally will strengthen local site, can save costs and avoid hurdles associated with specimen transport. Here we report the optimization and validation of an Intracellular Cytokine Staining (ICS) assay which was undertaken in preparation for a phase I HIV vaccine trial conducted in Thailand. Intra-, and inter-operator variability were easily established. However, while attempting to set population cut offs for a positive response we found 4/36 (11%) high background responses of IFNγ+ and/or IL-2+ CD8+ T cells (>1%) in normal healthy volunteers. The determinates of these unexpected responses were explored and minimized.

Keywords

IFNγ+/IL-2+ T cells; Intracellular cytokine staining; Validation; Phase I vaccine trial; Thailand
Development of postural control during gait in typically developing children: The effects of dual-task conditions

Sujitra Boonyong, Ka-Chun Siu, Paul van Donkelaar, Li-Shan Chou, Marjorie H. Woollacott

The purpose of this study was to investigate the typical development of postural control in younger (5–6 yrs) and older (7–16 yrs) children (YTD and OTD) during two gait tasks, including level walking and obstacle-crossing, using a dual-task paradigm, and to compare the results of the children’s performance with that of healthy young adults (HYA). Our findings revealed that gait control in typical children requires attentional resources to maintain stability. Moreover, dual-task interference was less in HYA compared to YTD and OTD. Gait performance decrements in the dual-task context were greater in YTD compared to OTD, whereas cognitive performance decrements in YTD and OTD were similar. In addition, dual-tasking affected cognitive performance more in YTD when gait task difficulty was increased. Results suggest a developmental trend in attentional resources used to control gait in typical children. Postural control during gait under dual-task conditions was improved when children were more mature, as attentional resources increased with age.

Keywords
Gait; Gait stability; Dual task; Development of gait; Gait in children
Drug reimbursement decision-making in Thailand, China, and South Korea

Surachat Ngorsuraches, Wei Meng, Bo-Yeon Kim, Vithaya Kulsomboon

Objective
To provide a comparison of national drug reimbursement decision-making, including an update of economic evaluation roles and barriers, in Thailand, China, and South Korea.

Methods
Documentary reviews supplemented by experiences of policymakers.

Results
National health insurance policy in all the three countries has been developed toward coverage for all. It leads to higher health-care expenditures and requires a good reimbursement system for health-care services, including drugs. Drug reimbursement decision-making in these countries is to develop a reimbursement list with the help of various committees having different roles. Primarily, they assess the clinical and safety evidence. Economic evidence, including budget impact and pharmacoeconomic evaluation, has also been very important for their reimbursement decision-making. This evidence is sometimes used in negotiation mechanism, which allows pharmaceutical companies to lower their drug prices and leads to lower overall drug expenditures. Several common barriers, for example, human capacity and data availability, for obtaining economic evidence in all the three countries, however, still exist.

Conclusions
Drug reimbursement decision-making in Thailand, China, and South Korea is in its transition period. It seems to run in the same direction, for example, guideline development and pharmacoeconomic evaluation agency establishment. Pharmacoeconomic evaluation plays important roles in the efficiency of drug reimbursement decision-making, even though there are several barriers to be overcome.

Keywords
Drug reimbursement; Health insurance; Reimbursement decision-making
AOS25 prevalence of PTEN loss in triple negative breast cancer in the Thai population

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Background

Triple negative breast cancer (TNBC) is worse and more aggressive and rapidly relapsing than hormone-receptor-positive breast cancer. PTEN, one of the important pathways in TNBC, could significantly worsen the disease progression. Primary outcome was the prevalence of PTEN loss in Thai patients with TNBC. Secondary outcome was the relation between PTEN loss and the progression of disease.

Methods

Female patients were diagnosed with TNBC and treated at King Chulalongkorn Memorial Hospital where PTEN was detected by use of immunohistochemistry (28H6 antibody) during June 2006 to December 31, 2011. Micro-array FISH was used to confirm those tumour samples that were HER2 positive.

Findings

Twenty-four (29.3) of 82 TNBC samples were PTEN negative. The average age of the patients with PTEN loss was 50.3 years and the women were mainly premenopausal (53.7%). The PTEN-negative disease was characterised by a tumour larger than 2 cm compared with PTEN-positive tumours (80% versus 68.8%), but not related to the severity of disease, lymphovascular invasion, and lymph node involvement. Although, the average disease recurrence time was worse in the PTEN-negative group than in the PTEN-positive group (17 months versus 24 months, hazard ratio 1.31, 95% confidence interval (CI) 11.13–22.87; p = 0.05), the survival rate was not different.

Interpretation

The PTEN loss reported in the patients with TNBC in Thailand is less than that reported in other studies. Although it is not prognostic for disease progression, we suggest that a longer follow-up to ascertain the survival rate of patients with the disease. Our study is the first report of PTEN loss in TNBC in Thailand.

The authors declared no conflicts of interest.
New insights into the pelvic organ support framework

Tanvaa Tansatit, Prawit Apinuntrum, Thavorn Phetudom, Piyaporn Phanchart

Objective

It is important to understand the underlying mechanisms of the physiological framework of the pelvic organ support system to develop more effective interventions. Developing more successful interventions for restoration of defects of the pelvic floor will lead to symptomatic improvement of pelvic floor prolapse and stress incontinence disorders. The purpose of the current study was to investigate the physiological framework related to the pelvic organ support system and propose the underlying mechanisms of pelvic organ support based on the anatomical findings.

Study design

Ten female soft embalmed cadavers were dissected after a colorectal hands-on workshop to visualize components of the pelvic organ support system.

Results

The puborectalis attached at the superior pubic ramus above the arcus tendineus fasciae pelvis. The anterior half of the iliococcygeus originated at the level of the arcus tendineus fasciae pelvis but descended from the arcus tendineus fasciae pelvis before it reached the ischial spine. The fibrous visceral sheath of the endopelvic fascia covered both the bladder and the upper vagina and bound these structures together. The levator ani muscle was separated into a horizontal and a vertical part at the medial attachment of the fibrous visceral sheath. A well-circumscribed adipose cushion pillow, in the ischioanal fossa and its anterior recess, supported the horizontal part of the levator ani muscle and pressed the vertical part against the pelvic viscera. Perivascular sheaths and pelvic nerve plexuses were reinforced by condensed endopelvic fascia, they suspended the pelvic organs posterolaterally.

Conclusion

The pelvic organ support framework consists of two mechanical structures: (1) the supporting system of the levator ani muscle, the arcus tendineus fasciae pelvis and the adipose cushion pillow, and (2) the suspension system of the neurovascular structures and the associated endopelvic fascia condensation.
Early versus deferred antiretroviral therapy for children older than 1 year infected with HIV (PREDICT): a multicentre, randomised, open-label trial


Background
The optimum time to start antiretroviral therapy for children diagnosed with HIV infection after 1 year of age is unknown. We assessed whether antiretroviral therapy could be deferred until CD4 percentages declined to less than 15% without affecting AIDS-free survival.

Methods
In our multicentre, randomised, open-label trial at nine research sites in Thailand and Cambodia, we enrolled children aged 1–12 years who were infected with HIV and had CD4 percentages of 15–24%. Participants were randomly assigned (1:1) by a minimisation scheme to start antiretroviral therapy at study entry (early treatment group) or antiretroviral therapy to start when CD4 percentages declined to less than 15% (deferred treatment group). The primary endpoint was AIDS-free survival (based on US Centers for Disease Control and Prevention category C events) at week 144, assessed with the Kaplan-Meier analysis and the log-rank approach. This study is registered with number .

Findings
Between March 28, 2006, and Sept 10, 2008, we enrolled 300 Thai and Cambodian children infected with HIV, with a median age of 6.4 years (IQR 3.9–8.4). 150 children were randomly allocated early antiretroviral therapy (one participant was excluded from analyses after withdrawing before week 0) and 150 children were randomly allocated deferred antiretroviral therapy. Median baseline CD4 percentage was 19% (16–22%). 69 children (46%) in the deferred treatment group started antiretroviral therapy during the study. AIDS-free survival at week 144 in the deferred treatment group was 98.7% (95% CI 94.7–99.7; 148 of 150 patients) compared with 97.9% (93.7–99.3; 146 of 149 patients) in the early treatment group (p=0.6).
**Interpretation**

AIDS-free survival in both treatment groups was high. This low event rate meant that our study was underpowered to detect differences between treatment start times and thus additional follow-up of study participants or future studies are needed to answer this clinical question.

**Funding**

US National Institutes of Health, Division of AIDS; National Institute of Allergy and Infectious Diseases; National Institute of Child Health and Human Development; and National Institute of Mental Health.
Rabies is an almost invariably fatal disease that can present as classic furious rabies or paralytic rabies. Recovery has been reported in only a few patients, most of whom were infected with bat rabies virus variants, and has been associated with promptness of host immune response and spontaneous (immune) virus clearance. Viral mechanisms that have evolved to minimise damage to the CNS but enable the virus to spread might explain why survivors have overall good functional recovery. The shorter survival of patients with furious rabies compared with those with paralytic rabies closely corresponds to the greater amount of virus and lower immune response in the CNS of patients with the furious form. Rabies virus is present in the CNS long before symptom onset: subclinical anterior horn cell dysfunction and abnormal brain MRI in patients with furious rabies are evident days before brain symptoms develop. How the virus produces its devastating effects and how it selectively impairs behaviour in patients with furious rabies and the peripheral nerves of patients with paralytic rabies is beginning to be understood. However, to develop a pragmatic treatment strategy, a thorough understanding of the neuropathogenetic mechanisms is needed.
We reported a case of an African American woman who went to the hospital with palpable right breast lump with bloody nipple discharge at University of Texas Medical Branch at Galveston. The modalities of breast imagings included mammography and ultrasoundography. The method used for viral identification was Linear Array HPV genotyping test. Intraductal papilloma revealed as high density tubular or rounded lobular masses with partially circumscribed, obscured margins and clustered punctate microcalcifications on mammograms. Ultrasound showed as intraductal masses with dilated ducts. The core biopsy demonstrated duct filled with papillary lesion and post excision revealed intraductal papilloma. HPV DNA types 16, 33, 58 and 71 were detected after use of Linear Array HPV genotyping test.

Keywords
Human papilloma virus; Preoncogenic gene; Breast cancer; Mammography; Ultrasound
Randomized study of intradermal compared to intramuscular hepatitis B vaccination in HIV-infected children without severe immunosuppression

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HIV infected individuals have poorer response to hepatitis B vaccine (HBV) compared to normal host. Intradermal administration (ID) facilitates the exposure of antigen to antigen-presenting cells compared to intramuscular administration (IM).

HIV-infected children aged 1–18 years with CD4% ≥ 15% or 200 cells/mm³ who had negative HBs Ag, antiHBs, and antiHBc were randomized to receive 3-dose of HBV via ID (2 μg/dose) or IM (10 μg/dose) route at months 0, 2, and 6. AntiHBs titers were measured at months 2, 6 and 7 after first HBV. AntiHBs ≥ 10 mIU/mL was considered protective and AntiHBs > 100 mIU/mL was considered good response.

Participants included 41 in ID and 39 in IM arms. 64% had completed 3-doses HBV during infancy. The mean (SD) of age, nadir CD4% and current CD4% were 12 (3.3) years, 10.6 (7.9)% and 28 (8.0)% respectively. 91% were on HAART and 84% had undetectable HIV-RNA.

Proportion of children with protective antiHBs in ID vs. IM group were 19.5% vs. 25.6% at month 2, 56.1% vs. 76.9% at month 6, and 90.2% vs. 92.3% at month 7 (NS, all). The geometric mean (95% confidence interval) of antiHBs titer in ID vs. IM group were 112.5 (34.4–367.6) vs. 141.2 (49.4–404.1) mIU/mL at month 2 \( (p = 0.74) \), 70.4 (39.8–124.4) vs. 132.1 (79.4–219.8) mIU/mL at month 6 \( (p = 0.10) \), and 157.0 (103.0–239.3) vs. 458.9 (324.0–647.0) mIU/mL at month 7 \( (p < 0.001) \). However, only 56.1% of the ID arm had good response to HBV compared to 82.1% in the IM arm \( (p = 0.01) \). The predictors for being a good responder to HBV were IM administration \( [OR 4.0, 95\% CI 1.4–11.8, p = 0.012] \) and body weight <35 kg at baseline \( [OR 3.8, 95\% CI 1.3–10.8, p = 0.013] \). No adverse events grade 3/4 occurred.
In conclusion, HIV-infected children without severe immune suppression, both ID and IM routes of HBV resulted in similar rates of protective antibody titers. However, high antibody titers to HBV were more common with IM; therefore, IM administration is preferred.

**Keywords**

HIV-infected children; Hepatitis B vaccine; AntiHBs; Immune recovery
Cost and effectiveness evaluation of prophylactic HPV vaccine in developing countries

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Background

Approximately 80% of cervical cancer cases occur in developing countries. In Thailand, cervical cancer has been the leading cancer in females, with an incidence of 24.7 cases per 100,000 individuals per year.

Objectives

We constructed a decision model to simulate the lifetime economic impact for women in the context of human papillomavirus (HPV) infection prevention. HPV-related diseases were of interest: cervical cancer, cervical intraepithelial neoplasia, and genital warts. The two strategies used were 1) current practice and 2) prophylactic quadrivalent vaccine against HPV types 6, 11, 16, and 18.

Methods

We developed a Markov simulation model to evaluate the incremental cost-effectiveness ratio of prophylactic HPV vaccine. Women transition through a model either healthy or developing HPV or its related diseases, or die from cervical cancer or from other causes according to transitional probabilities under the Thai health-care context. Costs from a provider perspective were obtained from King Chulalongkorn Memorial Hospital. Costs and benefits were discounted at 3% annually.

Results

Compared with no prophylactic HPV vaccine, the incremental cost-effectiveness ratio was 160,649.50 baht per quality-adjusted life-year. The mortality rate was reduced by 54.8%. The incidence of cervical cancer, cervical intraepithelial neoplasia grade 1, cervical intraepithelial neoplasia grade 2/3, and genital warts was reduced by up to 55.1%.
Conclusion

Compared with commonly accepted standard thresholds recommended by the World Health Organization Commission on Macroeconomics and Health, the nationwide coverage of HPV vaccination in girls is likely to be cost-effective in Thailand.

Keywords

Cost-effectiveness; Developing countries; HPV vaccine
A low-cost intervention for improving gait in Parkinson’s disease patients: A cane providing visual cues

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Objective
Stable walking is problematical for many Parkinson’s disease (PD) patients, sometimes experienced as “Freezing of Gait” (FOG), a brief interruption of their natural walking rhythm usually limited to advanced stages of PD. Visual cues have been found to reduce FOG so that patients are able to continue their walking without interruption, thereby reducing falls. This study assessed the difference in the impact on FOG with a group of PD patients receiving visual cues from an innovative “laser cane” and with a traditional cane with no cues.

Methods
This study of 30 PD patients compares the impact on FOG of a cane that provided visual cues from a laser beam with a cane providing no cues during both ‘on’ and ‘off’ responses to medications. For each test the individual subjects were videotaped walking two rounds on a 5-meter track and their footsteps were printed on paper tracking sheets.

Results
The visual cues of the laser beam cane significantly increased both stride length and velocity during the ‘off’ medication period in all of the participating patients. Greater improvements of the gait parameters were experienced in PD patients with the moderate stage (H & Y = 3) (17 patients) than those in the mild stage (H & Y = 2) (13 patients); with the biggest differences in reduced FOG and increased stride length.

Conclusions
This study demonstrates that an effective, low-cost intervention can be designed and implemented in low and middle-income countries for solving the problem of FOG in PD patients using locally available technology.

Keywords
Parkinson’s disease; Gait; Cane; Assistive device; Cues; External stimuli
TM4SF20 ancestral deletion and susceptibility to a pediatric disorder of early language delay and cerebral white matter hyperintensities


White matter hyperintensities (WMHs) of the brain are important markers of aging and small-vessel disease. WMHs are rare in healthy children and, when observed, often occur with comorbid neuroinflammatory or vasculitic processes. Here, we describe a complex 4 kb deletion in 2q36.3 that segregates with early childhood communication disorders and WMH in 15 unrelated families predominantly from Southeast Asia. The premature brain aging phenotype with punctate and multifocal WMHs was observed in ~70% of young carrier parents who underwent brain MRI. The complex deletion removes the penultimate exon 3 of TM4SF20, a gene encoding a transmembrane protein of unknown function. Minigene analysis showed that the resultant net loss of an exon introduces a premature stop codon, which, in turn, leads to the generation of a stable protein that fails to target to the plasma membrane and accumulates in the cytoplasm. Finally, we report this deletion to be enriched in individuals of Vietnamese Kinh descent, with an allele frequency of about 1%, embedded in an ancestral haplotype. Our data point to a constellation of early language delay and WMH phenotypes, driven by a likely toxic mechanism of TM4SF20 truncation, and highlight the importance of understanding and managing population-specific low-frequency pathogenic alleles.
Mechanism of arctigenin-mediated specific cytotoxicity against human lung adenocarcinoma cell lines

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The lignan arctigenin (ARG) from the herb Arctium lappa L. possesses anti-cancer activity, however the mechanism of action of ARG has been found to vary among tissues and types of cancer cells. The current study aims to gain insight into the ARG mediated mechanism of action involved in inhibiting proliferation and inducing apoptosis in lung adenocarcinoma cells. This study also delineates the cancer cell specificity of ARG by comparison with its effects on various normal cell lines. ARG selectively arrested the proliferation of cancer cells at the G₀/G₁ phase through the down-regulation of NPAT protein expression. This down-regulation occurred via the suppression of either cyclin E/CDK2 or cyclin H/CDK7, while apoptosis was induced through the modulation of the Akt-1-related signaling pathway. Furthermore, a GSH synthase inhibitor specifically enhanced the cytotoxicity of ARG against cancer cells, suggesting that the intracellular GSH content was another factor influencing the susceptibility of cancer cells to ARG. These findings suggest that specific cytotoxicity of ARG against lung cancer cells was explained by its selective modulation of the expression of NPAT, which is involved in histone biosynthesis. The cytotoxicity of ARG appeared to be dependent on the intracellular GSH level.

Keywords
Arctigenin (ARG); Mechanism; Specific; Cytotoxicity
Fragile X syndrome: Clinical, cytogenetic and molecular screening among autism spectrum disorder children in Indonesia

Winarni, T.I., Utari, A., Mundhofir, F.E.P., Hagerman, R.J., Faradz, S.M.H.

Fragile X testing is a priority in the evaluation of autism spectrum disorders (ASD) cases because identification of the FMR1 mutation leads to new treatment options. This study is focused on determining the prevalence of the FMR1 gene mutation among ASD cases in Indonesia. DSM-IV-TR criteria were administered to diagnose ASD; symptom severity was classified using the Childhood Autism Rating Scale. Cytogenetic analysis, polymerase chain reaction, and Southern blot for FMR1 gene analysis were carried out to confirm the diagnosis of fragile X syndrome. The fragile X site and FMR1 full mutation allele were identified in 3 out of 65 (4.6%) and 4 out of 65 (6.15%) children aged 3–17 years (57 boys and 8 girls), respectively. The Fragile X laboratory workup is essential in the evaluation of patients with ASD. Molecular analysis is most accurate, while cytogenetic documentation of the fragile X site can also be useful if molecular testing is not available.

Keywords
FMR1 screening; Indonesia; Autism spectrum disorders; Fragile X site; Fragile X syndrome
Genetic counseling/consultation in South-East Asia: A report from the workshop at the 10th Asia Pacific Conference on Human Genetics


This paper reports on the workshop ‘Genetic Counseling/Consultations in South-East Asia’ at the 10th Asia Pacific Conference on Human Genetics in Kuala Lumpur, Malaysia, in December 2012. The workshop brought together professionals and language/communication scholars from South-East Asia, and the UK. The workshop aimed at addressing culture- and context-specific genetic counseling/consultation practices in South-East Asia. As a way of contextualizing genetic counseling/consultation in South-East Asia, we first offer an overview of communication-oriented research generally, drawing attention to consultation and counseling as part of a communicative continuum with distinctive interactional features. We then provide examples of genetic counseling/consultation research in Hong Kong. As other countries in South-East Asia have not yet embarked on communication-oriented empirical research, we report on the current practices of genetic counseling/consultation in these countries in order to identify similarities and differences as well as key obstacles that could be addressed through future research. Three issues emerged as ‘problematic’: language, religion and culture. We suggest that communication-oriented research can provide a starting point for evidence-based reflections on how to incorporate a counseling mentality in genetic consultation. To conclude, we discuss the need for creating a platform for targeted training of genetic counselors based on communication-oriented research findings.
Simultaneous treatment with azelnidipine and olmesartan inhibits apoptosis of HL-1 cardiac myocytes expressing E334K cMyBPC


Background: Apoptosis appears to play an important role in the pathogenesis of hypertrophic cardiomyopathy (HCM). We have previously reported 3 HCM patients carrying the E334K MYBPC3, and that heterologous expression of E334K cMyBPC in cultured cells induced apoptosis. The purpose of this study was to identify pharmacological agents that would inhibit apoptosis in HL-1 cardiomyocytes expressing E334K cMyBPC.

Methods And Results: E334K cMyBPC expression in cells increased levels of pro-apoptosis (p53, Bax and cytochrome c) and decreased levels of anti-apoptosis (Bcl-2 and Bcl-XL). While the beta blocker carvedilol (1 μM) normalized the level of p53 and Bcl-2 and the calcium channel blocker (CCB) bepridil (0.5 μM) normalized that of Bcl-2, both the CCB azelnidipine (1 μM) and the angiotensin receptor blocker (ARB) olmesartan (10 μM) normalized those of p53, Bax, cytochrome c, and Bcl-XL. Among those proteins, cytochrome c was the one which showed the highest degree of change. Both azelnidipine (0.1 μM) and olmesartan (1 μM) reduced the level of cytochrome c by 40.2 ± 4.3% and 31.3 ± 5.1%, respectively. The CCB amlodipine and the ARB valsartan reduced it only by 19.1 ± 2.1% and 20.1 ± 5.2%, respectively. Flow cytometric analysis and annexin V staining showed that treatment of cells with azelnidipine (0.1 μM) plus olmesartan (0.3 μM) or that with amlodipine (0.1 μM) plus valsartan (0.3 μM) reduced the number of apoptotic cells by 35.8 ± 10.5% and 18.4 ± 3.2%, respectively.

Conclusion: Azelnidipine plus olmesartan or amlodipine plus valsartan inhibited apoptosis of HL-1 cells expressing E334K cMyBPC, and the former combination was more effective than the latter.

Keywords
Hypertrophic cardiomyopathy; Mutant cardiac myosin binding protein C; Calcium channel blocker; Angiotensin receptor blocker; Apoptosis
The gene effect of growth hormone on body weight and egg production in divergent selection for five generation of Japanese quail (*Coturnix coturnix japonica*)

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The aim of this study was to determine the gene effect of Growth Hormone (GH) on divergent selection of Japanese quail. Quails were grouped into high weight (Q-H), low weight (Q-L) and random weight (Q-R) females as a treatment for divergent selection. Parameter phenotype observed in each generation is the weight at four weeks of age and egg production at ten weeks of age for five generations. The results showed that the dominance level on body weight of Q-L was incomplete dominance, Q-R was over dominance and Q-H was lack of dominance. While the dominance level on egg production of Q-L and Q-H were over dominance and Q-R was lack of dominance. The gene effect of GH on body weight of Q-H is 1.53 times greater than the Q-L and 12.37 times greater when compared with Q-R. Whereas the gene effect of GH on egg production of Q-H is 1.53 times greater than the Q-L but only 4 times greater when compared with Q-R. Should be developed that to increase the low-weight (Q-L) is in the BB genotype and the high weight (Q-H) is in the AA genotype groups. Otherwise, to increase the low-weight (Q-L) and high-egg production are in the AA and BB genotypes and the high weight (Q-H) and low-egg production are in the AA and AB genotypes groups.
Body image and sexuality in Indonesian adults with a disorder of sex development (DSD)

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In Indonesia, disorders of sex development (DSDs) are not well recognized and medical care for affected individuals is scarce. Consequently, many patients live with ambiguous genitalia and appearance. We compared reported outcomes on body image, sexual functioning, and sexual orientation of 39 adults with DSDs (aged 18 to 41) and 39 healthy controls matched for gender, age, and residential setting (urban, suburban, rural). Differences in gender and treatment status (treated or untreated) were also explored. On body image, adults with DSDs reported dissatisfaction with sex-related body parts. Compared to the matched controls, women with DSDs reported greater sexual distress, and men with DSDs reported lower erectile and ejaculation frequencies, and more dissatisfaction with sexual life but not with sexual desire and activities. Men with DSDs who had undergone genital surgery reported higher erectile and ejaculation frequencies than untreated men. More women than men in the DSDs group reported a nonexclusive heterosexual orientation. DSDs and infertility had a great impact on sexuality. Fear of ostracism complicated DSD acceptance. Findings were compared to those of Western studies. Based on these results, education about DSDs and their psychosexual consequences may help reduce the sexual distress and problems in adults with DSDs and improve quality of life.
Width of abnormal ganglion cell complex area determined using optical coherence tomography to predict glaucoma


**Purposes:** We examined the relationships of ganglion cell complex (GCC) parameters determined on spectral-domain optical coherence tomography (SD-OCT), especially the width of abnormal areas, and its ability to detect various stages of glaucoma.

**Methods:** OCT parameters of glaucomatous and normal eyes were determined with the RTVue SD-OCT. Widths of abnormal GCC areas marked by either red or yellow on the OCT significance map were quantified with image J software. The relationships between the abnormal GCC area and other GCC parameters [thickness, focal loss volume (FLV), and global loss volume (GLV)] and the peripapillary retinal nerve fiber layer (RNFL) thickness were determined using regression analyses. The potential of using the GCC and RNFL parameters to discriminate between glaucomatous and normal eyes was examined using the area under the curve (AUC) of receiver operating characteristics (ROC).

**Results:** One hundred and eighteen glaucomatous eyes and 45 normal control eyes were studied. Nonlinear models best described the relationships between abnormal GCC area and other GCC parameters. Scatter plots showed changes in the average thickness of the GCC and RNFL, and the average sizes of the GLV preceded changes of abnormal areas of the GCC. The width of the abnormal areas on the GCC thickness map was comparable with other parameters for diagnosing glaucoma.

**Conclusions:** OCT thickness parameters appeared to decrease faster than the area parameter at the initial stage of glaucoma. The sizes of abnormal areas of the GCC were the most pertinent parameters for detecting glaucoma.

**Keywords**
Ganglion cell complex (GCC); Abnormal GCC area; Glaucoma; Optical coherence; Tomography
Activation of invariant natural killer T cells by α-galactosylceramide ameliorates myocardial ischemia/reperfusion injury in mice


Invariant natural killer T (iNKT) cells orchestrate tissue inflammation via regulating various cytokine productions. However the role of iNKT cells has not been determined in myocardial ischemia/reperfusion (I/R) injury. The purpose of this study was to examine whether the activation of iNKT cells by α-galactosylceramide (α-GC), which specifically activates iNKT cells, could affect myocardial I/R injury. I/R or sham operation was performed in male C57BL/6J mice. I/R mice received the injection of either α-GC (I/R + α-GC, n = 48) or vehicle (I/R + vehicle, n = 49) 30 min before reperfusion. After 24 h, infarct size/area at risk was smaller in I/R + α-GC than in I/R + vehicle (37.8 ± 2.7% vs. 47.1 ± 2.5%, P< 0.05), with no significant changes in area at risk. The numbers of infiltrating myeloperoxidase- and CD3-positive cells were lower in I/R + α-GC. Apoptosis evaluated by TUNEL staining and caspase-3 protein was also attenuated in I/R + α-GC. Myocardial gene expression of tumor necrosis factor-α and interleukin (IL)-1β in I/R + α-GC was lower to 46% and 80% of that in I/R + vehicle, respectively, whereas IL-10, IL-4, and interferon (IFN)-γ were higher in I/R + α-GC than I/R + vehicle by 2.0, 4.1, and 9.6 folds, respectively. The administration of anti-IL-10 receptor antibody into I/R + α-GC abolished the protective effects of α-GC on I/R injury (infarct size/area at risk: 53.1 ± 5.2% vs 37.4 ± 3.5%, P< 0.05). In contrast, anti-IL-4 and anti-IFN-γ antibodies did not exert such effects. In conclusion, activated iNKT cells by α-GC play a protective role against myocardial I/R injury through the enhanced expression of IL-10. Therapies designed to activate iNKT cells might be beneficial to protect the heart from I/R injury.

Keywords
2,3,5-triphenyltetrazolium chloride; AAR; Cytokines; I/R; IFN-γ; IL; IS; Inflammation; Invariant natural killer T cells; LV; MI; MNCs; MPO; Myocardial ischemia/reperfusion injury; NK; T cell receptor; T(H)1; T(H)2; T-helper type 1; T-helper type 2; TCR; TGF-β; TNF-α; TTC; Area at risk; iNKT; Infarct size; Interferon-γ; Interleukin; Invariant natural killer T; Ischemia/reperfusion; Left ventricle; Mononuclear cells; Myeloperoxidase; Myocardial infarction; Natural killer; qRT-PCR; Quantitative reverse transcriptase-polymerase chain reaction; Transforming growth factor-β; Tumor necrosis factor-α; α-galactosylceramide; α-GC
Design the cervical cancer detector use the artificial neural network

Af’Idah, D.I., Widianto, E.D., Setyawan, B.

Cancer is one of the contagious diseases that become a public health issue, both in the world and in Indonesia. In the world, 12% of all deaths caused by cancer and is the second killer after cardiovascular disease. Early detection using the IVA is a practical and inexpensive (only requiring acetic acid). However, the accuracy of the method is quite low, as it can not detect the stage of the cancer. While other methods have a better sensitivity than the IVA method, is a method of PAP smear. However, this method is relatively expensive, and requires an experienced pathologist-cytologist. According to the case above, Considered important to make the cancer cervics detector that is used to detect the abnormality and cervical cancer stage and consists of a digital microscope, as well as a computer application based on artificial neural network. The use of cervical cancer detector software and hardware are integrated each other. After the specifications met, the steps to design the cervical cancer detection are: Modifying a conventional microscope by adding a lens, image recording, and the lights, Programming the tools, designing computer applications, Programming features abnormality detection and staging of cancer.
Fragile X-associated tremor/ataxia syndrome (FXTAS) in grey zone carriers

Liu, Y., Winarni, T., Zhang, L., Tassone, F., Hagerman, R.

The grey zone (GZ; 45-54 CGG repeats in the FMR1 gene) is considered a normal allele; however, several studies have found a high frequency of GZ in movement disordered populations. Here, we describe neurological features of fragile X-associated tremor/ataxia syndrome (FXTAS) in two carriers of GZ alleles, although FXTAS has been defined as occurring only in premutation carriers (55-200 CGG repeats). Both patients had family members who had premutation and were diagnosed with FXTAS. The presence of relatively high GZ alleles with elevated fragile X mental retardation 1 mRNA (FMR1-mRNA) combined with a family history of FXTAS that may represent a facilitating genetic background for FXTAS are the factors that led to the presence of FXTAS in these individuals with a GZ allele. Further research into clinical involvement of GZ alleles is recommended and the definition of FXTAS may require revision.

Keywords
Ataxia; FMR1-mRNA; FXTAS; Grey zone; Premutation; Tremor
Variable loss of functional activities of androgen receptor mutants in patients with androgen insensitivity syndrome


Androgen receptor (AR) mutations in androgen insensitivity syndrome (AIS) are associated with a variety of clinical phenotypes. The aim of the present study was to compare the molecular properties and potential pathogenic nature of 8 novel and 3 recurrent AR variants with a broad variety of functional assays. Eleven AR variants (p.Cys177Gly, p.Arg609Met, p.Asp691del, p.Leu701Phe, p.Leu723Phe, p.Ser741Tyr, p.Ala766Ser, p.Arg775Leu, p.Phe814Cys, p.Lys913X, p.Ile915Thr) were analyzed for hormone binding, transcriptional activation, cofactor binding, translocation to the nucleus, nuclear dynamics, and structural conformation. Ligand-binding domain variants with low to intermediate transcriptional activation displayed aberrant Kd values for hormone binding and decreased nuclear translocation. Transcriptional activation data, FxXX-like peptide binding and DNA binding correlated well for all variants, except for p.Arg609Met, p.Leu723Phe and p.Arg775Leu, which displayed a relatively higher peptide binding activity. Variants p.Cys177Gly, p.Asp691del, p.Ala766Ser, p.Phe814Cys, and p.Ile915Thr had intermediate or wild type values in all assays and showed a predominantly nuclear localization in living cells. All transcriptionally inactive variants (p.Arg609Met, p.Leu701Phe, p.Ser741Tyr, p.Arg775Leu, p.Lys913X) were unable to bind to DNA and were associated with complete AIS. Three variants (p.Asp691del, p.Arg775Leu, p.Ile915Thr) still displayed significant functional activities in in vitro assays, although the clinical phenotype was associated with complete AIS. The data show that molecular phenotyping based on 5 different functional assays matched in most (70%) but not all cases.
Clinical experience with insulin detemir: Results from the Indonesian cohort of the international A1chieve study

Soewondo, P., Kshanti, I.A., Pramono, R.B., Langi, Y.A., Dalem-Pemayun, T.G.

Aim: To determine the safety and efficacy of insulin detemir in Indonesian patients with type 2 diabetes (T2D) as a sub-analysis of the 24-week, prospective, multinational, non-interventional A1chieve study.

Methods: This study included 477 Indonesian T2D patients starting insulin detemir at the discretion of their physicians. Safety and efficacy was measured in routine clinical practice at baseline, interim (around 12 weeks from baseline) and final (around 24 weeks from baseline) visit.

Results: At baseline the mean age, duration of diabetes and mean BMI were 55.3±8.5 years, 5.9±4.0 years and 24±3.6kg/m\(^2\), respectively. Of these patients, 78% were insulin-naive and 22% were prior insulin users. Glycaemic control was poor at baseline. After 24 weeks, significant reductions were observed in mean HbA\(_1c\) (2.2%, p < 0.001), fasting plasma glucose (90.0 mg/dL, p < 0.001) and postprandial plasma glucose (115.4 mg/dL, p < 0.001) levels, in the entire cohort. Similar significant reductions were also seen in insulin-naive patients and prior insulin users. In the entire cohort, 32.5% patients achieved HbA\(_1c\) levels <7.0% while 32.0% insulin-naive patients and 33.9% prior insulin users achieved this target after 24 weeks. No hypoglycaemic events were reported in the entire cohort. Modest increase in body weight was noted in the insulin-naive group, while mean body weight decreased in prior insulin users after 24 weeks of insulin detemir therapy.

Conclusion: This sub-analysis suggests that insulin detemir can be a safe and effective option for initiating insulin therapy in people with T2D in Indonesia.

Keywords

Insulin detemir; Indonesia; A1chieve
Clinical safety and effectiveness of biphasic insulin aspart 30 in type 2 diabetes patients switched from biphasic human insulin 30: Results from the Indonesian cohort of the A1chieve study

Soewondo, P., Lindarto, D., Wibisono, S., Renaldi, O., Dalem-Pemayun, T.G.

**Aim:** To evaluate the safety and effectiveness of biphasic insulin aspart 30 (BIAsp 30) in Indonesian type 2 diabetes patients switched from biphasic human insulin 30 (BHI 30) as a sub-analysis of the A1chieve study.

**Methods:** Clinical safety and effectiveness over 24 weeks was evaluated in Indonesian patients who switched from BHI 30 to BIAsp 30 at the discretion of their physician.

**Results:** A total of 244 patients with mean age ± SD 55.6±9.5 years, BMI 24.6±3.8kg/m², and mean diabetes duration 7.8±5.7 years were included. The mean pre-study BHI 30 dose was 0.56±0.25 IU/kg and the baseline BIAsp 30 dose was 0.60±0.26U/kg titrated up to 0.65±0.25 U/kg by Week 24. No serious adverse drug reactions were reported throughout the study. Overall hypoglycaemia decreased from 2.18 to 0.06 events/patient-year with a significant decrease in the proportion of patients affected (p < 0.0001). No nocturnal or major hypoglycaemia was reported at Week 24. HbA1c improved from 8.8±1.2% at baseline to 7.3±0.8% at Week 24. A total of 45 patients achieved HbA1c <7.0% as compared to 5 patients with HbA1c <7.0% at baseline. FPG and PPPG improved significantly after 24 weeks (p < 0.001). Quality of life was positively impacted (change in visual analogue scores, 3.0±11.6 points, p < 0.001).

**Conclusion:** Switching from BHI 30 to BIAsp 30 in this Indonesian cohort was well-tolerated and improved glycaemic control with a decreased risk of hypoglycaemia.

**Keywords**
Switch: Biphasic human insulin 30; Biphasic insulin aspart 30; Indonesia
The role of uncoupling protein 2 and 3 genes polymorphism and energy expenditure in obese Indonesian children


Aim: Uncoupling protein (UCP) genes, which may contribute to energy metabolism in mitochondria, may be involved in the pathogenesis of obesity. We analyzed the differences in energy expenditure between single nucleotide polymorphisms (SNPs) UCP3 - 55C/T , UCP3 Y210Y , and UCP2 A55V among Indonesian children.

Methods: The study included 76 schoolchildren (36 obese and 40 healthy; mean age, 12.8 years) in Semarang, Indonesia. Body composition was measured by bioelectrical impedance analysis; resting energy expenditure (REE) by indirect calorimetry; physical activity by uniaxial accelerometer; and total energy expenditure (TEE) by the equations extrapolated from REE and physical activity. UCP3-55C/T , UCP3 Y210Y , and UCP2 A55V were examined by restriction length fragment polymorphism analysis.

Results: The TEE of the subjects with the T/T genotype at UCP3-55C/T after adjusting for fat-free mass (63.2 ± 7.2 kcal/ kg/day) and T/T at UCP2 A55V (62.8 ± 5.6 kcal/kg/day) was lower than that of the subjects with the C/C and C/T genotypes (p < 0.05). The REE of the subjects with these T/T genotypes tended to be lower than that of the subjects with C/C and C/T (p = 0.05). No significant differences in REE or TEE were found between the UCP3 Y210Y genotypes.

Conclusions: The subjects with the T/T genotypes of UCP3-55C/T or UCP2 A55V had lower TEE than those with other genotypes.

Keywords
Children; Energy expenditure; Indonesia; Obesity; UCP genes
Gram-negative bacilli (GNB) cause many cases of pneumonia in Indonesia. We investigated nasopharyngeal carriage of GNB in Semarang, Indonesia. *Klebsiella pneumoniae* carriage in adults (15%) was higher than in children (7%) (P=0.004), while that of other GNB was comparable. Poor food and water hygiene are determinants of carriage of these bacteria.
A randomized double-blind, placebo-controlled trial of minocycline in children and adolescents with fragile x syndrome

Leigh MJ1, Nguyen DV, Mu Y, Winarni TI, Schneider A, Chechi T, Polussa J, Doucet P, Tassone F, Rivera SM, Hessl D, Hagerman RJ.

Objective: Minocycline rescued synaptic abnormalities and improved behavior in the fragile X mouse model. Previous open-label human studies demonstrated benefits in individuals with fragile X syndrome (FXS); however, its efficacy in patients with FXS has not been assessed in a controlled trial.

Method: Randomized, double-blind, placebo-controlled, crossover trial in individuals with FXS, aged 3.5 years to 16 years (n = 55, mean age 9.2 [SD, 3.6] years). Participants were randomized to minocycline or placebo for 3 months and then switched to the other treatment.

Results: Sixty-nine subjects were screened and 66 were randomized. Fifty-five subjects (83.3%) completed at least the first period and 48 (72.7%) completed the full trial. Intention-to-treat analysis demonstrated significantly greater improvements in one primary outcome, Clinical Global Impression Scale - Improvement after minocycline compared with placebo (2.49 ± 0.13 and 2.97 ± 0.13, respectively, p = .0173) and greater improvement in ad hoc analysis of anxiety and mood-related behaviors on the Visual Analog Scale (minocycline: 5.26 cm ± 0.46 cm, placebo: 4.05 cm ± 0.46 cm; p = .0488). Side effects were not significantly different during the minocycline and placebo treatments. No serious adverse events occurred on minocycline. Results may be potentially biased by study design weaknesses, including unblinding of subjects when they completed the study, drug-related side effects unblinding, and preliminary efficacy analysis results known to investigators.

Conclusions: Minocycline treatment for 3 months in children with FXS resulted in greater global improvement than placebo. Treatment for 3 months appears safe; however, longer trials are indicated to further assess benefits, side effects, and factors associated with a clinical response to minocycline.
Geometric survey on magnetic resonance imaging of growth hormone producing pituitary adenoma

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Apart from the radiologic features regarding size and invasiveness, we had noticed some differences in morphology among types of pituitary adenomas. We conducted this study to verify the differences in radiologic morphology between growth hormone producing pituitary adenomas (GHoma) and nonfunctioning pituitary adenomas (NFoma). Pre-surgical magnetic resonance images (MRIs) were assessed in 50 cases of GHoma and 50 cases of NFoma. Geometric parameters on MRI were set in accordance with sellar anatomy. Intensity of T1-weighted image was not different between the two groups, but hypo-intensity of T2-weighted image was more frequently seen in GHoma. Predominant inferior extension of tumor was seen mostly in GHoma (88 vs. 38 %). Extension of the tumor to the superior compartment of cavernous sinus was more frequent in NFoma. Pituitary gland was generally located superior to GHoma and postero-superior to NFoma. Growth characteristics of pituitary adenoma were confirmed to differ between GHoma and NFoma.

Keywords
MR image; Growth hormone; Pituitary adenoma; Sellar region
The fragile X-associated tremor ataxia syndrome (FXTAS) in Indonesia

Winarni TI, Mundhofir FE, Ediati A, Belladona M, Nillesen WM, Yntema HG, Hamel BC, Faradz SM, Hagerman RJ.

Fragile X-associated disorders caused by the premutation of the FMR1 gene, includes the fragile X-associated tremor/ataxia syndrome (FXTAS). FXTAS affects more than 40% of premutation males over the age of 50 and 75% over the age of 80. FMR1 molecular analysis was done using PCR and confirmed by Southern Blot. Three premutation males were diagnosed FXTAS using quantification based on the standard neurological examination. Cognitive impairment was assessed using Raven and WAIS-R test. MRI was done to identify the middle cerebellar peduncle (MCP) sign, white matter disease and/or cerebral atrophy. Three cases of FXTAS are identified, of five individuals older than 50 years in one family tree two met criteria for definite FXTAS and the third with sub-clinical symptoms, although cognitive and radiological criteria are met. These cases are the first identified FXTAS cases in rural Indonesia. In addition with lack of routine medical follow-up, complications of FXTAS, such as hypertension may go unrecognized and untreated, which may further exacerbate the central nervous system (CNS) findings of FXTAS.
Aims: Caucasian patients with disorders of sex development (DSD) are at a high risk of developing germ cell cancer (GCC). GCC is prominent in young adults in Western countries, while the incidence is significantly lower in Asia. So far, the risk of GCC in Asian DSD patients is unknown.

Methods and Results: A detailed study of gonad histology, morphology and immunohistochemistry (OCT3/4, testis-specific protein Y-encoded, VASA, SCF/ KITLG, SOX9, FOXL2) of 16 Indonesian DSD patients was undertaken. 13 cases could be analysed, including ovarian tissue (n=3), streak gonad (n=1), undifferentiated gonad (n=1) and testicular tissue (n=8), diagnosed as 46, XX (n=1), 46, XY (n=7) and sex chromosome DSD (n=5). The precursor lesion gonadoblastoma or carcinoma in situ, or GCC was diagnosed in four cases (30.8%; three 46, XY and one sex chromosome DSD). A hormone producing ovarian Leydig cell tumour was identified in a 46, XX patient, supposed to be a late onset congenital adrenal hyperplasia.

Conclusions: In spite of the significantly lower risk of GCC in the general Asian population, DSD is a dominant risk factor. The study demonstrates the power of immunohistochemical markers for (early) diagnosis. This knowledge will deepen understanding of the pathobiology of GCC and clinical handling of patients with DSD, globally.
The role of anti-dengue virus NS-1 and anti-protein disulfide isomerase antibodies on platelet aggregation in secondary dengue infection.

Rachman, A., Harahap, A.R., Widhyasih, R.M.

To observe the correlation between anti-NS-1 and anti PDI antibodies against platelets function disorder on secondary dengue infection. 50 patients with secondary DV infection according to WHO criteria were observed by a cross sectional study. Patient’s blood was collected on day 3, 5 and 7 after fever onset. Platelets aggregation test was done to prove the possibility of platelets dysfunction. Anti-NS-1 and anti-PDI antibodies were determined by solid phase ELISA. the inhibition of platelets aggregation was increased among day of observation. Means value of inhibition on day 3 is 46.6%, day 5 is 52.5% and day 7 is 56%. There is a significant difference (p<0.05) of inhibition of platelet aggregation value between days of observation. The antibodies against NS-1 DV and PDI were detected in all 50 sera with the positive rate of 90% develop NS-1 antibodies and 72% of PDI antibodies, on day 3 of symptoms. The highest OD of NS-1 antibodies is detected on the day 3 and decreased on day 7. The OD of PDI antibodies was increased on day 3 and still increasing on day 7. There is a significant correlation between anti NS-1 and PDI antibodies (r=0.386-0.490), while the differences of OD between observation days are not significant (p>0.05). the kinetics profile of NS1 and PDI antibodies responses, which were detected by the third day of symptoms. Dengue patients’ sera inhibited platelets aggregation. NS-1 antibodies and PDI antibodies might have a role on the platelets aggregation dysfunction; however, there is no correlation between them. It is possible that other mechanism involve in the inhibition of platelets aggregation.
Phenotype characterization of Beta-lactamase producing enterobacteriaceae in the intensive care unit (ICU) of Cipto Mangunkusumo Hospital in 2011.

Saharman, Y.R., Lestari, D.C.

The goal of this study is to understand the phenotype characteristic of beta-lactamase enzymes producing Enterobacteriaceae, such as ESBL, AmpC, and carbapenemase. Three different methods are performed to confirm those phenotypic characteristics, namely double disk diffusion method to confirm ESBL, AmpC disk test (cefoxitin-based) to confirm AmpC, and modified Hodge test to confirm carbapenemase. Using double disk diffusion method, we found 58.42% isolates are ESBL-producing, whereas the outcomes of AmpC disk test shows 1.98% are AmpC-producing. By conducting modified Hodge test (MHT), 27.59% isolates are confirmed as carbapenemase-producing bacteria. This study confirmed the prevalence of beta-lactamase producing Klebsiella pneumoniae is very high. Nevertheless, AmpC and carbapenemase should not be ignored despite their low prevalence.

Keywords
Enterobacteriaceae; Antibiotic resistance; ESBL; AmpC; Carbapenemase
Background: Several studies have shown that lipid-lowering therapy to address hypercholesterolemia is generally inadequate because the target cholesterol goal is not achieved. Our study reviews the cholesterol goal attainment among patients receiving lipid lowering therapy in Indonesian hypercholesterolemic patients.

Methods: This survey was part of the Pan-Asian CEPHEUS (CEntralized Pan-Asian survey on tHE Under-treatment of hypercholeSterolemia) study, involving hypercholesterolemic patients 18 years of age, who were on lipid lowering treatment for 3 months. Lipid concentrations were measured, demographic and other clinically relevant information were collected. Definitions and criteria set by the updated 2004 National Cholesterol Education Program - Adult Treatment Program III was applied.

Results: In this survey, 149 physicians enrolled 979 patients, of whom only 834 were included in the final analysis. The mean age was 56.5 years, 53.5% male, and 82.3% were on statin monotherapy. The LDL-C goal attainment rate amongst Indonesians (31.3%) was below that of the overall Asian rate (49.1%). The lowest attainment (12.1%) was found in patients with a therapeutic target < 70mg/dL. Additionally, the goal attainment rate in patients with metabolic syndrome (28%) was significantly lower than in patients without metabolic syndrome (37.5%, p = 0.006). Goal attainment was inversely related to cardiovascular risk and baseline LDL-C (p < 0.001). It was also noted that approximately 65.1% of patients believed he/she could miss a dosage without affecting his/her blood cholesterol concentration.

Conclusions: High proportions of Indonesian hypercholesterolemic patients on lipid-lowering drug are not at the recommended LDL-C levels, and remain at risk for cardiovascular disease.
Hepatitis B virus (HBV) reactivation after chemotherapy or immunosuppressive therapy is a serious cause of liver-related morbidity and mortality. The mechanism of HBV reactivation is still unclear, but it is believed due to the suppression of immune response hence increasing the viral load. No uniform diagnostic criteria are available, HBV reactivation can be confirmed by an increase in serum HBV-DNA level. There are many consensus regarding this issue, including the type and duration of nucleoside analogue therapy which need to be understood as not all chronic hepatitis B patients will lead to HBV reactivation. Recently, there has been an increased awareness of reactivation of occult hepatitis B virus, especially in hepatitis B virus endemic area, including Indonesia as part of Asia Pacific region. Preemptive antiviral therapy was the best approach to prevent the HBV reactivation.

**Keywords**

Hepatitis B virus reactivation; Chemotherapy; Immunosuppressive
Hypertensive crises in the adolescent: evaluation of suspected renovascular hypertension.

Wijaya, I., Siregar, P.

Hypertensive crises can be divided into two categories as hypertensive emergency and hypertensive urgency. Most authorities have defined hypertensive emergency as a situation that requires immediate reduction in blood pressure (BP) with parenteral agents because of acute or progressive target organ damage, whereas hypertensive urgency is a situation with markedly elevated BP but without severe symptoms or progressive target organ damage, wherein the BP should be reduced within hours, often with oral agents. Adolescent with hypertension should be suspected of having renovascular hypertension in spite of other causes. This case is presenting a 16-year-old boy with hypertensive crises due to suspected renovascular hypertension. His blood pressure was 240/120 at admission with hypertensive retinopathy grade III and there was increase in creatinine after administering ACE-inhibitor but his renal arteriography revealed normal, other physical examination and laboratory findings was normal. Regarding these findings, the conclusion was this patient got essential hypertension. As many hypertensive crises occur in any ages, clinicians should aware the possibility of renovascular hypertension in young patients with hypertensive crises. An early detection and urgent treatment are needed to prevent the implication of progressive target organ damage.

Keywords
Hypertensive crises; Adolescent
Zinc combined with vitamin A reduces upper respiratory tract infection morbidity in a randomised trial in preschool children in Indonesia

Kartasurya, M.I., Ahmed, F., Subagio, H.W., Rahfiludin, M.Z., Marks, G.C.

Zn supplementation has shown inconsistent effects on respiratory morbidity in young children in developing countries. Few studies have focused on upper respiratory tract infection (URTI), a frequent cause of morbidity in this group, and potential benefit from Zn supplementation or factors that influence its efficacy. We investigated the effects of Zn supplementation on URTI before and after vitamin A supplementation. This randomised double-blinded controlled Zn supplementation study was conducted on 826 children aged 2-5 years. Placebo or Zn (10 mg/d) was given in syrup daily for 4 months, with 200 000 IU vitamin A (60 mg retinol) given to all children at 2 months. Health workers visited children every 3 d for compliance and morbidity information. We found that 84 % of children experienced URTI during the study. Zn supplementation reduced the percentage of days with URTI (12 % reduction; P = 0.09), with greater impact following vitamin A supplementation (20 % reduction; P = 0.01). Vitamin A supplementation was associated with a decreased number but an increased duration of URTI episodes. We conclude that Zn combined with vitamin A supplementation significantly reduced the percentage of days with URTI in a population of preschool Indonesian children with marginal nutritional status. The results suggest that vitamin A status modifies the efficacy of Zn supplementation on URTI.
Monosomy 9pter and trisomy 9q34.11qter in two sisters due to a maternal pericentric inversion

Mundhofir FE1, Smeets D, Nillesen W, Winarni TI, Yntema HG, de Leeuw N, Hamel BC, Faradz SM, van Bon BW.

Pericentric inversions of chromosome 9 leading to unbalanced live-born offspring are relatively rare and so far only four cases have been reported. Here we present two sisters with an unbalanced recombinant chromosome 9 which resulted from a large maternal pericentric inversion inv(9)(p24.3q34.1). Further molecular characterisation of the aberrant chromosome 9 by 250k SNP array analysis showed a terminal 460 kb loss of 9p24.3 and a terminal 8.9 Mb gain of 9q34.11. We compared the clinical features of these two patients with the previous reported four cases as well as with patients with similar sized 9pter deletions or 9qter duplications. Based upon this study, we suggest that the recombinant chromosome 9 phenotype is mainly the result of duplication of a 3.4 Mb region of chromosome 9q34.11q34.13.
Electrophysiological properties of prion-positive cardiac progenitors derived from murine embryonic stem cells


Background

The prion protein (PrP) has been reported to serve as a surface maker for isolation of cardiomyo-genic progenitors from murine embryonic stem (ES) cells. Although PrP-positive cells exhibited automaticity, their electrophysiological characteristics remain unresolved. The aim of the present study was therefore to investigate the electrophysiological properties of PrP-positive cells in comparison with those of HCN4p- or Nkx2.5-positive cells.

Methods and Results

Differentiation of AB1, HCN5p-EGFP and hcgp7 ES cells into cardiac progenitors was induced by embryoid body (EB) formation. EBs were dissociated and cells expressing PrP, HCN4-EGFP and/or Nkx2.5-GFP were collected via flow cytometry. Sorted cells were subjected to reverse transcriptase-polymerase chain reaction, immunostaining and patch-clamp experiments. PrP-positive cells expressed mRNA of undifferentiation markers, first and second heart field markers, and cardiac-specific genes and ion channels, indicating their commitment to cardiomyogenic progenitors. PrP-positive cells with automaticity showed positive and negative chronotropic responses to isoproterenol and carbamylcholine, respectively. Hyperpolarization-activated cation current (If) was barely detectable, whereas Na\(^{+}\) and L-type Ca\(^{2+}\) channel currents were frequently observed. Their spontaneous activity was slowed by inhibition of sarcoplasmic reticulum Ca\(^{2+}\) uptake and release but not by blocking If. The maximum diastolic potential of their spontaneous firings was more depolarized than that of Nkx2.5-GFP-positive cells.

Conclusions

PrP-positive cells contained cardiac progenitors that separated from the lineage of sinoatrial node cells. PrP can be used as a marker to enrich nascent cardiac progenitors.
Imbalance of angiopoietin-1 and angiopoietin-2 in severe dengue and relationship with thrombocytopenia, endothelial activation, and vascular stability


The pathogenesis of plasma leakage during dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) is largely unknown. Angiopoietins are key regulators of vascular integrity: Angiopoietin-1 is stored in platelets and maintains vascular integrity, and endothelium-derived angiopoietin-2 promotes vascular leakage. We determined angiopoietin-1 and angiopoietin-2 levels in a cohort of children in Indonesia with DHF/DSS and related them to plasma leakage markers. Patients with DHF/DSS had reduced angiopoietin-1 and increased angiopoietin-2 plasma levels on the day of admission when compared with levels at discharge and in healthy controls. There was an inverse correlation between angiopoietin-1 and markers of plasma leakage and a positive correlation between angiopoietin-2 and markers of plasma leakage. Angiopoietin-1 levels followed the same trend as the soluble platelet activation marker P-selectin and correlated with platelet counts. Dengue-associated thrombocytopenia and endothelial activation are associated with an imbalance in angiopoietin-2: angiopoietin-1 plasma levels. This imbalance may contribute to the transient plasma leakage in DHF/DSS.
Identification of a novel nonsense mutation in RP1 that causes autosomal recessive retinitis pigmentosa in an Indonesian family


**Purpose:** The purpose of this study was to identify the underlying molecular genetic defect in an Indonesian family with three affected individuals who had received a diagnosis of retinitis pigmentosa (RP).

**Methods:** Clinical evaluation of the family members included measuring visual acuity and fundoscopy, and assessing visual field and color vision. Genomic DNA of the three affected individuals was analyzed with Illumina 700k single nucleotide polymorphism (SNP) arrays, and homozygous regions were identified using PLINK software. Mutation analysis was performed with sequence analysis of the retinitis pigmentosa 1 (RP1) gene that resided in one of the homozygous regions. The frequency of the identified mutation in the Indonesian population was determined with TaqI restriction fragment length polymorphism analysis.

**Results:** A novel homozygous nonsense mutation in exon 4 of the RP1 gene, c.1012C>T (p.R338*), was identified in the proband and her two affected sisters. Unaffected family members either carried two wild-type alleles or were heterozygous carriers of the mutation. The mutation was not present in 184 Indonesian control samples.

**Conclusions:** Most of the previously reported RP1 mutations are inherited in an autosomal dominant mode, and appear to cluster in exon 4. Here, we identified a novel homozygous p.R338* mutation in exon 4 of RP1, and speculate on the mutational mechanisms of different RP1 mutations underlying dominant and recessive RP.
Effect of *Staphylococcus aureus* and *Staphylococcus epidermidis* debris and supernatant on bone marrow stromal cells growth.

Rahyussalim, Andriansjah, Kusnadi, Y., Ismail, H., Lubis, A., Kurniawati, T., Merlina, M.

The goal of this study is to observe the effect of SA and SE debris and supernatant on BMSCs growth. SA and SE were isolated and cultured from lesion materials of spondylitis patients which were determined by gram staining and biochemical tests. BMSCs were cultured and incubated for 11 days to be further sub-cultured and tripinisized for cell counting before seeded. 0.1 mg/ml SA and SE debris and supernatant were added into the BMSCs culture media. Cell counting was performed 2, 5, 7, and 9 days after debris and supernatant addition to get the growth profile of BMSCs. debris and supernatant decreases BMSCS number at initial day. At day 5, BMSCs in the group debris were growing down, mean while BMSCs in the group supernatant were able to retain the cell number. Viability of all groups was more than 80%. both debris and supernatant from SA and SE have inhibitory effect of the growth BMSCs in the initial day. BMSCs could provide barrier to survive from the debris and supernatant environment of both bacteria in day five. BMSCs can use supernatant to retain the growth to replace the lack of nutrition.

**Keywords**

*Staphylococcus aureus; Staphylococcus epidermidis; Debris; Supernatant; Bone marrow stromal cells*
To evaluate endoscopic retrograde cholangiopancreatography (ERCP) benefits in treating patients with clinical appearance of yellowish discoloration, a descriptive retrospective cross-sectional study was performed on 122 patients at Cipto Mangunkusumo Hospital from January 2008 to December 2010. The main complained was yellowish discoloration of the skin. ERCPs were performed as appropriate, and then the distribution of disease entity, results of procedure and complications were noted. Subjects of this study consist of 63 males (52%) and 59 females (48%), 7 patients have undergone ERCP 2 times. Data showed 63 cases (51%) were indicated by stone and 52 cases (43%) by tumor/mass and 7 cases by infection (6%). Ten out of 122 cases (7%) showed normal results. Difficult cannulation was encountered in 23 cases (18%) as access to the CBD could not be obtained. From 53 cases with stone, the extraction was successful in 43 (81%) including while 12 procedures with high grade of difficult ERCP left stone remnants (23%), and the remaining 10 procedures entailed stones retention (19%). Radioopaque stones found in 2 cases (4%) and radiolucent in 51 cases (96%). Stent placement was done in CBD (30 cases, 83%), pancreatic duct (4 cases, 11%), and extraneous CBD (2 cases, 5%). Complications found 3 cases (2%) migration stent outside CBD in 2 cases, 1 case with crand radiolucentin 51 acked basket. ERCP procedure is really helpful in assisting clinicians to diagnose and manage therapeutic measures, especially in pancreaticobilliar tract disorder, while performing stone extraction and stent placement.
Diagnostic approach and management of acute abdominal pain.

Abdullah, M., Firmansyah, M.A.

The incidence of acute abdominal pain ranges between 5-10% of all visits at emergency department. Abdominal emergencies of hospital visits may include surgical and non-surgical emergencies. The most common causes of acute abdomen are appendicitis, biliary colic, cholecystitis, diverticulitis, bowel obstruction, visceral perforation, pancreatitis, peritonitis, salpingitis, mesenteric adenitis and renal colic. Good skills in early diagnosis require a sound knowledge of basic anatomy and physiology of gastrointestinal tract, which are reflected during history taking and particularly, physical examination of the abdomen. Advanced diagnostic approaches such as radiography and endoscopy enhance the treatment for acute abdomen including pharmacological and surgical treatment. Therapeutic endoscopy, interventional radiology treatment and therapy using adult laparoscopy are the common modalities for treating patients with acute abdomen.

Keywords
Abdominal pain; Acute abdomen; History taking; Abdominal physical examination
Immune-mediated disorders among women carriers of fragile X premutation alleles


The relative risk of immune-mediated disorders (IMDs) among women carriers of premutation alleles is estimated by a survey for IMDs among 344 carrier women (age 19-81 years; mean 46.35 and SD 12.60) and 72 controls (age 18-87 years; mean 52.40 and SD 15.40). One hundred fifty four (44.77%) women carrier had at least one IMD, as did 20 controls (27.78%). Among women carriers, autoimmune thyroid disorder was the most common (24.4%), then fibromyalgia (10.2%), irritable bowel syndrome (IBS; 9.9%), Raynaud’s phenomenon (7.6%), rheumatoid arthritis (RA; 3.8%), Sjögren syndrome (2.6%), systemic lupus erythematosus (SLE; 2.03%), multiple sclerosis (1.74%). Of 55 carriers age 40 or older with FXTAS, 72.73% had at least one IMD, compared to 46.54% of those without FXTAS (n=159), and 31.58% of controls (n=57). The estimated odds ratio (OR) for IMD is 2.6 (95% CI 1.2-5.6, P=0.015) for women with FXTAS relative to those without FXTAS; the likelihood of IMD in carriers without or with FXTAS was also significantly higher than for controls (OR 2.1, 95% CI 1.1-4.2, P=0.034; OR 5.5, 95% CI 2.4-12.5, P<0.001, respectively). Similarly, the odds of having an IMD among carriers with FXPOI is about 2.4 times higher when compared to carriers without FXPOI (95% CI 1.1-5.0; P=0.021). The likelihood of IMD in carriers with or without FXPOI is greater (OR 2.4, 95% CI 1.1-5.0; P=0.021) compared to that of controls.
Incidence and outcome of prenatally diagnosed, chromosomally normal congenital heart defects in Singapore

Dhanardhono, T., Thia, E., Wei, X., Saktini, F., Dewi, P.K., Yeo, G.S.H.

Introduction Congenital heart defect (CHD) is a significant cause of neonatal and infant mortality. We aimed to evaluate the incidence and pregnancy outcome of foetuses diagnosed with chromosomally normal CHD in KK Women’s and Children’s Hospital (KKH), Singapore, in 2008-2009.

Methods We reviewed the medical records of pregnant women who underwent first trimester screening and were diagnosed with foetal CHD at KKH. Additional information was obtained from the Birth Defect Registry for the period 2008-2009. Foetuses with abnormal karyotype or minor lesions not expected to be detected by ultrasonography were excluded.

Results 38 out of 9,834 euploid foetuses were diagnosed with CHD. Major defects were found in 26 (68%) foetuses, while 12 (32%) had minor CHDs. Tetralogy of Fallot, atrioventricular septal defect, hypoplastic left heart syndrome, transposition of the great arteries and ventricular septal defect constituted the five most common major CHDs observed. In 14 (54%) foetuses with prenatally diagnosed major CHD, the outcome was termination of pregnancy, while 12 (46%) pregnancies continued to birth. Among the live-born babies with major CHD, eight (67%) underwent surgery.

Conclusion The incidence of non-chromosomal major CHD in Singapore was about 2.6 per 1,000 foetuses. A detection rate of 88.5% was achieved for major CHD during the study period. Advances in CHD management have thrown up new challenges for clinicians in the area of diagnosis, treatment and ethics. Therefore, it may be beneficial to constitute a regulatory entity as a fundamental guide to improve the future management of foetuses diagnosed with CHD.
Activation of natural killer T cells ameliorates postinfarct cardiac remodeling and failure in mice


Rationale

Chronic inflammation in the myocardium is involved in the development of left ventricular (LV) remodeling and failure after myocardial infarction (MI). Invariant natural killer T (iNKT) cells have been shown to produce inflammatory cytokines and orchestrate tissue inflammation. However, no previous studies have determined the pathophysiological role of iNKT cells in post-MI LV remodeling.

Objective

The purpose of this study was to examine whether the activation of iNKT cells might affect the development of LV remodeling and failure.

Methods And Results

After creation of MI, mice received the injection of either α-galactosylceramide (αGC; n=27), the activator of iNKT cells, or phosphate-buffered saline (n=31) 1 and 4 days after surgery, and were followed during 28 days. Survival rate was significantly higher in MI+αGC than MI+PBS (59% versus 32%, P<0.05). LV cavity dilatation and dysfunction were significantly attenuated in MI+αGC, despite comparable infarct size, accompanied by a decrease in myocyte hypertrophy, interstitial fibrosis, and apoptosis. The infiltration of iNKT cells were increased during early phase in noninfarcted LV from MI and αGC further enhanced them. It also enhanced LV interleukin (IL)-10 gene expression at 7 days, which persisted until 28 days. Anti-IL-10 receptor antibody abrogated these protective effects of αGC on MI remodeling. The administration of αGC into iNKT cell-deficient Jα18 (-/-) mice had no such effects, suggesting that αGC was a specific activator of iNKT cells.

Conclusions

iNKT cells play a protective role against post-MI LV remodeling and failure through the enhanced expression of cardioprotective cytokines such as IL-10.
Background

The mode of death has not been investigated in the registry data of patients with heart failure and reduced ejection fraction (HFREF) vs. preserved ejection fraction (HFPEF). The aim of the present study was therefore to carry out this comparison.

Methods and Results

The Japanese Cardiac Registry of Heart Failure in Cardiology (JCARE-CARD) prospectively studied the characteristics and treatments in a broad sample of 2,675 patients hospitalized with worsening HF, and followed them for an average of 2.1 years. This study included 323 patients in whom information on both the mode of death and left ventricular EF on echocardiography could be obtained. The mode of death was cardiovascular (CV) in 63% (including 17% sudden, 36% HF, 3% myocardial infarction, and 3% stroke), non-CV in 23%, and unknown in 14%. The prevalence of CV death including sudden death was high in patients with HFREF compared to HFPEF (68% vs. 58%, P=0.020). HF death, the most common mode of death, was similar between groups (37% vs. 35%, P=0.694). In contrast, non-CV mortality was significantly higher in HFPEF than those with HFREF (28% vs. 18%, P=0.021).

Conclusions

In 60-70% of deaths the mode was CV, and HF death was the most common mode of death in either HFREF or HFPEF. The prevalence of sudden death was lower, and that of non-CV death higher, in HFPEF compared with HFREF.
Genetic factors play a significant role in the etiology of intellectual disability (ID). The goal of this study was to identify microscopically visible chromosomal abnormalities in an Indonesian ID population and to determine their frequency, pattern, and clinical features. A total of 527 intellectually disabled individuals from special schools and institutions in 4 different areas on Java Island, Indonesia, were screened for cytogenetic abnormalities. Additional analyses were carried out for verification or further characterization by using fluorescence in situ hybridization, multiplex ligation-dependent probe amplification, or analysis of the FMR1 promoter CGG(n) repeat. Of the 527 individuals with ID, chromosomal abnormalities were found in 87 (16.5%). Trisomy 21 was the major chromosomal abnormality, identified in 74 patients (14%). Other chromosome abnormalities included 8 X-chromosomal and 5 autosomal aberrations. Details on chromosome aberrations and confirmation analyses are discussed. This study shows that chromosomal abnormalities are an important cause of ID in Indonesia. Cytogenetic analysis is important for an adequate diagnosis in patients and subsequent genetic counseling for their families, especially in developing countries with such as Indonesia.
Severe dengue is associated with consumption of von Willebrand factor and its cleaving enzyme ADAMTS-13


**Background:** Thrombocytopenia, bleeding and plasma leakage are cardinal features of severe dengue. Endothelial cell activation with exocytosis of Weibel-Palade bodies (WPBs) may play an etiological role in this condition.

**Methods and Principal Findings:** In a cohort of 73 Indonesian children with dengue hemorrhagic fever (DHF), of which 30 with dengue shock syndrome (DSS), we measured plasma levels of the WPB constituents von Willebrand factor antigen (VWF:Ag), VWF propeptide and osteoprotegerin (OPG), together with activity levels of the VWF-cleaving enzyme ADAMTS-13 and the amount of VWF in a platelet binding conformation (VWF activation factor). Compared with healthy controls (n = 17), children with DHF/DSS had significantly higher levels of VWF:Ag, VWF propeptide and OPG and decreased ADAMTS-13 activity. The VWF activation factor was also significantly higher in DHF/DSS and highest in children who died. There were significant differences in the kinetics of the various WPB constituents: VWF propeptide and OPG levels decreased toward discharge, while VWF:Ag levels were lower than expected at enrollment with plasma levels increasing toward discharge. Moreover, VWF propeptide levels correlated better with markers of disease severity (platelet count, liver enzymes, serum albumin and pleural effusion index) than corresponding VWF levels. Together, these findings suggest that there is consumption of VWF in DHF/DSS. In 4 out of 15 selected children with low ADAMTS-13 levels on admission, we found a remarkable reduction in the large and intermediate VWF multimers in the discharge blood samples, consistent with an acquired von Willebrand disease.

**Conclusion:** These findings suggest that severe dengue is associated with exocytosis of WPBs with increased circulating levels of VWF:Ag, VWF propeptide and OPG. High circulating levels of VWF in its active conformation, together with low ADAMTS-13 activity levels, are likely to contribute to the thrombocytopenia and complications of dengue. During the convalescence phase, qualitative defects in VWF with loss of larger VWF multimers may develop.
Coronary artery disease (CAD) remains the leading cause of cardiovascular death. The CAD risk factors dyslipidemia, hypertriglyceridemia, and diabetes are related to dietary intake and their metabolism. However, the association between carbohydrate, lipid, and protein components of dietary intake and the significant CAD remains elusive; and it never been reported among Asian population. The purpose of this study was to identify the risk factor profile of significant CAD of young Indonesian patients and to compare those components of dietary intake in those patients with and without significant CAD. Within the framework of this Cardiometabolic Investigation study, a case/control group was established comprising 22 patients with significant CAD (case group) and 14 patients without or non-significant CAD (control group) aged ≤50 years all of whom were admitted to the Dr. Kariadi Hospital. The multivariate analysis of the risk factors for significant CAD were energy intake >1750 kcal/day (OR=14.4; p=0.005) and smoking habit (OR=7.7; p=0.036). The energy intake of the patients with significant CAD was significantly higher than that of the control (2005.25±85.91 vs. 1695.56±128.19 kcal/day; p=0.003). While the lipid and protein component of the energy intake did not vary significantly between those two groups, the carbohydrate intake in the significant CAD group was significantly higher than that of the control group (1142.99±38.11 vs. 950.00±75.88 kcal/day; p=0.018). Conclusion: In addition to the smoking habit, a high carbohydrate intake could pose a risk factor for the significant CAD in young Indonesian patients.

Keywords
Carbohydrate; Coronary artery disease; Young Indonesian patients
Association of TSH receptor antibody, thyroid stimulating antibody, and thyroid blocking antibody with clinical activity score and degree of severity of Graves ophthalmopathy.

Subekti, I., Boedisantoso, A., Moeloek, N.D., Waspadji, S., Mansyur, M.

To evaluate the association between TSH receptor antibody (TRAb), thyroid stimulating antibody (TSAb), and thyroid stimulation blocking antibody (TBAb) and TSAb/TBAb ratio with clinical activity score (CAS) and degree of severity of GO, this was a cross sectional study involving 75 consecutive Graves’ disease patients admitted at Cipto Mangunkusumo hospital between December 2009 until January 2011. Bartley criteria were used as clinical criteria for GO. In addition to clinical criteria, orbital CT scan and measurement of extraocular muscle thickness and increment of retroorbital fat volume were carried out. Furthermore, TSH, FT4, FT3 and TRAb were measured using ELISA method, TSAb and TBAb using RIA method. Clinical activity of GO was measured using clinical activity score (CAS). Degree of severity of GO was measured using Eckstein modified NOSPECS system. subjects consisted of various different ethnic groups in Indonesia, with the range of age between 20-63 years old. There were 28 (37%) and 61 (83.6%) GO subjects with clinical-based and CT scan-based respectively. Among all GD subjects, the proportion of TSAb were 70 (93.3%) and TBAb were 13 (17.3%). There was no correlation between TRAb and CAS nor the severity of GO, either clinical-based and CT scan-based GO. There was also no correlation between TSAb and CAS. No correlation between TSAb and severity of CT scan-based GO, but significant correlation between TSAb and severity of clinical-based GO (r=0.274; p=0.009) was noted. There was no correlation between TBAb and severity of GO. We also found no correlation between TBAb and CAS of clinical-based GO, but we found strong negative correlation with CAS CT scan-based GO (r=-0.565; p=0.035). The TSAb/TBAb ratio was also strongly correlated with all parameters evaluated, CAS of clinical-based GO (r=0.730; p=0.031), CAS of CT scan-based GO (r=0.607; p=0.024), degree of severity of clinical-based GO (r=0.563; p=0.023), and degree of severity of CT scan-based GO (r=0.762; p=0.001). TRAb was not correlated with CAS and degree of severity of clinical-based and CT scan-based GO, while TSAb was correlated with degree of severity of GO. There was negative correlation between TBAb and CAS of clinical-based GO, whereas TSAb/TBAb ratio was correlated with CAS and degree of severity of both clinical-based and CT scan-based GO.

Keywords
Clinical activity score (CAS); Graves’ ophthalmopathy; TBAb; TRAb; TSAb
Faecal carriage of extended-spectrum β-lactamase-producing Enterobacteriaceae among humans in Java, Indonesia, in 2001-2002


Objective: To characterise commensal Escherichia coli and other Enterobacteriaceae with reduced susceptibility to cefotaxime that were collected in a large survey carried out among 3995 patients and healthy persons in two urban regions on Java, Indonesia, in 2001-2002.

Methods: The putative extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae were analysed using double-disk synergy tests, isoelectric focusing, PCR assays, DNA sequencing, and pulsed-field gel electrophoresis (PFGE).

Results: On the day of discharge after five or more days of hospitalisation, at least 95 of 999 (9.5%) patients carried ESBL-positive Enterobacteriaceae as dominant faecal flora. Six patients were simultaneously colonised with E. coli and Klebsiella pneumoniae isolates with ESBL activity. On admission, only 6 of 998 (0.6%) patients were colonised. Faecal carriage of ESBL-producing Enterobacteriaceae among healthy persons or persons visiting a public health centre was not detected. The 107 ESBL-positive strains included 68 E. coli, 35K. pneumoniae, and four other Enterobacteriaceae. blaCTX-M-15 was the most prevalent ESBL in both E. coli (47.1%) and K. pneumoniae (45.7%), but the E. coli O25b-ST131 clone was virtually absent. Other ESBL types found were: SHV-2, -2a, -5, -12, CTX-M-3, -9, -14, and TEM-19. PFGE revealed extensive genetic diversity among the isolates.

Conclusions: In 2001-2002, faecal carriage of ESBL-producing Enterobacteriaceae as dominant flora in Indonesia was almost exclusively hospital-associated. The presence of various blaESBL genes and the extensive genetic diversity among isolates argue against a single/dominant strain outbreak.

Keywords: Asia; Antibiotic resistance; Colonisation; ESBL; CTX-M-15
The role of ultrasonography in the management of lung and pleural diseases.

Rumende, C.M.

Ultrasonographic examination in pulmonology provides a revolutionary advance because it is very helpful in the diagnosis and management of various pleural and peripheral pulmonary defects. Lung ultrasonography allows the clinicians to diagnose some pulmonary abnormalities more rapidly, including the diagnosis of pleural effusion. Ultrasound examination also provides great assistance for the clinicians to perform invasive techniques in the field of pulmonology, which may increase the success rate and reduce the likelihood of complications. In addition to pleural effusion, other lung disorders can be diagnosed by ultrasound such as peripheral lung tumors and other pleural abnormalities caused by pleural fibrosis and tumor metastasis as well as the primary pleural tumor (mesothelioma). Ultrasound-guided invasive procedures include aspiration of minimal effusion, Transthoracal Needle Aspiration, Transthoracal biopsies and chest tube insertion. Lung ultrasound also offers other advantages, i.e. free from radiation hazards, portable, non-invasive and relatively inexpensive. Ultrasonography in the thorax also has its limitations, especially in detecting mediastinal abnormalities.

Keywords

Ultrasonography; Transducer; Lung examination; Pleural disease.
The value of fecal tumor M2 pyruvate kinase as a diagnostic tool for colorectal cancer screening.

Abdullah, M., Rani, A.A., Simadibrata, M., Fauzi, A., Syam, A.F.

To evaluate the performance of fecal tumor M2 pyruvate kinase (M2PK) as a diagnostic biomarker for colorectal cancer (CRC) screening in high-risk or symptomatic populations, consecutive patients (N=328) who were referred for elective colonoscopy were prospectively enrolled. One walnut-sized stool sample was collected from each patient for analysis of tumor M2PK content using an ELISA kit. No dietary restrictions were applied. The clinical pathologists who conducted the M2PK analyses were blinded to the patients’ confirmed diagnoses. Levels of fecal tumor M2PK were compared with histopathological results from colorectal biopsies. Of the 328 patients who underwent colonoscopy examinations, 197 (60.1%) were men and 131 (39.9%) were women. Based on histopathological examination, 83 (25.3%) patients had normal bowel histology, 42 (12.8%) patients had CRC, 67 (20.4%) patients had adenoma, 19 (5.8%) patients had inflammatory bowel disease, three (0.9%) patients had amoebic colitis, and 114 (34.8%) patients had infective colitis. The cutoff level for tumor M2PK concentration was defined as 4.00 U/mL. The sensitivity, specificity, positive predictive value, and negative predictive value of the M2PK test were 71.4%, 71.0%, 73.5%, and 94.4%, respectively. There was a significant association between CRC and fecal tumor M2PK level (P<0.001). The M2PK test detected 16 tumors among 67 (23.9%) cases of adenoma, eight tumors among 19 (42.1%) cases of inflammatory bowel disease, 35 tumors among 114 (30.7%) cases of infective colitis, and two tumors among three (66.7%) cases of amoebic colitis. The fecal tumor M2PK test has good sensitivity and specificity for CRC detection, especially in high-risk or symptomatic populations.
ACE gene polymorphism and atherosclerotic lesion of carotid artery among offsprings of type 2 diabetes mellitus.

Purnamasari, D., Widjojo, B.D., Antono, D., Syampurnawati, M.

To investigate the association among ACE gene polymorphism, serum ACE level and atherosclerotic lesion in offspring of type 2 diabetes in Jakarta, Indonesia, a cross sectional study was conducted among 73 nondiabetic and normotensive offspring of type 2 diabetes subjects. Each subject underwent medical history taking, physical examination, laboratory examination (oral glucose tolerance test, lipid profile, ace gene polymorphism, serum ace level) and atherosclerotic lesions (carotid intima media thickness or atherosclerosis plaque) examination using B-mode USG. among 73 subjects, the proportions of genotype DD, ID and II are 10, 38, and 52% respectively. There is association between ACE gene polymorphism and serum ACE level (p=0.000). Among 3 genotypes, II has the lowest value of serum ace level which is statistically significant. The prevalence of atherosclerotic lesion in this study is 45.2%. There is no correlation between ACE gene polymorphism and atherosclerotic lesion. the insertion/deletion (I/D) polymorphism of the ACE gene was associated with serum ACE level but not with atherosclerotic lesion in carotid arteries among offspring of type 2 diabetes subjects.

Keywords
ACE gene polymorphism; Serum ACE level; Atherosclerotic lesion; Offspring of type 2 diabetes
Sixteen years experience in six cases of Conn syndrome in Jakarta.

Siregar, P.

Primary hyperaldosteronism or Conn syndrome is the syndrome formed from the triad of hypertension, hypokalemia, and metabolic alkalosis. Six patients of Conn syndrome, two females (21 and 50 years) and 4 males (30, 33, 46, dan 51 years), were reported. All of the cases came with the symptoms of weakness of the lower extremities in conjunction with hypertension. The plasma aldosterone level was high with the very low plasma renin activity in all of the cases. All of the patients in this case had metabolic alkalosis. Unilateral adrenal mass was found on CT-Scan or MRI imaging. Following adrenalectomy, three patients (one female and two males) still needed one type of anti hypertension drug. All of the patients did not require anti aldosterone anymore. The plasma aldosterone returned to normal value in three patients while in three other patients were not checked. The histopathology of the adrenal revealed the adenoma of the adrenal cortex in all of the six cases.

Keywords

Hyperaldosteronism; Adrenalectomy
Hepatitis B virus (HBV) reactivation is a serious but preventable complication of immunosuppression. Chemotherapy in patients with lymphoma without specific anti-HBV prophylaxis leads to significant impairment of liver function and results in an overall liver-related mortality of greater than 5%. Prevention is a better approach than intervention at the time of reactivation. The cause of death is usually HBV-related fulminant liver failure. We reported a case of a male patient aged 42 years old who was present with acute liver failure related to chemotherapy for treatment of gastric lymphoma. He was later known as having chronic carrier hepatitis B, with high elevated transaminases and hyperbilirubinemia and signs of decompensated liver. The patient was admitted to High Care Unit for best supportive care but his condition was deteriorating and eventually died eventhough he had been already given antiviral agent.

**Keywords**

HBV reactivation; Chemotherapy; Liver failure
To find whether there is a correlation between CD4+ count and TB form in TB-HIV Cointected patients in Indonesia. this is a cross-sectional study of the TB-HIV patients at National HIV Center POKDISUS, Cipto Mangunkusumo Hospital in 2008-2011. We classified TB form as pulmonary TB, extrapulmonary TB, mililiary TB, and combination form. The data were analyzed by Spearman and lambda correlation test. We also did partial correlation test to eliminate some confounding factors, including demography and clinical characteristics, that had been determinated before. there were 122 TB-HIV patients (aged median 31 [18-34], 80% male) included in this study. The most common TB form was pulmonary TB (71.2%), then extrapulmonary TB (7.4%), the combined type (18.9%), and mililiary TB (2.5%). Median of CD4+ count was 40 cells/mL (IQR 17.5-100.6). There was a very weak correlation between CD4+ count and TB form in TB-HIV patients in Indonesia (r=0.185; p=0.042). The other factor that also showed a significant correlation to TB form is HIV staging (r=0.289; p=0.001). After adjusting those factors, we found an increase on correlation between CD4+ count and TB form (r=0.353; p=0.000). There was a correlation between CD4+ count and TB form in TB-HIV patients in Indonesia, but in a very weak correlation.

Keywords

TB-HIV coinfection; CD4+ count; TB form
The effects of oral plain kefir supplementation on proinflammatory cytokine properties of the hyperglycemia Wistar rats induced by streptozotocin.

Hadisaputro, S., Djokomoeljanto, R.R., Judiono, Soesatyo, M.H.

To validate the effect of plain kefir on immune responses of hyperglycemia wistar rats induced by Streptozotocin, the randomized pretest - posttest control group study design was conducted in male hyperglycemia Wistar rats induced by streptozotocin (STZ). Rats were randomized into four groups: (1) STZ-induced group were given insulin treatment 0.76 UI/200 g bw, (2) STZ-induced group and treated with plain kefir 3.6 cc/200 g bw/day for 30 days, (3) STZ-induced group as control, (4) normal animal group as a negative control. Blood glucose was measured from whole blood that was taken 0.1 ml from retroorbitalis vein by microhematocrit on day 1 (pretest) and day 30 (post test) by enzymatic methods. Immune responses (cytokines IL1, IL6, IL10, TNF) were measured by ELISA. Data were analyzed by one way Anova, Mann Whitney test and Duncan with significant level of p<0.05. plain kefir supplementation 3.6 cc/day affect blood glucose, proinflamatory cytokines (IL1, IL6, TNF) and antiinflamatory cytokine (IL10). Statistical analysis showed decrease of glucose -111.00±44.23 ml (p<0.001) and proinflamatory cytokines IL1 about -18.62±23.59 and IL6 -3.21±7.57 mU/mL (p<0.001), respectively compared to the control groups. TNF decreased 1.65±4.62 mU/mL, but not significant (p>0.05), except for controls group. In addition, antiinflamatory (IL10) showed also increase about 15.11±2.16 (p<0.05), except for the control. plain kefir supplementation significantly decreased blood glucose, level of cytokines (IL1, IL6) and lowered TNF level. On the contrary, the level of IL10 is increased compare to control groups.

Keywords
Probiotic; Plain kefir; Diabetes mellitus; Hyperglycemia; Free radicals; Proinflammatory cytokines
Alpha-glucosidase inhibitor activity and characterization of endophytic actinomycetes isolated from some Indonesian diabetic medicinal plants

Pujiyanto, S., Lestari, Y., Suwanto, A., Budiarti, S., Darusman, L.K.

An alpha glucosidase inhibitor is one of the compounds for the treatment of diabetes. This inhibitor can retard the liberation of glucose from dietary complex carbohydrates and delay glucose absorption, resulting in reduced postprandial plasma glucose levels and suppress postprandial hyperglycaemia. The purpose of this study was to isolate and select alpha glucosidase inhibitor-producing endophytic actinomycetes from various diabetic medicinal plants. Endophytic actinomycetes were isolated from the roots, leaves and stems of diabetic medicinal plants: Alloe vera, Tinospora crispa, Phaleria macrocarpa, Curcuma aeruginosa, Centella asiatica, Xoncus arvensis, Andrographis paniculata, Caesalpinia sappan, Curcuma xanthoriza, Parcia speciosa, Gynura procumbens, Physalis peruviana and Hibiscus sabdariffa. Sterilized plant sample were inoculated on the HV Agar medium containing 50 ppm cycloheximide and 30 ppm nalidixic acid and were incubated for 2-3 weeks at room temperature. Sixty-five isolates were obtained and tested for their ability to inhibit the alpha-glucosidase. Identification for the selected isolates was based on 16S rDNA sequences. The inhibitor activity to alpha glucosidase was determined spectrophotometrically at 400 nm using p-Nitrophenyl-alpha-D-glucopyranoside as a substrate, and acarbose as a positive control. Production of alpha-glucosidase inhibitor compounds in this plant largely related with the contribution of its actinomycetes endophytes. The results showed that endophytic actinomycetes isolated from selected antidiabetic plants produced various inhibition activities. The highest inhibition activity to alpha-glucosidase was shown by BWA65 found from Tinospora crispa. The molecular identification based on 16S rDNA gene revealed that the potential BWA65 isolate showed 92% similarity to Streptomyces olivochromogenes.

Keywords
Alpha-glucosidase inhibitor; Endophytic actinomycete; Diabetes mellitus; Indonesian medicinal plants
Identification of expanded alleles of the FMR1 gene among high-risk population in Indonesia by using blood spot screening

Winarni, T.I., Utari, A., Mundhofir, F.E.P., Tong, T., Durbin-Johnson, B., Faradz, S.M.H., Tassone, F.

The prevalence of Fragile X Syndrome (FXS) is 1 in 4000 in males and 1 in 2500 in males and females, respectively, in the general population. Several screening studies aimed at determining the prevalence of FXS have been conducted in individuals with intellectual disabilities (IDs) with a prevalence varying from 1.15% to 6.3% across different ethnic groups. A previous study in Indonesia showed an FXS prevalence of 1.9% among the ID population. A rapid, effective, and inexpensive method for FMR1 screening, using dried blood spots capable of detecting an expanded FMR1 allele in both males and females, was recently reported. We used this approach to screen 176 blood spots, collected from Central Java, Indonesia, for the presence of expanded FMR1 gene alleles. Samples were collected from high-risk populations: 112 individuals with ID, 32 obtained from individuals with diagnosis of autism spectrum disorders, and 32 individuals with a known family history of FXS. Fourteen subjects carrying an FMR1 expanded allele were identified including 7 premutations (55-200CGG repeats) and 7 full mutations (>200 repeats). Of the seven subjects identified with a full mutation, one subject was from a non-fragile X family, and six from were families with a history of FXS.
Antimicrobial resistance among pathogenic bacteria in Southeast Asia

Sri Lestari, E., Severin, J.A., Verbrugh, H.A.

Antimicrobial drug resistance is a problem in both developing and developed countries, in hospitals as well as in the community. Much data exists about antimicrobial resistance in Southeast Asia, but this information is fragmented, being published in different papers from different countries over several decades. We reviewed all available information about antimicrobial resistance in Southeast Asia using the PubMed database, concentrating on bacteria that commonly cause infection. From January 1, 1995 to January 1, 2007, 97 reports were published with accurate data regarding resistance patterns among the major pathogens. Thailand was the country where most of the published data were found. No reports were published for East Timor. From the available data, the following trends were observed: 1) there was a high prevalence of resistance to penicillin among Streptococcus pneumoniae and Neisseria gonorrhoeae; 2) pathogens causing diarrheal diseases are now often resistant to inexpensive, older antibiotics; 3) among Enterobacteriaceae and nonfermenting gram-negative bacteria, resistance to virtually all antibiotic classes has been reported, but it is unclear whether multidrug resistant gram-negative bacteria have emerged as a major problem; 4) the prevalence of methicillin-resistant Staphylococcus aureus (MRSA) is not clear; in some countries, such as Singapore, MRSA is endemic in the health care system. This review shows that antimicrobial resistance to pathogenic bacteria has been and still is on the rise in Southeast Asia. However, there is great variation in resistance by hospital, patient type and country.

Keywords
Pathogenic bacteria; Antimicrobial resistance; Southeast Asia
Influence of storage on the volatile oil content of *Curcuma* rhizome

Sukrasno, Kartika, Fidrianny, I., Elfahmi, Anam, K.

*Curcuma xanthorrhiza* is one the most important of Indonesian crude drug. Its pharmacological activities are usually associated with curcuminoid and the essential oil content. This study was aimed at studying the influence of the crude drug preparation on the content and the composition of volatile oil *Curcuma* rhizome. The bulky rhizomes were stored at room temperatures and their volatile oil contents measured. The composition of the oil was analyzed by GC-MS. The rhizomes were sliced, dried, comminuted and their oil content measured. Storage of bulky rhizome at room temperature continuously decreased the yield of volatile oil from bulky fresh rhizome. Storage did not change the number and the identity of the oil component: However, it altered their composition. Germacron, xanthorrhizol and α-curcumene increased while dipi-α-cedren decreased during storage. Upon slicing, drying under the sun, drying in an air oven, grinding and storage of the dried *Curcuma* rhizome, most of the volatile oil was still retained in the crude drug. Storage of bulky *Curcuma* rhizome continuously decreased its volatile oil content and the lost of oil reach 57% after 12 weeks. It is suggested that to assure the highest level of volatile oil content in the preparation of *Curcuma* crude drug, the rhizome should be immediately sliced and dried after harvest.

**Keywords**

*Curcuma* rhizome; Germacron; Xanthorrhizol
Application of the new classification on patients with a disorder of sex development in Indonesia


Disorder of sex development (DSD) patients in Indonesia most often do not receive a proper diagnostic evaluation and treatment. This study intended to categorize 88 Indonesian patients in accordance with the new consensus DSD algorithm. Diagnostic evaluation including clinical, hormonal, genetic, imaging, surgical, and histological parameters was performed. Fifty-three patients were raised as males, and 34 as females. Of 22 patients with 46, XX DSD, 15 had congenital adrenal hyperplasia, while in one patient, an ovarian Leydig cell tumor was found. In all 58 46, XY DSD patients, 29 were suspected of a disorder of androgen action (12 with an androgen receptor mutation), and in 9, gonadal dysgenesis was found and, in 20, severe hypospadias e.c.i. Implementation of the current consensus statement in a resource-poor environment is very difficult. The aim of the diagnostic workup in developing countries should be to end up with an evidence-based diagnosis. This is essential to improve treatment and thereby to improve the patients’ quality of life.
A novel homozygous 5bp deletion in FKBP10 causes clinically Bruck syndrome in an Indonesian patient


We report an Indonesian patient with bone fragility and congenital joint contractures. The initial diagnosis was Osteogenesis Imperfecta type III (OI type III) based on clinical and radiological findings. Because of (i) absence of COL1A1/.2 mutations, (ii) a consanguineous pedigree with a similarly affected sibling and (iii) the existence of congenital joint contractures with absence of recessive variants in PLOD2, mutation analysis was performed of the FKBP10 gene, recently associated with Bruck syndrome and/or recessive OI. A novel homozygous deletion in FKBP10 was discovered. Our report of the first Indonesian patient with clinically Bruck syndrome, confirms the role of causative recessive FKBP10 mutations in this syndrome.

Keywords
Bruck syndrome; FKBP10; Collagen type I
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Molecular genetic analysis of retinitis pigmentosa in Indonesia using genome-wide homozygosity mapping

Siemiatkowska AM; Arimadyo K; Moruz LM; Astuti GD; de Castro-Miro M; Zonneveld MN; Strom TM; de Wijs IJ; Hoefsloot LH; Faradz SM; Cremers FP; den Hollander AI; Collin RW

Purpose: Retinitis pigmentosa (RP) is a clinically and genetically heterogeneous retinal disorder. Despite tremendous knowledge about the genes involved in RP, little is known about the genetic causes of RP in Indonesia. Here, we aim to identify the molecular genetic causes underlying RP in a small cohort of Indonesian patients, using genome-wide homozygosity mapping.

Methods: DNA samples from affected and healthy individuals from 14 Indonesian families segregating autosomal recessive, X-linked, or isolated RP were collected. Homozygosity mapping was conducted using Illumina 6k or Affymetrix 5.0 single nucleotide polymorphism (SNP) arrays. Known autosomal recessive RP (arRP) genes residing in homozygous regions and X-linked RP genes were sequenced for mutations.

Results: In ten out of the 14 families, homozygous regions were identified that contained genes known to be involved in the pathogenesis of RP. Sequence analysis of these genes revealed seven novel homozygous mutations in ATP-binding cassette, sub-family A, member 4 (ABCA4), crumbs homolog 1 (CRB1), eyes shut homolog (Drosophila) (EYS), c-mer proto-oncogene tyrosine kinase (MERTK), nuclear receptor subfamily 2, group E, member 3 (NR2E3) and phosphodiesterase 6A, cGMP-specific, rod, alpha (PDE6A), all segregating in the respective families. No mutations were identified in the X-linked genes retinitis pigmentosa GTPase regulator (RPGR) and retinitis pigmentosa 2 (X-linked recessive; RP2).

Conclusions: Homozygosity mapping is a powerful tool to identify the genetic defects underlying RP in the Indonesian population. Compared to studies involving patients from other populations, the same genes appear to be implicated in the etiology of recessive RP in Indonesia, although all mutations that were discovered are novel and as such may be unique for this population.
Increase of plasminogen activator inhibitor-1 and decrease of transforming growth factor-β1 in children with dengue haemorrhagic fever in Indonesia

Djamiatun, K., Faradz, S.M.H., Setiati, T.E., Netea, M.G., van der Ven, A.J.A.M., Dolmans, W.M.V.

Mortality in children with severe dengue haemorrhagic fever (DHF) in Indonesia is high. The origin of the elevated plasminogen activator inhibitor-1 (PAI-1) levels in these children is unclear. We measured PAI-1, transforming growth factor-β1 (TGF-β1), platelet counts, plasma leakage and liver function in 71 children with DHF (3-15 years old) and in 30 healthy children. We found that PAI-1 concentrations in children with DHF were significantly higher on admission than on Day 2. Circulating TGF-β1 concentrations on admission were significantly lower in DHF than in controls, but on Day 2 increased towards levels in controls. TGF-β1 and PAI-1 concentrations were not correlated on either day. PAI-1 was correlated with platelet count and serum albumin on admission, and with degree of pleural effusion. Liver function tests were mildly elevated but not correlated with PAI-1. In conclusion, elevated PAI-1 concentrations in DHF were associated with platelet counts and plasma leakage.
Immunophenotypic patterns of childhood acute leukemias in Indonesia


**Background:** Immunophenotyping, as suggested by WHO, may improve diagnosis of childhood leukemia since it offers a better classification of the hematopoietic lineage of malignant cells as compared to morphology. Therefore, we aimed to determine the proportion of the immunophenotypic subtypes of acute leukemia in Indonesian children.

**Methods:** Samples were obtained from patients (0-14 years of age) in 4 hospitals in Indonesia. We analyzed 541 suspected leukemia samples presented over a 4-year period (March 2006 - July 2010) by flow cytometry. Immunophenotyping allowed classification into acute myeloid leukemia (AML) and ALL (B-lineage and T-lineage ALL).

**Results:** Of 541 samples, 136 were tested using a single color method and 405 with a three-color method. Concordance with morphology was very good ($\kappa=0.82$) using the three-color method with a panel of 15 monoclonal antibodies ($n=387$). A relatively high percentage of acute leukemia was classified as AML (23%). Of the ALL samples 83% were B-lineage ALL and 17% T-lineage ALL. Nine out of 239 morphological ALL were labeled AML, and 12/79 morphological AML were in fact ALL.

**Conclusion:** Immunophenotyping in a multi-center study proved feasible and appears particularly important for prognostic assessment of childhood leukemia in low income countries such as Indonesia.

**Keywords**
Childhood leukemia; AML; ALL; Immunophenotyping; Indonesia
Removal of cyanides from gadung (Dioscorea hispida Dennst.) Tuber chips using leaching and steaming techniques

Kumoro, A.C., Retnowati, D.S., Budiyati, C.S.

Gadung (Dioscorea hispida Dennst.) has been considered as one of staple foods in Indonesia. However, its high cyanides content has limited its utilisation for commercial food production. This work is aimed to investigate the removal of cyanides content from gadung tuber chips through two consecutive treatments, i.e. leaching and steaming and to propose mathematics model for the leaching process. The results showed that processing water flow rate and leaching time affected the efficiency of cyanides removal in the leaching process. The proposed mathematical model was able to represent the removal of cyanides through leaching process very well. The cyanides content removal was also found to be affected by steaming time. Best processing condition was at leaching using $5.00 \times 10^{-5} \text{m}^3\text{s}^{-1}$ for 3,600 s, followed by steaming for 3,600 s to obtain cyanides content of 29.9 mg kg$^{-1}$. While the yielded gadung tuber chips are considered as safe for consumption, further research on physicochemical characteristic of the gadung tuber flour is necessary for its utilisation consideration.

**Keywords**

Cyanogens; Dioscoreae; Leaching; Mathematics model; Steaming
Antimicrobial susceptibility of bacterial pathogens associated with community-acquired respiratory tract infections in Asia: Report from the Community-Acquired Respiratory Tract Infection Pathogen Surveillance (CARTIPS) study, 2009-2010


A multicentre resistance surveillance study [Community-Acquired Respiratory Tract Infection Pathogen Surveillance (CARTIPS)] investigating the susceptibilities of 2963 clinical isolates of Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Klebsiella pneumoniae, meticillin-susceptible Staphylococcus aureus (MSSA) and Streptococcus spp. from Asia against 12 antimicrobial agents was undertaken from 2009 to 2010. Based on the breakpoints for oral penicillin V recommended by the Clinical and Laboratory Standards Institute, the prevalence of penicillin-non-susceptible S. pneumoniae (PNSSP) ranged from 46% to 100%. Azithromycin and clarithromycin exhibited variable resistance rates of 0-88% against S. pneumoniae, 0-57% against MSSA and 0-76.5% against Streptococcus spp. isolates. The prevalence of extended-spectrum ß-lactamase-producing K. pneumoniae varied from 5.1% to 58.5%. ß-Lactamase production rates amongst H. influenzae isolates ranged from 15% to 46.6% and amongst M. catarrhalis isolates from 90% to 100%. Amongst M. catarrhalis isolates, macrolide resistance and cefaclor resistance rates of 5.8% and 1.2%, respectively, were found, mainly in Mainland China. Levofloxacin resistance rates of 0-3.9% with a MIC<sub>90</sub> (minimum inhibitory concentration causing inhibition of 90% of isolates) of 1-2 mg/L and moxifloxacin resistance rates of 0-1.7% with a MIC<sub>90</sub> of 0.125-0.5 mg/L were found amongst PNSSP isolates. Moxifloxacin was very active against Streptococcus spp., H. influenzae and M. catarrhalis isolates, with MIC<sub>90</sub> values of 0.125-0.25, 0.032-0.5 and 0.064-0.125 mg/L, respectively. These results from the CARTIPS study have confirmed some significant regional differences in the antimicrobial susceptibilities of S. pneumoniae, MSSA, K. pneumoniae, H. influenzae and Streptococcus spp. and emphasise the importance of antimicrobial surveillance programmes for guiding empirical therapy and for focusing interventional control of antimicrobial resistance in distinct geographic areas.

Keywords
Antibiotic resistance; Surveillance
Incidence and predictors for delirium in hospitalized elderly patients: a retrospective cohort study.

Isfandiay, R., Harimurti, K., Setiati, S., Roosheroe, A.G.

To determine the incidence and predictors for delirium and to develop a prediction model for delirium in hospitalized elderly patients in Indonesia, a retrospective cohort study was conducted in elderly patients (aged 60 years and older) who were hospitalized in Internal Medicine Ward and Acute Geriatric Ward Cipto Mangunkusumo Hospital from January 2008 until December 2010. Patients were not delirious on admission. Twelve predefined predictors for development of delirium during hospitalization were identified on admission. Independent predictors for delirium were identified by Cox’s proportional hazard regression analysis and each independent predictor was quantified to develop delirium prediction model. The calibration performance of the model was tested by Hosmer-Lemeshow test and its discrimination ability was determined by calculating area under the receiver operating characteristic curve (AUC).

Subjects consist of 457 patients, predominantly male (52.5%) and were in 60-69 age group (55.8%), with mean age of 69.6 (SD 7.09) years old. Delirium developed in 86 patients (cumulative incidence 18.8%, incidence density 0.021 per person-days) during first fourteen-days of hospitalization. Three independent predictors for delirium were identified, including: infection (without sepsis, adjusted HR 1.83 (95% CI 0.82-4.10); with sepsis, adjusted HR 4.86, 95% CI 2.14-11.04), cognitive impairment (adjusted HR 3.12; 95%CI 1.89-5.13) and decrease of functional status (adjusted HR 1.74; 95% CI 1.07-2.82). Predictive model was performed using the final model of multivariate analysis and stratified into three levels: low- (rate of delirium 4.4%), intermediate- (32.8%), and high-risk (54.7%) groups. The Hosmer-Lemeshow test revealed good precision (p-value 0.066) and the AUC showed good discrimination ability (0.82, 95% CI 0.78-0.88). Incidence of delirium is 18.8% in hospitalized elderly patients, with incidence density of 0.021 per person days. Infections, cognitive impairment, and decrease of functional status on admission are independent predictors for the development of delirium during hospitalization.

Keywords

Elderly; Delirium; Incidence; Prediction model
Correlation between androstenedione and 17-hydroxyprogesterone levels in the saliva and plasma of patients with congenital adrenal hyperplasia

Juniarto, A. Z.; Goossens, K.; Setyawati, B. A.; et al.

Introduction:
Congenital adrenal hyperplasia (CAH) or adrenogenital syndrome is the most common cause of female ambiguous genitalia. Management of such patients involves medical treatment using glucocorticoids such as hydrocortisone, prednisone or dexamethasone. Monitoring is done by measurement of 17-hydroxyprogesterone (17-OHP) or androstenedione in serum, plasma or saliva. The aim of this study was to develop a system of monitoring steroid treatment in CAH patients using only saliva.

Methods:
We studied the saliva of 24 CAH patients who received glucocorticoid replacement therapy. The patients were asked to collect saliva upon awakening, and in the afternoon and evening. The levels of 17-OHP and androstenedione in the saliva as well as in serum were then measured by immunoassay.

Results:
There was a significant positive correlation between 17-OHP in serum and in saliva (R equals 0.929, p-value less than 0.01). A significant positive correlation between androstenedione level in saliva and serum was also found (R equals 0.611, p-value less than 0.01). This study also revealed a significant positive correlation between androstenedione and 17-OHP in serum (R equals 0.647, p-value less than 0.01) and saliva (R equals 0.799, p-value less than 0.01). All patients showed increased level of 17-OHP and androstenedione in the sample collected upon awakening.

Conclusion:
Determination of salivary androstenedione and 17-OHP in CAH patients could be a useful alternative to the measurement of these hormones in serum.
Toll-like receptor 4 polymorphisms in dengue virus-infected children

Djamiatun, Kis; Ferwerda, Bart; Netea, Mihai G.; et al.

Differential viral recognition by cells bearing Toll-like receptor 4 (TLR4) polymorphisms Asp299Gly and Thr399Ile may influence susceptibility and severity of dengue virus infection. In central Java, Indonesia, we investigated 201 children with dengue hemorrhagic fever (DHF) and 179 healthy controls. Patients and controls were mostly ethnic Javanese. A nearly complete cosegregation of the two mutations was observed. The TLR4 299/399 genotype was found in five patients and four controls. Prevalence of the TLR4 299/399 genotype did not differ significantly between controls and DHF patients or between patients with different severities of DHF. Also, vascular leakage in patients with different TLR4 genotypes did not differ. Thus, the 299/399 TLR4 haplotype has only minor influence on susceptibility and severity of complicated dengue virus infection.
Chemical chaperone therapy: Chaperone effect on mutant enzyme and cellular pathophysiology in beta-galactosidase deficiency

Higaki, Katsumi; Li, Linjing; Bahrudin, Udin; et al.

Beta-Galactosidase deficiency is a group of lysosomal lipid storage disorders with an autosomal recessive trait. It causes two clinically different diseases, G(M1)-gangliosidosis and Morquio B disease. It is caused by heterogeneous mutations in the GLB1 gene coding for the lysosomal acid beta-galactosidase. We have previously reported the chaperone effect of N-octyl-4-epi-beta-valienamine (NOEV) on mutant beta-galactosidase proteins. In this study, we performed genotype analyses of patients with beta-galactosidase deficiency and identified 46 mutation alleles including 9 novel mutations. We then examined the NOEV effect on mutant beta-galactosidase proteins by using six strains of patient-derived skin fibroblast. We also performed mutagenesis to identify beta-galactosidase mutants that were responsive to NOEV and found that 22 out of 94 mutants were responsive. Computational structural analysis revealed the mode of interaction between human beta-galactosidase and NOEV. Moreover, we confirmed that NOEV reduced G(M1) accumulation and ameliorated the impairments of lipid trafficking and protein degradation in beta-galactosidase deficient cells. These results provided further evidence to NOEV as a promising chaperone compound for beta-galactosidase deficiency.
Prognostic of machine health estimates the remaining useful life of machine components. It deals with prediction of machine health condition based on past measured data from condition monitoring (CM). It has benefits to reduce the production downtime, spare-parts inventory, maintenance cost, and safety hazards. Many papers have reported the valuable models and methods of prognostics systems. However, it was rarely found the papers deal with censored data, which is common in machine condition monitoring practice. This work concerns with developing intelligent machine prognostics system using survival analysis and support vector machine (SVM). SA utilizes censored and uncensored data collected from CM routine and then estimates the survival probability of failure time of machine components. SVM is trained by data input from CM histories data that corresponds to target vectors of estimated survival probability. After validation process, SVM is employed to predict failure time of individual unit of machine component. Simulation and experimental bearing degradation data are employed to validate the proposed method. The result shows that the proposed method is promising to be a probability-based machine prognostics system.

Keywords
Machine prognostics; Survival probability; Support vector machine; Censored; Uncensored data
High plasma mid-regional pro-adrenomedullin levels in children with severe dengue virus infections

Michels M, Djamiatun K, Faradz SM, Koenders MM, de Mast Q, van der Ven AJ

Background:
Dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) is characterized by hemorrhage, plasma leakage and shock. Adrenomedullin and vasopressin are vaso-active hormones that mediate endothelial permeability, vascular tone and water balance and may therefore play a role during DHF/DSS. Adrenomedullin reduces endothelial permeability and has vasodilatory properties, while vasopressin is a potent vasoconstrictor with anti-diuretic effects.

Objectives:
To determine mid-regional pro-adrenomedullin (MR-proADM) and copeptin, which are reliable and stable markers for adrenomedullin and vasopressin response, respectively, and relate their plasma concentrations to outcome and markers of plasma leakage in Indonesian children with DHF and DSS.

Study design:
In this observational cohort study Indonesian children with DHF/DSS were enrolled. On study days 0 and 2, plasma MR-proADM and copeptin concentrations as well as parameters of plasma leakage were determined. Plasma MR-proADM and copeptin concentrations were compared to values of healthy controls.

Results:
MR-proADM was increased in both DHF (n = 43) and DSS (n = 28) vs. controls (n = 17), with median (IQR) values of 0.47 (0.40-0.68), 0.56 (0.44-1.00) vs. 0.22 (0.19-0.29) nmol/L, respectively. Additionally, MR-proADM correlated with signs of increased vascular leakage such as low albumin and increased pleural effusion. Copeptin concentrations showed no significant changes as compared to controls.
Conclusions:

MR-proADM concentrations are elevated in children with DHF and DSS and correlate with the severity of plasma leakage, in contrast to copeptin concentrations. We speculate that adrenomedullin has a functional role in limiting endothelial hyperpermeability during DHF/DSS. Finally, MR-proADM may be a candidate biomarker to predict development of DHF/DSS.

Keywords

Dengue hemorrhagic fever/dengue shock syndrome; Biomarkers; Adrenomedullin; Mid-regional pro-adrenomedullin; Vasopressin; Copeptin
Green building design concepts of healthcare facilities on the orthopedic hospital in the tropics

Erni Setyowati, Arnis Rochma Harani, Yasmina Nurul Falah

The issue of Global Warming is rapidly evolving, so every healthcare facility requires the Green Building Concepts. The Orthopaedic Hospital of Professor Dr. R. Soeharso is in Surakarta, Indonesia. It needs strategies on the green building concepts application. The purposes of this study are green concepts consisting of functional program, additional capacity of hospital services, and marketing strategies based on clinical approaches. Market share figures will be able to predict the number of patients coming up by the year of 2020. By this method, the researchers will be able to find out some essential facilities that should be built by the hospital.

Keywords

Green building concepts; Ortopaedic hospital; Services capacity
Suppressive chemoprophylaxis invites avoidable risk of serious illness caused by \textit{Plasmodium vivax} malaria

\textit{J. Kevin Baird}

Despite inadequacy in preventing vivax malaria after travel, suppressive chemoprophylaxis has dominated travel medicine strategy since the advent of chloroquine in 1946. The lethal threat of falciparum malaria versus the perceived benign consequence of vivax malaria underpins this strategic posture. Recent evidence demonstrating vivax malaria as often pernicious should prompt reconsideration of that posture. Causal prophylaxis kills early developing forms of plasmodia in the liver, thus preventing attacks of falciparum and vivax malaria during travel and delayed onset vivax malaria following travel. Primaquine is the only available drug for this application, and has good evidence of safety, tolerability and efficacy in non-pregnant, G6PD-normal travelers. The primaquine label, however, carries no such indication. Risk of pernicious vivax malaria from all across the endemic regions of the globe, including much of sub-Saharan Africa, should raise consideration of daily primaquine during travel as the preferred front-line option for chemoprophylaxis against malaria in travelers.
Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates


Background
Reliable estimates of populations affected by diseases are necessary to guide efficient allocation of public health resources. Sickle haemoglobin (HbS) is the most common and clinically significant haemoglobin structural variant, but no contemporary estimates exist of the global populations affected. Moreover, the precision of available national estimates of heterozygous (AS) and homozygous (SS) neonates is unknown. We aimed to provide evidence-based estimates at various scales, with uncertainty measures.

Methods
Using a database of sickle haemoglobin surveys, we created a contemporary global map of HbS allele frequency distribution within a Bayesian geostatistical model. The pairing of this map with demographic data enabled calculation of global, regional, and national estimates of the annual number of AS and SS neonates. Subnational estimates were also calculated in data-rich areas.

Findings
Our map shows subnational spatial heterogeneities and high allele frequencies across most of sub-Saharan Africa, the Middle East, and India, as well as gene flow following migrations to western Europe and the eastern coast of the Americas. Accounting for local heterogeneities and demographic factors, we estimated that the global number of neonates affected by HbS in 2010 included 5 476 000 (IQR 5 291 000–5 679 000) AS neonates and 312 000 (294 000–330 000) SS neonates. These global estimates are higher than previous conservative estimates. Important differences predicted at the national level are discussed.

Interpretation
HbS will have an increasing effect on public health systems. Our estimates can help countries and the international community gauge the need for appropriate diagnoses and genetic counselling to reduce the number of neonates affected. Similar mapping and modelling methods could be used for other inherited disorders.
The lack of a continuous culture method for Plasmodium vivax has given the impression that investigations on this important species are severely curtailed. However, the use of new or improved ex vivo methods and tools to study fresh and thawed isolates from vivax malaria patients is currently providing useful data on P. vivax, such as sensitivity to antimalarial drugs, invasion mechanisms and pathobiology. This review discusses a practical framework for conducting ex vivo studies on the asexual erythrocytic stages of P. vivax and considers the synergies between ex vivo defined phenotypes; Ex vivo derived ‘omic’ studies and in vivo clinical studies
Borobudur revisited: Soy consumption may be associated with better recall in younger, but not in older, rural Indonesian elderly

Eef Hogervorst, Fidiansjah Mursjid, Dewi Priandini, Henry Setyawan, Raden Irawati Ismael, Stephan Bandelow, Tri Budi Rahardjo

Previous reports have suggested that high frequent tofu consumption is associated with worse cognitive function in East Asian elderly. Some studies also found an increased risk of dementia with high tofu consumption in those older than 65 years of age. Tofu and other soy products, such as tempeh, contain high levels of plant estrogens or isoflavones. This study revisited a rural Central Javanese population (56–97 years of age) who were covered by the Borobudur District Health Centers. Data on cognitive performance were available for \( n = 142 \) participants. Results showed positive linear associations of weekly tofu (beta = .22, \( p < 0.05 \)) and tempeh (beta = .23, \( p < 0.01 \)) consumption with immediate recall, which were significant in those with an average age of 67 years. In those with an average age of 80 years, the earlier reported negative association of tofu with immediate recall was no longer significant. Lifestyle changes (reduction of tofu consumption after dissemination of results) or “healthy survivor effects” may have been responsible for this finding. These findings may be reminiscent of the “Window of Opportunity” theory, which suggests that estrogenic compounds can exert positive effects on verbal memory, but not in older men and women, when no or negative effects of these compounds on brain cells and cognition have been found. Long-term, placebo-controlled treatment studies should investigate whether tempeh, a fermented soybean product that also contains folate, can maintain cognitive function in middle-aged and elderly participants.
Implements in quality of life associated with insulin analogue therapies in people with type 2 diabetes: Results from the A1chieve observational study

Siddharth Shah, Alexey Zilov, Rachid Malek, Pradana Soewondo, Ole Bech, Leon Litwak

Aims
To determine the effects on quality of life after starting insulin with, or switching to, insulin analogue therapies in the 24-week, prospective, non-interventional, observational A1chieve study conducted across four continents in people with type 2 diabetes.

Methods
Health-related quality of life (HRQoL) was assessed at baseline and at 24 weeks by the validated EQ-5D questionnaire (visual analogue score [VAS] and five dimensions) in 66,726 people who had started using basal insulin detemir, mealtime insulin aspart (with or without a basal insulin) or biphasic insulin aspart 30.

Results
For the overall cohort, reported HRQoL increased significantly by 13.8 points from 63.4 points at baseline to 77.2 points at 24 weeks (p < 0.001) (scale 1–100, 100 = best health imaginable). Beginning or changing insulin was associated with a significant increase in HRQoL score (+15.0 points and +11.1 points, respectively), resulting in a similar score at 24 weeks in the two populations (77.8 and 75.9 points). Reported HRQoL also increased statistically significantly in people administering any insulin analogue regimen and across all regions, although there were some marked regional differences in reported HRQoL at baseline.

Conclusion
Compared with baseline scores, beginning insulin with, or switching to, insulin analogue therapies are associated with increased HRQoL.
Olive (Olea europaea) leaf extract effective in patients with stage-1 hypertension: Comparison with Captopril

Endang Susalit, Nafrialdi Agus, Imam Effendi, Raymond R. Tjandrawinata, Dwi Nofiariny, Tania Perrinjaquet-Moccetti, Marian Verbruggen

A double-blind, randomized, parallel and active-controlled clinical study was conducted to evaluate the anti-hypertensive effect as well as the tolerability of Olive leaf extract in comparison with Captopril in patients with stage-1 hypertension. Additionally, this study also investigated the hypolipidemic effects of Olive leaf extract in such patients. It consisted of a run-in period of 4 weeks continued subsequently by an 8-week treatment period. Olive (Olea europaea L.) leaf extract (EFLA®943) was given orally at the dose of 500 mg twice daily in a flat-dose manner throughout the 8 weeks. Captopril was given at the dosage regimen of 12.5 mg twice daily at start. After 2 weeks, if necessary, the dose of Captopril would be titrated to 25 mg twice daily, based on subject’s response to treatment. The primary efficacy endpoint was reduction in systolic blood pressure (SBP) from baseline to week-8 of treatment. The secondary efficacy endpoints were SBP as well as diastolic blood pressure (DBP) changes at every time-point evaluation and lipid profile improvement. Evaluation of BP was performed every week for 8 weeks of treatment; while of lipid profile at a 4-week interval. Mean SBP at baseline was 149.3 ± 5.58 mm Hg in Olive group and 148.4 ± 5.56 mm Hg in Captopril group; and mean DBPs were 93.9 ± 4.51 and 93.8 ± 4.88 mm Hg, respectively. After 8 weeks of treatment, both groups experienced a significant reduction of SBP as well as DBP from baseline; while such reductions were not significantly different between groups. Means of SBP reduction from baseline to the end of study were −11.5 ± 8.5 and −13.7 ± 7.6 mm Hg in Olive and Captopril groups, respectively; and those of DBP were −4.8 ± 5.5 and −6.4 ± 5.2 mm Hg, respectively. A significant reduction of triglyceride level was observed in Olive group, but not in Captopril group. In conclusion, Olive (Olea europaea) leaf extract, at the dosage regimen of 500 mg twice daily, was similarly effective in lowering systolic and diastolic blood pressures in subjects with stage-1 hypertension as Captopril, given at its effective dose of 12.5–25 mg twice daily.

Keywords

Olive leaf; Olea europaea; Oleuropein; Captopril; Hypertension; Stage-1; Blood pressure; Double-blind randomized study
Ovarian cancer identification using One-Pass clustering and k-Nearest Neighbors

Arieshanti, I., Purwananto, Y., Tjandrasa, H.

The identification of ovarian cancer using protein expression profile (SELDI-TOF-MS) is important to assists early detection of ovarian cancer. The chance to save patient’s life is greater when ovarian cancer is detected at an early stage. However, the analysis of protein expression profile is challenging because it has very high dimensional features and noisy characteristic. In order to tackle those difficulties, a novel ovarian cancer identification model is proposed in this study. The model comprises of One-Pass Clustering and k-Nearest Neighbors Classifier. With simple and efficient computation, the performance of the model achieves Accuracy about 97%. This result shows that the model is promising for Ovarian Cancer identification.

Keywords
Ovarian cancer; One-pass clustering; k-NN
Problem statement: An analysis of regression modeling which influenced by the characteristics of the region is very important. That modeling is the spatial autoregressive model. One type of spatial autoregressive model is a Spatial Durbin Model (SDM), which performs a lag effect of the dependent and independent variables. This model was developed because the dependencies in the spatial relationships doesn’t only occur in the dependent variable, but also on the independent variables. Modeling of diarrhea and the factors that influence is the case that followed this method.

Approach: This problem was solved by identification of spatial autocorrelation and modeling to get the influence factors of diarrhea. The modelings were Ordinary Least Square (OLS) and SDM. Then, it was compared between two models. This research located in Tuban Regency, East Java, Indonesia.

Results: There were a spatial autocorrelation on diarrhea and the factors variable that influence it. Furthermore, the SDM was giving better performance than OLS model. The results of SDM showed that the lag in the dependent and independent variables significantly affected. These independent variables were source of drinking water, health center and medical personnel which were significant at $\alpha = 5\%$.

Conclusion: SDM has good performance to identify influential factors of diarrhea which has spatial factors.

Keywords
Diarrhea; Spatial; Spatial durbin model
Extracting broadband tissue optics parameters from one source-detector CW diffuse optical spectroscopy

Nasution, A.

Human tissue by its nature is a kind of complex entity in structures and compositions, with their respective spectral properties. These properties make complex light-tissue interactions as the light propagates inside the tissue. Hence the information on broadband wavelength-dependency of optical parameters is important to assess the state of investigated tissue. Accurately determined tissue optics parameters (i.e. the absorption and scattering coefficients) are crucial for further derivation of many other ones related to hemodynamics states. Nowadays the Diffuse Optical Spectroscopy, which is based on spectral measurements of diffusely re-emanated of injected light source, plays an important role in many tissue diagnostics applications. Most of available extraction schemes are based on multiprobe/multidistance spectral measurements. This paper describes a novel and simple extraction scheme from only single distance of source-detector probe. The use of single pair source-detector probe will significantly reduce the complexity and cost of measurement system.

Keywords

Broadband tissue optical parameters; Diffuse optical spectroscopy; Tissue-parameters extraction-scheme; Single pair source-detector probe
Classification of hospital pharmaceutical drug inventory items by combining ABC analysis and fuzzy classification

Mahendrawathi, E.R., Nurul Laili, E., Kusumawardani, R.P.

The management of pharmaceutical inventory items in a hospital poses a unique problem. One of the most commonly used techniques in inventory management, the ABC analysis, lends simple and intuitive interpretation. However, it is based on a single quantifiable criterion, generally the annual dollar usage of the item; whereas the determination of importance of a pharmaceutical drugs item should also take into account other considerations, such as how severely its unavailability would affect patients. These other factors are often judged on the human experience, thus are hard to quantify. This paper proposes the use of the fuzzy-ABC technique, which is able to incorporate multiple factors, both quantitative and qualitative ones, into inventory management decisions in a computationally simple and easily interpretable manner. Differences observed in the results of classical ABC and fuzzy-ABC analysis clearly demonstrates that the fuzzy-ABC technique is able to better capture the intuition behind the importance of each pharmaceutical item as determined by multiple criteria beyond its dollar usage, including factors that are inexpressible as exact quantities.
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Preliminary results for hyperspectral videoendoscopy diagnostics on the phantoms of normal and abnormal tissues: Towards gastrointestinal diagnostics

Martin Hohmann, Alexandre Douplik, Janani Varadhachari, Aulia Nasution, Jonas Mudter, Markus Neurath, and Michael Schmidt

Cancer is the second most cause of death in the world after cardiovascular related disease. This paper presents the calibration and test results obtained by mean of a hyperspectral reflectance and flexible video endoscope setup. Its application field is intended to be gastrointestinal cancer detection. We fabricated hard tissue phantoms which mimic different types of tissue in terms of its reflection properties for evaluation. The reflectance properties of the phantoms are set by varying the concentration of ink or titanium oxide. The goal is to achieve a similar reflectance properties as in actual respective tissues in vivo. A modified endoscope was used to discriminate the normal and tumor tissue phantoms with reflectance measurements. This hyperspectral endoscope setup consists of a light source, a camera and a camera controller that are compatible for use with conventional video endoscopes and video monitors. This setup allows the operator to switch between conventional white light imaging mode (WLI) and hyperspectral imaging mode (HSI). A significant imaging contrast between normal and tumor tissue phantoms has been provided.
Ganoderol B: A potent alpha-glucosidase inhibitor isolated from the fruiting body of *Ganoderma lucidum*

Fatmawati, Sri; Shimizu, Kuniyoshi; Kondo, Ryuichiro

Apha-Glucosidase inhibitor has considerable potential as a diabetes mellitus type 2 drug because it prevents the digestion of carbohydrates. The search for the constituents reducing alpha-glucosidase activity led to the finding of active compounds in the fruiting body of *Ganoderma lucidum*. The CHCl₃ extract of the fruiting body of *G. lucidum* was found to show inhibitory activity on alpha-glucosidase *in vitro*. The neutral fraction, with an IC₅₀ of 88.7 µg/ml, had stronger inhibition than a positive control, acarbose, with an IC₅₀ of 336.7 µg/ml (521.5 µM). The neutral fraction was subjected to silica gel column chromatography and repeated p-HPLC to provide an active compound, (3 β,24E)-lanosta-7,9(11),24-trien-3,26-diol (ganoderol B). It was found to have high alpha-glucosidase inhibition, with an IC₅₀ of 48.5 µg/ml (119.8 µM).

**Keywords**

*Ganoderma lucidum*; [α]-Glucosidase inhibitor; Ganoderol B; Triterpenoid
Endovascular therapy for infected aortic aneurysms

Boonprasit Kritpracha, Dhanakom Premprabha, Jitpreedee Sungsiri, Wittawat Tantarattanapong, Sorracha Rookkapan, Pong Juntarapatin

Objective
To determine the outcome of endovascular therapy for an infected aortic aneurysm in patients with or without aorto-aerodigestive/aortocaval fistulas.

Methods
From September 2005 to May 2010, 21 patients, 17 abdominal and four thoracic infected aortic aneurysms were treated with an endovascular stent graft at Songklanagarind Hospital, Thailand. Five patients presented with fistula complications, 1 aortoesophageal, 1 aortobronchial, 1 aortocaval, and 2 aortoenteric fistulas. Lifelong antibiotics were planned for all patients. In-hospital mortality and follow-up outcomes were examined.

Results
The average age was 66 years (range, 42-84) and 18 patients were male. All five cases in the fistulous group presented with symptoms related to the organs involved, four massive bleedings and one congestive heart failure. Symptoms of patients in the nonfistulous group were abdominal, back, or chest pain in 94%, fever in 81%, and diarrhea in 19%. Blood culture was positive in 10 patients (48%): eight Salmonella spp and two Burkholderia pseudomallei. The overall in-hospital mortality was 19% (4/21): 60% (3/5) in the fistula group and only 6% (1/16) in the nonfistula group. One conversion to open repair was performed in the fistula group 2 weeks after the endovascular procedure. During the follow-up period, one of the two survivors in the fistula group died at 18 months from unrelated causes, while there were no deaths in the 15 patients of the nonfistula group with an average patient follow-up of 22 months (range, 1-54). Periaortic inflammation and aneurysms in the nonfistula group completely disappeared in 10 of the 15 patients (67%). The aneurysm significantly shrunk in four patients (27%), and was stable at 1 month in one patient. There were no late conversions.
Conclusion

Endovascular therapy, as a definite treatment for infected aortic aneurysms, provided excellent short- and medium-term results in patients without fistula complications. However, a poorer outcome was evident in patients with fistula complications.

Keywords

Pseudoaneurysm; Infectious aortitis; Infected aortic aneurysm; Stent graft; Endovascular; FDG/PET
Replacing the measles ten-dose vaccine presentation with the single-dose presentation in Thailand


Introduced to minimize open vial wastage, single-dose vaccine vials require more storage space and therefore may affect vaccine supply chains (i.e., the series of steps and processes involved in distributing vaccines from manufacturers to patients). We developed a computational model of Thailand’s Trang province vaccine supply chain to analyze the effects of switching from a ten-dose measles vaccine presentation to each of the following: a single-dose measles-mumps-rubella vaccine (which Thailand is currently considering) or a single-dose measles vaccine. While the Trang province vaccine supply chain would generally have enough storage and transport capacity to accommodate the switches, the added volume could push some locations’ storage and transport space utilization close to their limits. Single-dose vaccines would allow for more precise ordering and decrease open vial waste, but decrease reserves for unanticipated demand. Moreover, the added disposal and administration costs could far outweigh the costs saved from preventing open vial wastage.

Keywords
Measles vaccine; Vaccine supply chain; Single-dose
Maternal, neonatal, and child health in southeast Asia: towards greater regional collaboration

Cecilia S Acuin, Geok Lin Khor, Tippawan Liabsuetrakul, Endang L Achadi, Thein Thein Htay, Rebecca Firestone, Zulfiqar A Bhutta

Although maternal and child mortality are on the decline in southeast Asia, there are still major disparities, and greater equity is key to achieve the Millennium Development Goals. We used comparable cross-national data sources to document mortality trends from 1990 to 2008 and to assess major causes of maternal and child deaths. We present inequalities in intervention coverage by two common measures of wealth quintiles and rural or urban status. Case studies of reduction in mortality in Thailand and Indonesia indicate the varying extents of success and point to some factors that accelerate progress. We developed a Lives Saved Tool analysis for the region and for country subgroups to estimate deaths averted by cause and intervention. We identified three major patterns of maternal and child mortality reduction: early, rapid downward trends (Brunei, Singapore, Malaysia, and Thailand); initially high declines (sustained by Vietnam but faltering in the Philippines and Indonesia); and high initial rates with a downward trend (Laos, Cambodia, and Myanmar). Economic development seems to provide an important context that should be coupled with broader health-system interventions. Increasing coverage and consideration of the health-system context is needed, and regional support from the Association of Southeast Asian Nations can provide increased policy support to achieve maternal, neonatal, and child health goals.
Discriminatory attitudes toward people living with HIV among health care workers in Aceh, Indonesia: A vista from a very low HIV caseload region


Background

The aim of this study was to identify the level of discriminatory attitudes towards people living with HIV (PLHIV) among health care workers (HCWs) and the factors influencing discriminatory attitudes in very low HIV load region.

Methods

This research was conducted at seven regencies in Aceh, Indonesia. A cross-sectional study design was adopted and 589 HCWs selected purposively were included in this study. Research was conducted from October 2012 to January 2013. Correlation analysis, analysis of variance and independent sample t test analysis were used according to the type of data. Multiple linear regression models were used to identify the predictor factors.

Results

It was observed that the level of discriminatory attitudes is high. Bivariate analysis showed that regency, education, type of HCW, religion, direct contact experience with PLHIV, HIV/AIDS-related training, knowledge on transmission and prevention of HIV, value-driven stigma, overestimated risk to HIV transmission, and facility profile were significantly related to the level of discriminatory attitudes ($p < 0.05$). A multiple linear regression model identified the following correlate to discriminatory attitudes: being Muslim, low-level of knowledge on transmission and prevention of HIV, and high level of value-driven stigma and overestimated risk to HIV transmission ($R^2 = 0.205$).
Conclusions

Our study found that knowledge on transmission and prevention of HIV, value-driven stigma and overestimated risk to HIV transmission are the only significant predictors of discriminatory attitudes towards PLHIV among HCWs in Aceh. Therefore to reduce those factors, trainings on HIV-related discrimination to HCWs and clear guidelines and protocols related to PLHIV care are urgently needed.

Keywords

Discriminatory attitudes; Discrimination; PLHIV; HIV; Health care worker
5.5 Value in Health Regional Issues, In Press, Corrected Proof, Available online 10 June 2013

Revisit what is next for pharmacoeconomics and outcomes research in Asia

Hong Li, Surachat Ngorsuraches

As part of the global trend to address the constrained resources for population health care coverage, the concepts of pharmacoeconomics (PE) and health technology assessment (HTA) have been introduced to Asia in the last decade. Medicines are just one of numerous types of innovative technologies developed to address unmet medical need. Many of these medicines receive a great deal of attention because of their potential impact on limited health care budgets. There are a few key challenges for using PE and HTA in making informed decisions regarding the value of a given new health care technology in an Asian country. These challenges include 1) recognizing the multidimensional aspects of PE and HTA, which can include both health care and political considerations; 2) involving stakeholders (with a focus on patients) in decision making; 3) balancing short- and long-term overall benefits of innovative medicines; and 4) giving consideration to specific local cultural and health care characteristics.
The human population at large is exposed to many critical factors (e.g. bad food habits, chemical substances, and stress) leading to the development of serious diseases. Colon or colorectal cancer is one of the most prevalent types of cancer in many countries. Despite being a multi-factorial chronic disease, resulting from the interaction of multiple genetic and environmental factors, the critical factor is mostly a poor diet regimen. Therefore, an accumulation of constant mutations leads to a complex arrangement of events during tumor initiation, development and propagation. It is well known that many plants are rich in polyphenols with anti-oxidant, anti-atherogenic, anti-diabetic, anti-cancer, anti-viral, and anti-inflammatory properties. These compounds are secondary metabolites with the ability to donate electrons to free radicals through different mechanisms. In recent years, a large number of studies have attributed a protective effect to polyphenols and foods containing these compounds (e.g. plants, vegetables, cereals, tea, coffee or chocolate). Polyphenolic compounds have been described to inhibit cancer development and propagation, being used as chemopreventive agents. Some polyphenols reported a preventive action against colon cancer, e.g. curcumin, gallic acid, ellagic acid, and epigallocatechin-3-gallate. The present article focuses on the properties of these molecules as chemopreventive agents and the recent advances on their formulation in nanoparticulate systems for targeted therapy and increased bioavailability.

Keywords

Colon cancer; Ellagic acid; Curcumin; Epigallocatechin-3-gallate; Gallic acid; Nanotechnology
Anti Propionibacterium acnes activity of rhodomyrtone, an effective compound from Rhodomyrtus tomentosa (Aiton) Hassk. leaves

Jongkon Saising, Supayang Piyawan Voravuthikunchai

Propionibacterium acnes have been recognized as one of the main causative agents in pathogenesis of acne. Twenty one isolates of P. acnes isolated from acne lesions were screened for lipase and protease activity which are reported to be associated in acne and inflammation. Interestingly, all P. acnes isolates demonstrated lipase activity. Similarly, 90% of test P. acnes produced protease enzyme. Antibacterial activity of the ethanol extract of Rhodomyrtus tomentosa (Aiton) Hassk. leaves and rhodomyrtone, its principle compound were tested against P. acnes using broth macrodilution method. The MIC$_{90}$ values of the ethanol extract and rhodomyrtone were 32 and 0.5 μg/mL, respectively. The numbers of the bacterial cells were reduced at least 99% after treatment with the ethanol extract and rhodomyrtone within 72 and 24 h, respectively. Cytotoxicity test of the extract and rhodomyrtone was performed on human normal fibroblast. The IC$_{50}$ values of the ethanol extract and rhodomyrtone were 476 and more than 200 μg/mL, approximately 15 and 400 folds higher than the MIC$_{90}$ values indicating that both substances were very low cytotoxic which could be applied as topical therapeutic anti-acne agents.

Keywords

Rhodomyrtus tomentosa; Rhodomyrtone; Propionibacterium acnes; Cytotoxicity
Objective

To determine the risk factors of seizure recurrence and the most common comorbidities in elderly patients with epilepsy.

Method

We did a retrospective study of 278 patients older than 65 years with first seizure. We evaluated electrolytes, blood glucose, urea and creatinine levels, and performed electrocardiography (ECG), and routine electroencephalogram (EEG) on all patients. We evaluated seizure recurrence and comorbidities at 2 years.

Results

Univariate analysis found that significant (P < 0.05) factors affecting seizure recurrence were etiology of seizure, EEG, and status epilepticus at first presentation. In multivariate regression analysis, etiology of seizure and EEG were significant statistical factors in seizure recurrence at 2 years follow up. Age, sex, duration of time between first seizure and diagnosis of seizure, seizure type, misdiagnosis of non-epileptic seizure, and use of antiepileptic drugs were not significant factors for predicting seizure recurrence. Depression and anxiety were the most common comorbidities in our study, followed by sleep-related disorders and stroke. There were no statistically significantly differences in comorbidities between patients who remained seizure free and patients who had recurrent seizure.
Conclusion

Most of the new onset seizures in our elderly patients were focal onset. Acute symptomatic etiology, remote symptomatic etiology, progressive symptomatic etiology and abnormal EEG features were powerful predictors of seizure recurrence, and mood disorder, sleep disorder and stroke were the common comorbidities.

Keywords

Elderly; Co-morbidity; Recurrent seizure; Thailand
Safety and efficacy of everolimus with exemestane vs. exemestane alone in elderly patients with HER2-negative, hormone receptor–positive breast cancer in BOLERO-2


Background
Postmenopausal women with hormone receptor–positive (HR+) breast cancer in whom disease progresses or there is recurrence while taking a nonsteroidal aromatase inhibitor (NSAI) are usually treated with exemestane (EXE), but no single standard of care exists in this setting. The BOLERO-2 trial demonstrated that adding everolimus (EVE) to EXE improved progression-free survival (PFS) while maintaining quality of life when compared with EXE alone. Because many women with HR+ advanced breast cancer are elderly, the tolerability profile of EVE plus EXE in this population is of interest.

Patients and Methods
BOLERO-2, a phase III randomized trial, compared EVE (10 mg/d) and placebo (PBO), both plus EXE (25 mg/d), in 724 postmenopausal women with HR+ advanced breast cancer recurring/progressing after treatment with NSAI. Safety and efficacy data in elderly patients are reported at 18-month median follow-up.

Results
Baseline disease characteristics and treatment histories among the elderly subsets (≥ 65 years, n = 275; ≥ 70 years, n = 164) were generally comparable with younger patients. The addition of EVE to EXE improved PFS regardless of age (hazard ratio, 0.59 [≥ 65 years] and 0.45 [≥ 70 years]). Adverse events (AEs) of special interest (all grades) that occurred more frequently with EVE than with PBO included stomatitis, infections, rash, pneumonitis, and hyperglycemia. Elderly EVE-treated patients had similar incidences of these AEs as did younger patients but had more on-treatment deaths.
Conclusion

Adding EVE to EXE offers substantially improved PFS over EXE and was generally well tolerated in elderly patients with HR+ advanced breast cancer. Careful monitoring and appropriate dose reductions or interruptions for AE management are recommended during treatment with EVE in this patient population.

Keywords

Advanced breast cancer; Endocrine resistance; Geriatric; Progression-free survival; Safety
Emerging need to use phytopharmaceuticals in the treatment of HIV

L. Chaitra Narayan, V. Ravishankar Rai, Supinya Tewtrakul

Phytopharmaceuticals holds promise in the treatment of HIV because of its efficacy, lesser or no side effects coupled with no toxicity. Thus far, very few candidate species have been exploited for testing of anti-HIV activity. The plant kingdom being highly diverse holds many more biomolecules to be uncovered and explored for the treatment of HIV. For this, it becomes necessary to carry out extensive research and unearth new bioactive molecules. This review presents a comprehensive outlook into the presently available synthetic drugs and its vast side effects and hence, stresses on the importance of herbal therapy in the treatment regimen of HIV.

Keywords

HIV; Natural products; Phytopharmaceuticals; Herbal therapy
Kinetics of DNA load predict HPV 16 viral clearance


Introduction

While high HPV 16 viral load measured at a single time point is associated with cervical disease outcomes, few studies have assessed changes in HPV 16 viral load on viral clearance.

Objective

To measure the association between changes in HPV 16 viral load and viral clearance in a cohort of Thai women infected with HPV 16.

Study design

Fifty women (n = 50) between the ages of 18–35 years enrolled in a prospective cohort study were followed up every three months for two years. Women positive for HPV 16 DNA by multiplex TaqMan® assay at two or more study visits were selected for viral load quantitation using a type-specific TaqMan® based real-time PCR assay. The strength of the association of change in viral load between two visits and viral clearance at the subsequent visit was assessed using a GEE model for binary outcomes.

Results

At study entry, HPV 16 viral load did not vary by infection outcome. A >2 log decline in viral load across two study visits was found to be strongly associated with viral clearance (AOR: 5.5, 95% CI: 1.4–21.3). HPV 16 viral load measured at a single time point was not associated with viral clearance.
Conclusions

These results demonstrate that repeated measurement of HPV 16 viral load may be a useful predictor in determining the outcome of early endpoints of viral infection.

Keywords

HPV; DNA; Viral load; Epidemiology; Thailand
Receptor for Activated C Kinase-1 protein from *Penaeus monodon* (Pm-RACK1) participates in the shrimp antioxidant response

Netnapa Saelee, Moltira Tonganunt-Srithaworn, Warapond Wanna, Amornrat Phongdara

Cellular oxidative stress responses are caused in many ways, but especially by disease and environmental stress. After the initial burst of reactive oxygen species (ROS), the effective elimination of ROS is crucial for the survival of organisms and is mediated by antioxidant defense mechanisms. In this paper, we investigate the possible antioxidant function of *Penaeus monodon* Receptor for Activated C Kinase-1 (Pm-RACK1). When Pm-RACK1 was over-expressed in *Escherichia coli* cells or *Spodoptera frugiperda* (Sf9) insect cells exposed to H$_2$O$_2$, it significantly protected the cells from oxidative damage induced by H$_2$O$_2$. When recombinant Pm-RACK1 protein was expressed as a histidine fusion protein in *E. coli* and purified with a Ni$^{2+}$-column it possessed antioxidant functions that protected DNA from metal-catalyzed oxidation. Shrimp (*Penaeus vannamei*) held at an alkaline pH had a much higher hepatopancreatic expression of Pm-RACK1 than in those held at pH 7.4. The exposure of shrimp to alkaline pH is also known to increase ROS production. These results provide strong evidence that Pm-RACK1 can participate in the shrimp antioxidant response induced by the formation of ROS.

**Keywords**

Pm-RACK1; Antioxidant; Oxidative stress; White spot syndrome virus (WSSV); Shrimp
A survey of folk remedies for gastrointestinal tract diseases from Thailand’s three southern border provinces

Oratai Neamsuvan, Tuwaeyah Tuwaemaengae, Fatin Bensulong, Asma Asae, Kholeel Mosamae

**Ethnopharmacological relevance:**
Gastrointestinal tract diseases commonly occur in Thailand. However, surveying for finding out traditional drugs has never been done.

**Aim of study:**
To quantify and categorize the folk medicinal remedies that are used for healing the gastrointestinal tract by the traditional healers living in Thailand’s three southern border provinces.

**Materials and methods:**
The Pattani, Yala and Narathiwat provinces were selected. Semi-structured interviews of nine healers were conducted to collect information that included the remedy names, herbal ingredients, plant parts used, preparation, properties and treatment methods. The data were then further analyzed.

**Result:**
The results revealed that 39 multi-species remedies and 36 single-species remedies were used to treat gastrointestinal disorders. A total of 103 plant species and 5 other materia medica were used as therapeutics. Most of the plants used were of the Zingiberaceae, Fabaceae and Euphorbiaceae families. Furthermore, it was found that although most of the healers used different remedies for a particular disease, some of the ingredients might have been similar. For example, *Caesalpinia bonduc* (L.) Roxb. was an ingredient used for parasitic disease remedies, and *Senna alata* (L.) Roxb. was used for constipation remedies.
Conclusion:

A review of the literature revealed 57 plant species and 2 other materia medica that have already been tested for their biological activities, whereas 46 plant species and 3 materia medica have never been tested. Consequently, research should be performed to confirm the pharmacological properties of folk remedies.

Keywords

Folk remedies; Gastrointestinal tract; Thailand’s three southern border provinces
Health association of dental enamel loss with the pH and titratable acidity of beverages

Pojjanut Benjakul, Chanya Chuenarrom

Background/purpose
The purpose of this study was to evaluate how well the pH and titratable acidity (TA) of beverages can predict dental enamel erosion.

Materials and methods
The erosive potential of 16 beverages was assessed by measuring their pH and TA. Six beverages were used for training purposes to derive a prediction equation. The ten remaining beverages were set aside to test the prediction equation. Enamel samples were immersed in each beverage for 60 minutes. Enamel loss was measured before and after immersion in different beverages using a profilometer. The equation was formulated from the pH, TA, and enamel loss of the training group. The enamel loss of the test group was calculated using the prediction equation and was compared with the experimental results.

Results
Using the prediction equation \[\text{enamel loss (μm)} = 6.676 - 1.726 \text{pH} + 0.233 \text{TA}\], the difference between the calculated enamel loss and experimental enamel loss ranged 3.0–14.6% for these beverages.

Conclusions
The erosive potential of several beverages can be predicted by the pH and TA.
Deep vein thrombosis (DVT) is the third leading cause of morbidity in critically ill trauma patients but it can be prevented by performing appropriate risk assessment and preventive strategies. The purpose of this study was to evaluate the effectiveness of implementing a clinical nursing practice guideline (CNPG) for preventing DVT in critically trauma patients at Songklanagarind Hospital. The CNPG content with 37 items initially developed from evidence-based knowledge related to DVT and its prevention was validated and approved by the consensus of an expert panel. The ‘expert panel’ consisted of a clinical (critical surgical patients) nurse specialist, a trauma surgeon, a medical doctor who experts in developing CNPG, and two surgical care nurse educators. The revised 30 from 37 items were tested for reliability thereafter and yielded of 0.90 and 1.00, respectively. Forty-two nurses participated in this study. The effectiveness of this CNPG was evaluated in terms of (1) feasibility and difficulty of using the CNPG, (2) nurse’s satisfaction in implementation of CNPG, and (3) the patient’s femoral blood flow velocity before and after 7 days. Results have shown that 23 items were performed by more than 90% of nurses and there were 7 items performed at rates lower than 90%. 79% of nurses rated their satisfaction at high (M = 8.06, SD = 0.96). There were no differences in femoral venous blood flow velocity before and after 7 days and without signs of DVT. The findings indicated that the use of evidence-based clinical practice guidelines for deep vein thrombosis prevention could enhance the quality of care in terms of early detection for DVT and maintaining blood flow velocity in those patients who are at risk. Further study could be explored to confirm its effectiveness with the large sample size.

Keywords
Clinical nursing practice guideline; DVT prevention; Critically trauma patient
Cytotoxic activity of acetogenins and styryl lactones isolated from Goniothalamus undulatus Ridl. root extracts against a lung cancer cell line (COR-L23)

S. Tantithanaporn, C. Wattanapiromsakul, A. Itharat, N. Keawpradub

An investigation of the chemical constituents in a dichloromethane extract of Goniothalamus undulatus root led to the isolation of three known styryl lactones (5-acetoxyisogoniothalamin oxide, O-acetylaholactone and altholactone), and four known annonaceous acetogenins (annonacin, cis-annonacin, goniothalamicin and cis-goniothalamicin). These compounds were subjected to a sulphorhodamine B (SRB) cytotoxicity assay against human large cell lung carcinoma (COR-L23), and normal human fetal fibroblast (MRC-5), cell lines. The isolated acetogenins showed higher cytotoxic activity against COR-L23 compared to the styryl lactones, with IC<sub>50</sub> values in the range of 0.5–1.7 μM and 7.4–15.4 μM, respectively. A similar pattern of cytotoxicity was also observed against the other cell line (MRC-5); acetogenins IC50 values were in the range of 11.8–31.4 μM, and those for styryl lactones were in the range of 48.7–102.8 μM. This is the first report of a bioassay-guided isolation of chemical constituents from G. undulatus and on cytotoxic studies of the isolated compounds using these particular lung cancer cell lines.
Anthraquinone derivatives from the mangrove-derived fungus *Phomopsis* sp. PSU-MA214

Saranyoo Klaiklay, Vatcharin Rukachaisirikul, Souwalak Phongpaichit, Chaveng Pakawatchai, Saowanit Saithong, Jirayu Buatong, Sita Preedanon, Jariya Sakayaroj

One new tetrahydroanthraquinone derivative, (2R,3S)-7-ethyl-1,2,3,4-tetrahydro-2,3,8-trihydroxy-6-methoxy-3-methyl-9,10-anthracenedione (1), together with five known anthraquinones (2–6), two known phenylethyl alcohols (7–8) and one known butanamide (9), were isolated from the mangrove-derived fungus *Phomopsis* sp. PSU-MA214. Their structures were established by spectroscopic evidence. Compound 1 is a rare ethyltetrahydroanthraquinone and exhibited weak cytotoxicity against breast cancer (MCF-7) cell lines and antibacterial activity against the standard *Staphylococcus aureus* ATCC25923 and methicillin-resistant *S. aureus* SK1.

**Keywords**

*Phomopsis* sp.; Mangrove-derived fungus; Tetrahydroanthraquinone derivatives; Antibacterial activity; Cytotoxicity
Resource utilization and direct medical costs of chronic hepatitis C in Thailand: A heavy but manageable economic burden

Satawat Thongsawat, Teerha Piratvisuth, Chutima Pramoolsinsap, Anuchit Chutaputti, Tawesak Tanwandee, Dittaya Thongsuk

Objective
To estimate the cost for the management of chronic hepatitis C (CHC) and related morbidities by using a payer perspective in Thailand.

Methods
Data elements were extracted from medical records of 542 patients newly diagnosed with CHC in five tertiary care hospitals across Thailand. All patients were divided into five health states: noncirrhotic CHC, hepatitis C virus (HCV)-related compensated cirrhosis, HCV-related decompensated cirrhosis, HCV-related hepatocellular carcinoma, and HCV-related liver transplantation. Resource utilization data for each patient during a 12-month follow-up study period were compiled, and reference prices published by the Thai government were used to estimate the cost for each health state. The average cost was calculated and categorized into various groups, for example, laboratory and diagnostic tests, procedures, medication, and hospitalization.

Results
The average number of outpatient visits per patient was approximately six visits in all cohorts. The HCV-related hepatocellular carcinoma and liver transplantation cohorts had a higher average number of inpatient admissions per patient. The average number of days per admission varied from fewer than 3 days to 1 week or more across all the health states. The average annual total cost per patient varied across all health states from approximately 170,000 to 600,000 baht, and medication cost was the largest portion in every cohort, except the HCV-related liver transplantation cohort in year 1. Among all medications, the average annual antiviral medication cost per patient was the largest portion in the noncirrhotic CHC and HCV-related compensated cirrhosis cohorts.
Conclusions

CHC was a costly disease in Thailand. The average annual medication cost was the largest portion in every health state, except HCV-related liver transplantation.

Keywords

Direct medical cost; Economic burden; Hepatitis C virus; Resource utilization
Rhodomyrtone from *Rhodomyrtus tomentosa* (Aiton) Hassk. leaf extract has a strong antibacterial activity against the bacterial pathogen *Streptococcus pyogenes*. Our previous studies indicated that the bactericidal activity of rhodomyrtone might involve intracellular targets. In the present studies we followed a proteomics approach to investigate the mode of action of rhodomyrtone on *S. pyogenes*. For this purpose, *S. pyogenes* was cultivated in the presence of 0.39 μg/ml rhodomyrtone, which corresponds to 50% of the minimal inhibitory concentration. The results show that the amounts of various enzymes associated with important metabolic pathways were strongly affected, which is consistent with the growth-inhibiting effect of rhodomyrtone. Additionally, cells of *S. pyogenes* grown in the presence of rhodomyrtone produced reduced amounts of known virulence factors, such as the glyceraldehyde-3-phosphate dehydrogenase, the CAMP factor, and the streptococcal pyrogenic exotoxin C. Taken together, these findings indicate that rhodomyrtone has both antimicrobial and anti-infective activities, which make it an interesting candidate drug.

**Keywords**

Rhodomyrtone; *Rhodomyrtus tomentosa*; Glycolysis; Proteomics; *Streptococcus pyogenes*; Two-dimensional gel electrophoresis
Pharmacodynamics of meropenem in critically ill patients with febrile neutropenia and bacteraemia

Sutep Jaruratanasirikul, Thanya Limapichat, Monchana Jullangkoon, Nanchanit Aeiniang, Natnicha Ingviya, Wibul Wongpoowarak

The bactericidal activity of β-lactams is determined by the time that concentrations in tissue and serum are above the minimum inhibitory concentration ($T > MIC$) for the pathogen. The aim of this study was to compare the probability of target attainment (PTA) and the cumulative fraction of response (CFR) for meropenem between administration by bolus injection and a 3-h infusion. The study was a randomised, three-way, cross-over design in eight febrile neutropenic patients with bacteraemia. Each subject received meropenem in three regimens consecutively: (i) a bolus injection of 1 g every 8 h (q8h) for 24 h; (ii) a 3-h infusion of 1 g q8h for 24 h; and (iii) a 3-h infusion of 2 g q8h for 24 h. For pathogens with an MIC of 4 μg/mL, the PTA of achieving 40% $T > MIC$ following administration of meropenem by a bolus injection of 1 g q8h, a 3-h infusion of 1 g q8h and a 3-h infusion of 2 g q8h was 75.7%, 99.24% and 99.96%, respectively. Only the 3-h infusion of 2 g q8h achieved a PTA >99% for 40% $T > MIC$ for a MIC of 8 μg/mL. By referral to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) MIC distributions, the three regimens of meropenem were predicted to achieve a CFR ≥ 90% against *Escherichia coli* and *Klebsiella* spp. In conclusion, a 3-h infusion of 2 g of meropenem q8h resulted in the highest PTA rates. The three regimens of meropenem had high probabilities of achieving optimal impact against *E. coli* and *Klebsiella* spp.

**Keywords**

Carbapenem; Pharmacokinetic/pharmacodynamic; β-Lactam
5.21 Short questionnaire for Parkinson’s disease as a screening instrument

Suwanna Setthawatcharawanich, Pornchai Sathirapanya, Kanitpong Phabphal, Kitti Limapichat

Objective
To validate and simplify a screening questionnaire for the determination of PD.

Methods
The screening questionnaire for PD was developed with the permission of the author. Reliability of the questionnaire was tested. To validate the questionnaire, 40 patients with PD and 93 controls completed the questionnaire. Multiple logistic regression analysis was used to determine the questions independently associated with PD and a risk score was calculated. The predictive performance of the risk score was evaluated via the area under the curve (AUC) of a receiver operating characteristics (ROC) curve.

Results
The questionnaire showed a Cronbach’s alpha coefficient of 0.73 with no difference between the initial and follow up scores. The mean content validity was 0.86. Of the 11 questions, 4 were independently associated with PD and were used to calculate the risk score. The scores of these questions were 2 (clumsiness) + 4 (tremor) + 2 (masked face) + 2 (loss of balance while turning). The AUC of a ROC curve for the sum of risk score was 0.95. With a cutoff score of 5 or higher, the sensitivity and specificity were 0.88 and 0.95, respectively.

Conclusions
The screening questionnaire for PD is a reliable and valid instrument. The predictive performance of the simplified questionnaire is as good as the original.

Keywords
Short; Questionnaire; Parkinson’s disease; Validate; Screening
Smooth muscle tumors of the tonsil are rare. Recently, the occurrence of Epstein-Barr virus-associated smooth muscle tumor (EBV-SMT) has been increasingly recognized in immunocompromised patients, mainly post-transplantation and AIDS patients. The clinicopathologic features of EBV-SMT are different from conventional smooth muscle tumors. To the best of our knowledge, EBV-SMT involving the tonsil in an AIDS patient has not been reported. A 27-year-old man presented with a 2.2 cm right tonsillar mass six months after AIDS diagnosis. The tumor was composed of a cellular proliferation of oval to spindle-shaped cells with mitotic count up to 10 in 10 high-power fields. The diagnosis of EBV-SMT was confirmed by in situ hybridization for EBV-encoded RNA (EBER) transcripts. Synchronous lesions were also detected in the liver and peritoneum by an abdominal computed tomographic scan. EBV-SMT should be included in the differential diagnoses of a mesenchymal tumor in immunocompromised patients, and in the differential diagnoses of a smooth muscle tumor occurring in uncommon sites including the tonsil.
Anti-cancer activity of compounds from Bauhinia strychnifolia stem

Supreeya Yuenyongsawad, Kingkan Bunluepuech, Chatchai Wattanapiromsakul, Supinya Tewtrakul

Ethnopharmacological relevance

The stem and root of Bauhinia strychnifolia Craib (Fabaceae family) have been traditionally used in Thailand to treat fever, alcoholic intoxication, allergy and cancer. An EtOH extract of Bauhinia strychnifolia showed good inhibitory activity against several cancer cell lines including HT-29, HeLa, MCF-7 and KB. As there has been no previous reports on chemical constituents of Bauhinia strychnifolia, this study is aimed to isolate the pure compounds with anti-cancer activity.

Materials and methods

Five pure compounds were isolated from EtOH extract of Bauhinia strychnifolia stem using silica gel, dianion HP-20 and sephadex LH-20 column chromatography and were tested for their cytotoxic effects against HT-29, HeLa, MCF-7 and KB cell lines using the Sulforhodamine B (SRB) assay.

Results

Among five compounds, 3, 5, 7, 3′, 5′-pentahydroxyflavanonol-3-O-α-L-rhamnopyranoside (2) possessed very potent activity against KB (IC₅₀=0.00054 μg/mL), HT-29 (IC₅₀=0.00217 μg/mL), MCF-7 (IC₅₀=0.0585 μg/mL) and HeLa cells (IC₅₀=0.0692 μg/mL). 3,5,7-Trihydroxychromone-3-O-α-L-rhamnopyranoside (3) also showed good activity against HT-29 (IC₅₀=0.02366 μg/mL), KB (IC₅₀=0.0412 μg/mL) and MCF-7 (IC₅₀=0.297 μg/mL), respectively. The activity of 2 (IC₅₀=0.00054 μg/mL) against KB cell was ten times higher than that of the positive control, Camptothecin (anti-cancer drug, IC₅₀=0.0057 μg/mL). All compounds did not show any cytotoxicity with normal cells at the concentration of 1 μg/mL.
Conclusion

This is the first report of compounds 2 and 3 on anti-cancer activity and based on the anti-cancer activity of extracts and pure compounds isolated from *Bauhinia strychnifolia* stem, it might be suggested that this plant could be useful for treatment of cancer.

Keywords

Anti-cancer activity; *Bauhinia strychnifolia*; Fabaceae
**HPV genotyping in adenocarcinoma of the uterine cervix in Thailand**

Sumalee Siriaunkgul, Utaiwan Utaipat, Cheepsomon Suthipintawong, Kobkul Tungsimmunkong, Surang Triaratanachat, Surapan Khunamornpong

**Objective**

To determine the distribution of human papillomavirus (HPV) genotypes in cervical adenocarcinoma in Thailand and to evaluate the clinicopathologic characteristics associated with common HPV genotypes.

**Methods**

Formalin-fixed, paraffin-embedded tissues from 150 patients with adenocarcinoma were collected from 4 areas of Thailand. Infection with HPV was detected by nested polymerase chain reaction (PCR) with primers MY09/11 and GP5 +/6 +. Genotyping was performed using a linear array assay, followed by type-specific PCR targeting the E6/E7 regions of HPV-16, HPV-18, and HPV-52 if the linear array test was negative.

**Results**

Human papillomavirus DNA was detected in 145 (97%) adenocarcinomas (132 single infections; 11 multiple infections; 2 tumors with undetermined HPV type). Genotype 18 was most common (66%), followed by HPV-16 (30%) and HPV-45 (3%). Infection with only HPV-16 and/or HPV-18 accounted for 88% of the HPV-positive tumors. Patients with HPV-18 infection had a younger age ($P = 0.009$) and higher tumor grade ($P < 0.001$) than patients with HPV-16 infection.

**Conclusion**

The HPV detection rate in cervical adenocarcinomas in Thailand is high. The predominant genotype is HPV-18, being twice as common as HPV-16. Genotype variations are associated with patient age and tumor grade. Vaccination against HPV-16/HPV-18 might prevent almost 90% of adenocarcinomas.

**Keywords**

Adenocarcinoma; Genotyping; Human papillomavirus; Prevalence; Uterine cervix
Malnutrition assessment in patients with cancers of the head and neck: A call to action and consensus

Tanadech Dechaphunkul, Lisa Martin, Cathy Alberda, Karin Olson, Vickie Baracos, Leah Gramlich

**Purpose of research**

A state of the science review to assess how nutritional status and malnutrition are defined by the community of researchers studying head & neck cancer (HNC) patients.

**Principal results**

In 117 publications, nutritional status was described diversely, ranging from merely one to all six of the following features: weight loss, body composition, quantity/type of food intake, symptoms impacting oral intake, inflammation and altered metabolism. Methods of assessment of each feature were inconsistent. Cancer- and treatment-related symptoms impacting oral intake were a prominent theme. Metabolic changes potentially related to weight loss and efficacy of nutritional therapy were rarely described (<15% of articles). There were 24 different explicit definitions for malnutrition.

**Conclusion**

Consensus is needed regarding the criteria to adequately describe HNC-associated malnutrition. Standardization of assessments will permit aggregation of data, and integration into clinical practice—specifically, development of consensus criteria for implementation and termination of nutrition therapies.

**Keywords**

Head and neck cancer; Nutrition; Nutrition support; Malnutrition; Cachexia; Assessment
Assessing the spreading patterns of dengue infection and chikungunya fever outbreaks in lower southern Thailand using a geographic information system

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Purpose
The aims of this study were to assess the incidence of dengue infection (DEN) and chikungunya fever (CHIK) and determine the direction and speed of CHIK between August 2008 and June 2009 in lower southern Thailand.

Methods
The National Communicable Disease Surveillance System database and a geographic information system containing data on case locations were combined. R and ArcView were used for identifying incidence, direction, and speed of disease outbreaks.

Results
A total of 27,166 patients were identified, of which 3,319 and 23,847 had DEN and CHIK, with incidences of 73 and 521 per 100,000, respectively. The direction of the CHIK outbreak moved from south to north with a median speed of 7.5 km per week. CHIK cases increased after 6 weeks of increasing cumulative rainfall with variation of average daily temperatures (23.7–30.7°C) per week. There was no clear association of DEN with climate variables.

Conclusions
The combination of surveillance and geographic information system data of DEN and CHIK can be used to determine the speed and direction of disease spread. DEN is endemic, but CHIK is an emerging disease. Because of the rapid spread of CHIK, strict and timely integrated vector control programs after case notification must be implemented.

Keywords
Chikungunya fever; Dengue; Geographic Information System; Lower Southern Thailand; Outbreak
Noise exposure assessment in a dental school

Thitiworn Choosong, Wandee Kaimook, Ratchada Tantisarasart, Puwanai Sooksamear, Satith Chayaphum, Chanon Kongkamol, Wisarut Srisintorn, Pitchaya Phakthongsuk

Objectives:
This cross-sectional study was performed in the Dental School of Prince of Songkla University to ascertain noise exposure of dentists, dental assistants, and laboratory technicians. A noise spectral analysis was taken to illustrate the spectra of dental devices.

Methods:
A noise evaluation was performed to measure the noise level at dental clinics and one dental laboratory from May to December 2010. Noise spectral data of dental devices were taken during dental practices at the dental services clinic and at the dental laboratory. A noise dosimeter was set following the Occupational Safety and Health Administration criteria and then attached to the subjects’ collar to record personal noise dose exposure during working periods.

Results:
The peaks of the noise spectrum of dental instruments were at 1,000, 4,000, and 8,000 Hz which depended on the type of instrument. The differences in working areas and job positions had an influence on the level of noise exposure (p < 0.01). Noise measurement in the personal hearing zone found that the laboratory technicians were exposed to the highest impulsive noise levels (137.1 dBC). The dentists and dental assistants who worked at a pedodontic clinic had the highest percent noise dose (4.60 ± 3.59%). In the working areas, the 8-hour time-weighted average of noise levels ranged between 49.7-58.1 dBA while the noisiest working area was the dental laboratory.
Conclusion:
Dental personnel are exposed to noise intensities lower than occupational exposure limits. Therefore, these dental personnel may not experience a noise-induced hearing loss.

Keywords
Noise-induced hearing loss; Noise; Dental practice; Dental school; Dental instruments
Development of a burden scale for caregivers of dementia patients

Unchulee Taemeeyapradit, Dussadee Udomittipong, Sawitri Assanangkornchai

Objective
To develop a scale to measure the burden of care for caregivers of patients with dementia and explore its factor structure.

Methods
The initial draft of the Thai dementia patients’ caregiver burden (Thai-DCAB) scale was developed based on literature review, in-depth interviews and expert opinions. The drafted scale was administered to 203 caregivers of dementia patients treated at two large public hospitals in southern Thailand. An exploratory factor analysis using maximum likelihood extraction with varimax rotation was conducted. The reliability of the scale was assessed using Cronbach’s alpha.

Results
The Thai-DCAB scale consisted of 18 questions. Three factors were obtained, covering psychological, physical and financial burdens of the caregivers in taking care of dementia patients. These three factors accounted for 67% of the variance. The Cronbach’s alpha coefficient was 0.95.

Conclusion
The Thai-DCAB scale has high internal consistency and captures key theoretical constructs of the perceived burden among caregivers of patients with chronic and deteriorating dementia and in accordance with the social and cultural contexts and the way of life of the Thai people.

Keywords
Burden scale; Dementia; Caregiver; Factor structure
Health how influenza vaccination policy may affect vaccine logistics


Background

When policymakers make decision about the target populations and timing of influenza vaccination, they may not consider the impact on the vaccine supply chains, which may in turn affect vaccine availability.

Purpose

Our goal is to explore the effects on the Thailand vaccine supply chain of introducing influenza vaccines and varying the target populations and immunization time-frames.

Methods

We Utilized our custom-designed software HERMES (Highly Extensible Resource for Modeling Supply Chains), we developed a detailed, computational discrete-event simulation model of the Thailand’s National Immunization Program (NIP) supply chain in Trang Province, Thailand. A suite of experiments simulated introducing influenza vaccines for different target populations and over different time-frames prior to and during the annual influenza season.

Results

Introducing influenza vaccines creates bottlenecks that reduce the availability of both influenza vaccines as well as the other NIP vaccines, with provincial to district transport capacity being the primary constraint. Even covering only 25% of the Advisory Committee on Immunization Practice-recommended population while administering the vaccine over six months hinders overall vaccine availability so that only 62% of arriving patients can receive vaccines. Increasing the target population from 25% to 100% progressively worsens these bottlenecks, while increasing influenza vaccination time-frame from 1 to 6 months decreases these bottlenecks.
Conclusion

Since the choice of target populations for influenza vaccination and the time-frame to deliver this vaccine can substantially affect the flow of all vaccines, policy-makers may want to consider supply chain effects when choosing target populations for a vaccine.

Keywords

Influenza vaccine; Supply chain; Immunization policy
Toxoplasma gondii infection: What is the real situation?

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The prevalence of chronic Toxoplasma infections reported in the literature varies enormously. We hypothesize that one factor could be due to the different methods used in the evaluation of infections. Serological evidence of Toxoplasma infections in 450 pregnant women (PW) and 300 HIV-infected patients (HIV) were investigated by the Sabin–Feldman dye test and two other commercial ELISA kits (kit1 and kit2). Anti-Toxoplasma IgG antibodies obtained from the Sabin–Feldman dye test, ELISA kit1 and ELISA kit2 in the PW subjects were 14.7%, 29.6% and 38.7%, and in the HIV subjects were 13%, 34.7% and 36.3%, respectively. So there were significant differences in the seroprevalences when different diagnostic tests were used ($P < 0.05$). Regarding Sabin–Feldman dye test as the gold standard for anti-Toxoplasma antibodies detection, we found that the sensitivity and specificity of the ELISA kit1 and kit2 was in the range of their specification. However, as the two ELISA kits used in our study identified a much higher prevalence of Toxoplasma infections which indicated that false positive cases were being reported. Based on results obtained, it is therefore highly recommended that research workers should be aware that the reports of serological studies in terms of high positive results should be treated with some skepticism until additional precise diagnostic tools are developed.
Objective

This study aims to evaluate the costs and outcomes of offering the 10-valent pneumococcal conjugate vaccine (PCV10) and 13-valent pneumococcal conjugate vaccine (PCV13) in Thailand compared to the current situation of no PCV vaccination.

Methods

Two vaccination schedules were considered: two-dose primary series plus a booster dose (2 + 1) and three-dose primary series plus a booster dose (3 + 1). A cost-utility analysis was conducted using a societal perspective. A Markov simulation model was used to estimate the relevant costs and health outcomes for a lifetime horizon. Costs were collected and values were calculated for the year 2010. The results were reported as incremental cost-effectiveness ratios (ICERs) in Thai Baht (THB) per quality adjusted life year (QALY) gained, with future costs and outcomes being discounted at 3% per annum. One-way sensitivity analysis and probabilistic sensitivity analysis using a Monte Carlo simulation were performed to assess parameter uncertainty.

Results

Under the base case-scenario of 2 + 1 dose schedule and a five-year protection, without indirect vaccine effects, the ICER for PCV10 and PCV13 were THB 1,368,072 and THB 1,490,305 per QALY gained, respectively. With indirect vaccine effects, the ICER of PCV10 was THB 519,399, and for PCV13 was THB 527,378. The model was sensitive to discount rate, the change in duration of vaccine protection and the incidence of pneumonia for all age groups.

Conclusions

At current prices, PCV10 and PCV13 are not cost-effective in Thailand. Inclusion of indirect vaccine effects substantially reduced the ICERs for both vaccines, but did not result in cost.
Thai nurses’ experience of caring for persons with life-sustaining technologies in intensive care settings: A phenomenological study

Waraporn Kongsuwan, Rozzano C. Locsin

Technological competency as caring in nursing is grounded in the viewpoint that health care technologies are used to know persons. This study described the experiences of eight Thai nurses caring for persons with life-sustaining technologies in adult intensive care settings. Using individual semi-structured interviews, Van Manen’s hermeneutic phenomenological approach was used to analyse the data. Nine thematic categories formed the description of the experience of caring for. The experience of caring for is described as valuing competency to care despite differing insecurities in the use of technology. Influenced by relationships and compassion, the risk that technology prevented an appreciation of persons as wholes is embodied in the encouraging collaboration of fostering time to care regardless of being in a restricted space surrounded with technology. Locsin’s theory of Technological Competency as Caring in Nursing serves as theoretical lens through which findings are discussed. These findings should assist nurses achieve quality human care in intensive care settings.

Keywords
Thai nurse; Life-sustaining technology; Intensive care; Technological competency as caring
The development of clinical nursing practice guideline for initial assessment in multiple injury patients admitted to trauma ward

Wipa Sae-Sia, Praneed Songwathana, Pornpen Ingkavanich

Background

Missed diagnoses are very common in patients with multiple injuries. To help nurses identify missed injuries, this study aimed to develop and evaluate a clinical nursing practice guideline (CNPG) for the initial assessment of multiply injured patients admitted to the trauma ward in a provincial hospital in southern Thailand.

Method

The CNPG was developed using evidence-based knowledge of trauma assessment and the Advanced Trauma Life Support guideline. The CNPG was used by 18 nurses working in the trauma ward. They implemented the CNPG with 34 multiply injured patients. The outcome measures of the CNPG use were the nurses’ self-reported compliance with the use of the CNPG, the nurses’ satisfaction with using the CNPG, and the percentage of missed injuries detected as a result of the use of the CNPG.

Results

Most nurses (83.33%) reported complying with the CNPG and 72.2% of them indicated that their satisfaction with using the CNPG was at a high level. Missed injuries were discovered at a rate of 14.6% of the total injuries diagnosed in the injured patients within 24 h of ward admission.

Conclusion

Further research needs to be conducted to establish if the CNPG could be more widely applied to improve the quality of care and increase the safety of those with multiple injuries.

Keywords

Initial assessment; Trauma nursing; Clinical practice guideline; Evidence-based practice; Multiple injuries; Missed injury
Effect of spiritual intelligence, emotional intelligence, psychological ownership and burnout on caring behaviour of nurses: A cross-sectional study

Kaur D., Sambasivan M., Kumar N.

Aims and objectives:
To propose a model of prediction of caring behaviour among nurses that includes spiritual intelligence, emotional intelligence, psychological ownership and burnout.

Background:
Caring behaviour of nurses contributes to the patients’ satisfaction, well-being and subsequently to the performance of the healthcare organisations. This behaviour is influenced by physiological, psychological, sociocultural, developmental and spiritual factors.

Design:
A cross-sectional survey was used, and data were analysed using descriptive statistics and structural equation modelling.

Methods:
Data were collected between July-August 2011. A sample of 550 nurses in practice from seven public hospitals in and around Kuala Lumpur (Malaysia) completed the questionnaire that captured five constructs. Besides nurses, 348 patients from seven hospitals participated in the study and recorded their overall satisfaction with the hospital and the services provided by the nurses. Data were analysed using structural equation modelling (SEM).
Results:

The key findings are: (1) spiritual intelligence influences emotional intelligence and psychological ownership, (2) emotional intelligence influences psychological ownership, burnout and caring behaviour of nurses, (3) psychological ownership influences burnout and caring behaviour of nurses, (4) burnout influences caring behaviour of nurses, (5) psychological ownership mediates the relationship between spiritual intelligence and caring behaviour and between emotional intelligence and caring behaviour of nurses and (6) burnout mediates the relationship between spiritual intelligence and caring behaviour and between psychological ownership and caring behaviour of nurses.

Conclusions:

Identifying the factors that affect caring behaviour of nurses is critical to improving the quality of patient care. Spiritual intelligence, emotional intelligence, psychological ownership and burnout of nurses play a significant role in effecting caring behaviour of nurses. Relevance to clinical practice: Healthcare providers must consider the relationships between these factors in their continuing care and incorporation of these in the nursing curricula and training.

Keywords

Burnout; Caring behaviour; Emotional intelligence; Nurses; Psychological ownership; Public hospital; Spiritual intelligence
Candidiasis is a fungal infectious disease, caused by the opportunistic pathogens, Candida species. Incidences of candidiasis have become more common, as a result of prolonged antibiotic therapy and increased number of immunocompromised patients. This study was conducted to investigate the antifungal properties of Rhizome coptidis, Radix Sophorae flavescentis, Radix Stemonae, Etlingera elatior, Alpinia galangal and Cymbopogon citratus extracts in terms of inhibition zone and minimum inhibitory concentration (MIC) of plant extracts against some of clinically prevalent species of Candida outlined by CLSI susceptibility testing guidelines for yeast cells. Our favourable results demonstrated that R. coptidis has potential to show the strong antifungal activity against all Candida species tested as ranged from 64 to >1024 μg/ml. A. galangal was also able to inhibit the growth of Candida tropicalis and Candida glabrata, although to a lower extent. Moreover, the MIC value of A. galangal was 64 μg/ml for both Candida tested. Meanwhile, the majority of plant extracts tested did not show significant antifungal activity. Nonetheless, in vivo testing needs to be performed to support these findings.
Acute, reproductive toxicity and two-generation teratogy studies of a standardized quassinoid-rich extract of *Eurycoma longifolia* jack in Sprague-Dawley rats

Low B.S., Das P.K., Chan K.L.

The roots of *Eurycoma longifolia* Jack are popularly sought as herbal medicinal supplements to improve libido and general health amongst the local ethnic population. The major quassinoids of *E. longifolia* improved spermatogenesis and fertility but toxicity studies have not been well documented. The reproductive toxicity, two generation of foetus teratology and the up-and-down acute toxicity were investigated in Sprague-Dawley rats orally treated with quassinoid-rich *E. longifolia* extract (TAF273). The results showed that the median lethal dose (LD$_{50}$) of TAF273 for female and male rats was 1293 and $>2000$mg/kg, respectively. Fertility index and litter size of the TAF273 treated were significantly increased when compared with those of the non-treated animals. The TAF273-treated dams decreased in percentage of pre-implantation loss, post-implantation loss and late resorption. No toxic symptoms were observed on the TAF273-treated pregnant female rats and their foetuses were normal. The no-observed adverse effect level (NOAEL) obtained from reproductive toxicity and teratology studies of TAF273 in rats was 100mg/kg body weight/day, being more than 10-fold lower than the LD$_{50}$ value. Thus, any human dose derived from converting the rat doses of 100mg/kg and below may be considered as safe for further clinical studies.

**Keywords**

Acute toxicity; *Eurycoma longifolia* Jack; Quassinoids; Reproductive toxicity; Teratology
Estrogenic assessment of Labisia pumila extracts using a human endometrial cell line

Melissa, P.S.W., Navaratnam, V., Yin, C.Y.

Objective:

Labisia pumila (LP) has been used by Malay women for generations to regulate post-menopausal symptoms and contraction of the uterus after child birth. Its activity is due to phytoestrogens which could act like estrogen to bring about an estrogenic effect. This study aims to investigate the estrogenic activity of various LP extracts using an in-vitro model.

Methods:

Various extracts and fractions was obtained from LP and tested for estrogenic activity using an in-vitro alkaline phosphatase assay using Ishikawa cells. Highly estrogenic water extract was fractionated using preparative high pressure liquid chromatography (HPLC). The extracts and fractions were also tested for their effect on cell proliferation.

Results:

Standardized water extract of LP at 100μg/ml was highly estrogenic (2.56 fold of the control) thus was further fractionated. The last fraction eluted from HPLC presented the highest estrogenic activity (2.84 fold of the control), even higher than that of the water extract. Meanwhile, butanol, hexane and dichloromethane solvents did not significantly induce estrogenic activity. All the extracts showed minimal induction of cell proliferation (<20.00%) in comparison to estradiol (a positive control).

Conclusion:

The high estrogenic activity and lower cell proliferation induction of the water extract provides a good insight for its use as an estrogen replacement agent. Consequently, this provides a respectable outcome towards the commercial products which contains LP extracts.

Keywords:

Labisia pumila; Traditional medicine; Phytoestrogen; Estrogenic activity
Estrogenic and anti-proliferative activity of water extract of *Glycyrrhiza uralensis* (licorice root)

Melissa P.S.W., Yin C.Y.

Licorice is the root of *Glycyrrhiza uralensis*, which is a commonly used herb in traditional Chinese medicine. Licorice extract has been claimed to have anti-cancer, anti-viral, anti-inflammatory and anti-diabetic activities. This study evaluated the estrogenic effect of licorice root water extract on Ishikawa cells and related it to its effect on cell proliferation using various cell lines in comparison to glycyrrhizic acid (GA). This study showed that licorice root extract exhibited estrogenic property while decreasing cell proliferation thus suggesting possible use in estrogen replacement agent with anti-proliferative property. Even though GA is the most studied active component in licorice, these two properties were not seen in the cell lines tested; hence suggesting that GA is not responsible for these activities. These results showed that licorice could be further studied as an estrogen replacement agent as it does not cause an increase in cell proliferation in the breast and uterus.

**Keywords**

*Glycyrrhiza uralensis*; Glycyrrhizic acid; Health functional food; Licorice root; Phytoestrogen
Glycyrrhizic acid (GA), belonging to a class of triterpenes, is a conjugate of two molecules, namely glucuronic acid and glycyrrhetinic acid. It is naturally extracted from the roots of licorice plants. With its more common uses in the confectionery and cosmetics industry, GA extends its applications as a herbal medicine for a wide range of ailments. At low appropriate doses, anti-inflammatory, anti-diabetic, antioxidant, anti-tumor, antimicrobial and anti-viral properties have been reported by researchers worldwide. This review summarizes the effects of GA on metabolic syndrome, tumorigenesis, microbes and viruses, oxidative stress, and inflammation, as well as the reported side effects of the drug.

Keywords

Anti-diabetic; Anti-inflammatory; Anti-tumor; Anti-viral; Antimicrobial; Antioxidant; Glycyrrhizic acid
Maternal nutrition is one of the dominant factors in determining fetal growth and subsequent developmental health for both mother and child. This study aimed to explore the association between maternal consumption of food groups and birth size among singleton, termed newborns. One hundred and eight healthy pregnant women in their third trimester, aged 19 to 40 years who visited the Obstetrics and Gynecology Clinic of Hospital Universiti Sains Malaysia completed an interviewed-administered, validated semi-quantitative food frequency questionnaire. The maternal socio-demographic, medical and obstetric histories and anthropometry measurements were recorded accordingly. The pregnancy outcomes, birth weight, birth length and head circumference were obtained from the medical records. The data were analyzed using multiple linear regression by controlling for possible confounders. Among all food groups, fruits intake was associated with higher birth weight (p=0.018). None of the food intake showed evident association with birth length while only fruits intake was associated positively with head circumference (p=0.019). In contrast, confectioneries and condiments were associated with lower birth weight (p=0.013 and p=0.001, respectively). Also, condiments appeared to associate inversely with ponderal index (p=0.015). These findings suggest the potential beneficial effects of micronutrient rich food but detrimental effects of high sugar and sodium food on fetal growth. Such an effect may have long term health consequences to the lives of children.

**Keywords**

Birth weight; Food frequency questionnaire; Maternal intake; Pregnancy
Anatomical evaluation of first dorsal compartment of the hand – a study in South Indian cadavers.

Suhani, S and Mamatha, H and Bhaskarananda, K and Saraswathi, and Melanie, RD and Naveen, K

Morphology of the first dorsal compartment of the hand is often linked with several surgical or orthopaedic complications. It is frequently associated with splitting of the compartment into two sub compartments and more common in patients with de Quervain disease, which supports the claim that this anatomic variation is involved in the pathogenesis of de Quervain disease. Our aim was to evaluate the different anatomic variations of the first dorsal compartment and its possible clinical complications in south Indian cadaveric hands. We studied 94 formalin fixed isolated hands for the morphological study of the 1st dorsal compartment. The length and width of the compartment ranged between 14.07 to 24.17mm and 4.19 to 10.37mm, respectively and the thickness of the extensor retinaculum over the first dorsal compartment was found to vary between 0.11mm to 1.72mm. Septation was seen in 50.74% of the specimens. In majority of cases, extensor pollicis brevis presented with single tendon and in 2.98% cases, it was absent. In contrary to this, multiple tendons of abductor pollicis longus was common observation. Hence, it is handy to have a prior detailed knowledge of existence of the various anatomic variations of first dorsal compartment for the surgeons who treat de Quervian’s tenosynovitis or other related clinical complications, which require steroid treatment as it should be injected to both sub compartments when present.

Keywords

First dorsal compartment; Extensor pollicis brevis; Abductor pollicis longus; Septation; de Quervain tenosynovitis
Antioxidant activity of methanol extract of *Tinospora crispa* and *Tabernaemontana corymbosa*

Heida Nadia Zulkefli, and Jamaludin Mohamad, and Nurhayati Zainal Abidin

*Tinospora crispa* and *Tabernaemontana corymbosa* have been used traditionally to treat fever, diabetes, rheumatism and sinusitis. The objective of this study was to evaluate the antioxidant activity of *Tinospora crispa* and *corymbosa*. The presence of apigenin and magnoflorine was detected using LCMS/MS in *crispa* (Patawali) whereas appararicine, voafinine, conodusarine, conodurine, voacamine and voacangine were detected in *corymbosa* (Susur kelapa) methanol extract. The stem extract of *crispa* showed high antioxidant activity in the following order: DPPH radical scavenging, reducing power and metal chelating assay (98.8%, 0.957, 81.97%) than *corymbosa* of leaves (90.04%, 0.652, 69.64%), stem (82.78%, 0.819, 36.70%) and root extracts (63.25%, 0.469, 51.56%), respectively. The high antioxidant activity in the stem extract of *crispa* is due to the presence of apigenin and magnoflorine. The high antioxidant activity in *Tabernaemontana corymbosa* extract is due to its high phenol contents. There were significant linear positive correlation (r=0.788, p<0.001, r²=0.621) between the total phenolic content and DPPH free radical scavenging assay in the crude extracts of *Tinospora crispa* and *corymbosa*. Meanwhile, a significant moderate positive correlation was observed between the total phenolic content and ferric reducing power assay (r= 0.556, p<0.05, r²= 0.309). However, there was no significant difference in the correlation coefficient of total phenolic content and metal chelating assay.

**Keywords**

*Tabernaemontana corymbosa*; *Tinospora Crispa*; Total phenolic content
Developing correlation equations for converting among coliforms, *E. coli* and HPC for rainwater disinfection by sunlight.

M.T. Amin, Amin and M.Y. Han and Tschung-Il Kim and A.A. Alazba, Alazba and M.N. Amin, Amin

The application of solar disinfection for treating stored rainwater was investigated by the authors using indicator organisms. The multiple tube fermentation technique and pour plate method were used for the detection of microbial quality indicators like total and fecal coliforms, *E. coli* and heterotrophic plate count. These techniques have disadvantages mainly that these are laborious and time consuming. The correlation of total coliform with that of exposure time is proposed under different factors of weather, pH and turbidity. Statistical tools like root mean square error and coefficient of determination were used to validate these proposed equations. The correlation equations of fecal coliform, *E. coli* and heterotrophic plate count with total coliform are suggested by using four regression analysis including Reciprocal Quadratic, Polynomial Regression (2 degree), Gaussian Model and Linear Regression in order to reduce the tedious experimental work in similar types of experiments and treatment systems.

**Keywords**

Correlation; Microbial parameters; Rainwater; Sunlight
Ethnobotanical survey of medicinal plants used for the treatment of diabetes in Manisa, Turkey.

Durmuskahya, C. and Ozturk, M.

In this study, medicinal plants which are traditionally used for treatment of diabetes mellitus in Manisa and its environs have been investigated. A detailed market survey and ethnobotanical enquiry was performed in the region. In all, 121 medicinal herb dealers were interviewed together with the patients suffering from diabetes. After questionnaire studies, plant specimens were collected from medicinal herb markets known locally as ‘aktars’ or ‘baharatchi’, a total of 27 plant taxa belonging to 15 families were identified to be used for the treatment of diabetes. These taxa mostly belonged to the families Rosaceae (5 taxa), Lamiaceae (3 taxa), Fabaceae (2 taxa) and Asteraceae (2 taxa). The most important anti-diabetic plants are; Zizyphus jujube Mill. (jujube), Origanum onites L. (oregano), Ceracus mahaleb L. (mahaleb) and Trigonella foenum-graecum L. (fenugreek). Attempts are being made to investigate their active compounds responsible for the hypoglycemic activity.

Keywords

Diabetes; Ethnobotany; Manisa; Medicinal plants; Turkey
Natural diet of blue swimming crab, *Portunus pelagicus* at Strait of Tebrau, Johor, Malaysia


Knowledge of natural diet in *Portunus pelagicus* is essential to understand its nutritional requirements, its interactions with other organisms and its potential for culture. The natural diet of *P. pelagicus* was studied in Strait of Tebrau, Johor, Malaysia via gut content analysis and molecular analysis. A total of 30 identifiable fatty acids were detected in foregut content of *P. pelagicus*. Fatty acid 18:3ω3 act as a mangrove detritus marker was found to be the most abundant in foregut content of both sexes of *P. pelagicus* and has higher value in female. PUFA was the main fatty acid found in foregut content of *P. pelagicus* and major contributed by fatty acid 18:3ω3, 20:5ω3 and 22:6ω3. Marine animal’s marker was found to be the dominant in foregut content of *P. pelagicus* and that indicated that marine animals were the main food source of *P. pelagicus*. In conclusion, this study showed that *P. pelagicus* is a primarily omnivores crab with preference of marine animal and with addition and/or incidental fed plant items.

**Keywords**

Dietary composition; Fatty acid analysis; Foregut contents; Portunus pelagicus
Optimization of submerged culture conditions for the production of mycelial biomass and exopolysaccharides from *Lignosus rhinocerus*

Wei, Hong Lai and Saadiah Mohd Salleh, and Fauzi Daud, and Zamri Zainal, and Abas Mazni Othman, and Norihan Mohd Saleh

Tiger’s Milk mushroom (*Lignosus rhinocerus*) is a highly priced medicinal mushroom utilized in traditional medicine to treat various diseases. However, due to insufficient wild *L. rhinocerus*, submerged culture conditions and nutritional requirements for the production of mycelial biomass and exopolysaccharide (EPS) from *L. rhinocerus* were studied using one-factor-at-a-time and orthogonal matrix method in shake flask culture. The optimal pH and temperature for ideal production of mycelial biomass and EPS were found to be at pH6 and 25°C, respectively. The optimal compositions for mycelial biomass production were 80 g/L of glucose, 4 g/L of potassium nitrate, 0.4 g/L of FeSO$_4$.7H$_2$O and 0.1 g/L of CaCl$_2$. Subsequently, the optimal compositions for EPS production were 80 g/L of glucose, 4 g/L of potassium nitrate, 1.4 g/L of FeSO$_4$.7H$_2$O and 1.1 g/L of CaCl$_2$. The maximum mycelial biomass and EPS concentrations achieved in a 1.5 L stirred-tank bioreactor were 6.3788 g/L and 1.2 g/L, respectively. Mycelial biomass production was about 3 times higher than that at the basal medium. However, EPS production indicated no significant difference at the basal medium. In addition, the concentrations for α-amylase, β-amylase, cellulase and invertase in optimal medium were 2.87, 1.07, 3.0 and 3.0 mg/mL, respectively. Current findings suggest that the production of mycelial biomass and EPS of *L. rhinocerus* can be enhanced dramatically by controlling the culture conditions and modifying the medium’s composition.

**Keywords**
Exopolysaccharides; *Lignosus rhinoceros*; Mycelial biomass; Orthogonal matrix method; Submerged culture
Piper sarmentosum water extract attenuates diabetic complications in streptozotocin induced Sprague-Dawley rats

Farida Hussan, and Nur Nazilah Mat Zin, and Mohd Ramdzi Zulkifli, and Yow, Siew Choon and Noor Adibah Abdullah, and Teoh, Seong Lin

Piper sarmentosum has been shown to possess antihyperglycemic effect. The effect of water extract of PS leaves was determined on the diabetic complications in streptozotocin induced rats. Eighteen male Sprague-Dawley rats (n=18) were randomly divided into three groups with six rats each, namely, control, diabetic untreated and PS treated diabetic groups. Diabetes was induced with intramuscular injection of STZ (50 mg/kg). Ten days following the induction, the diabetes was confirmed with fasting blood sugar level more than 8 mmol/L and PS extract was administered orally (0.125 g/kg) for 28 days. The left kidneys were collected to analyze. The body weight and kidney weight index showed significant differences between control and diabetic groups (p<0.05). However, the lesser extent of body weight gain was observed in diabetic group compared with the control groups. The fasting blood sugar level was reduced in PS treated group. The percent area occupied by the glomerulus over a renal corpuscle was found to be 74.5% in DPS, 72% in DNT and 75% in C group; however it was statistically insignificant. Histological study revealed marked inflammatory cells infiltration and glomeruli contraction with widened urinary spaces revealed in DNT group following 28 days of hyperglycemic state whereas the DPS group showed features of improvement. The water extract of PS leaves has the potential preventive effect on the diabetic nephropathy by reducing hyperglycemia.

Keywords

Diabetic nephropathies; Piper sarmentosum; Streptozotocin
Psidium guajava fruit peel extract reduces oxidative stress of pancreas in streptozotocin-induced diabetic rats

Siti Balkis Budin, and Hawa Ismail, and Pek, Lian Chong

Abundant natural products with medicinal properties have been used as food and traditional medicine for diabetes mellitus all over the world. Psidium guajava fruit from the family of Myrtaceae has gained attention for its antioxidant potential. This study was conducted to determine the effects of P. guajava fruit peel aqueous extract on oxidative stress of pancreas in streptozotocin-induced (45 mg/kg) diabetic rats. Diabetic rats were administered with 400 mg/kg of aqueous extract of P. guajava fruit peel daily for 28 days duration. The results showed that diabetic rats supplemented with P. guajava extract did not cause significant difference in blood glucose level (p>0.05) as compared with diabetic rats alone. For oxidative stress evaluation, malondialdehyde (MDA) and protein carbonyl level were significantly lower and the activity of superoxide dismutase (SOD) and glutathione (GSH) level were significantly higher (p<0.05) in P. guajava supplemented rats compared with non-supplemented diabetic rats. However, histological observation showed that supplementation of P. guajava extract did not give protective effects towards alterations in pancreas histology in diabetic rats. The findings suggested that aqueous extract of P. guajava fruit peel supplementation has the ability to reduce oxidative stress in pancreas of diabetic rats and may play a role in reducing the development of diabetic complications.

Keywords
Antioxidant; Histopathology; Lipid peroxidation; Psidium guajava; Type 1 diabetes mellitus
Spatial analysis of infant mortality in Peninsular Malaysia over three decades using mixture models

Nuzlinda Abdul Rahman, and Abdul Aziz Jemain

Infant mortality is one of the central public issues in most of the developing countries. In Malaysia, the infant mortality rates have improved at the national level over the last few decades. However, the issue concerned is whether the improvement is uniformly distributed throughout the country. The aim of this study was to investigate the geographical distribution of infant mortality in Peninsular Malaysia from the year 1970 to 2000 using a technique known as disease mapping. It is assumed that the random variable of infant mortality cases comes from Poisson distribution. Mixture models were used to find the number of optimum components/groups for infant mortality data for every district in Peninsular Malaysia. Every component is assumed to have the same distribution, but different parameters. The number of optimum components were obtained by maximum likelihood approach via the EM algorithm. Bayes theorem was used to determine the probability of belonging to each district in every components of the mixture distribution. Each district was assigned to the component that had the highest posterior probability of belonging. The results obtained were visually presented in maps. The analysis showed that in the early year of 1970, the spatial heterogeneity effect was more prominent; however, towards the end of 1990, this pattern tended to disappear. The reduction in the spatial heterogeneity effect in infant mortality data indicated that the provisions of health services throughout the Peninsular Malaysia have improved over the period of the study, particularly towards the year 2000.

Keywords
Disease mapping; Infant mortality; Mixture model
In this paper, we examined a model of cell invasion focusing on the wavefront of the neural crest (NC) cells in the case of Hirschsprung’s disease (HSCR). Hirschsprung’s disease (HSCR) is a congenital defect of intestinal ganglion cells and causes patients to have disorders in peristalsis. This simulation model was performed using the fractional differential equations (FDEs) based upon two basic cell functions. Here, we simulated the mathematical model in a one-dimensional setting, based on the fractional trapezoidal numerical scheme and the results showed an interesting outcome for the mobility of the cellular processes under crowded environments.

**Keywords**

Fractional differential equation; Hirschsprung disease; Simulation
Validation of a food frequency questionnaire in assessing the omega-3 polyunsaturated fatty acids intake for Malays and Chinese elderly in Malaysia

Lai, Kuan Lee and Suzana Shahar, and Noor Aini Mohamad Yusoff, and Al-Vyrn , Chin

Omega-3 polyunsaturated fatty acids (PUFAs) is crucial to prevent a wide range of chronic diseases from a global view point. However, no suitable dietary assessment tool is available for usage among Malaysian population. The present study aimed to evaluate the validity of interviewer-administered semi-quantitative Food Frequency Questionnaire (FFQ) for assessing the omega-3 PUFAs intake among the Malays and Chinese elderly individuals in Klang Valley, Malaysia. Thirty-seven elderly people (54.1% women and 45.9% men), aged 60 years and above, were recruited from a community setting. Omega-3 PUFAs intake for the past one month was assessed using a 45-food item FFQ and validated against 3 days Food Record (FR). Wilcoxon signed rank test indicated no significant mean intake difference between two assessment methods. Significant correlation was found for total omega-3 PUFAs (r=0.926), α-linolenic acid (ALA) (r=0.745), eicosapentaenoic acid (EPA) (r=0.579) and docosahexaenoic acid (DHA) (r=0.912). Bland-Altman analysis exhibited no apparent systematic bias between the two methods for total omega-3 PUFAs intake, while quartile analysis classified 73% subjects assigned into the same quartile. Conclusively, the newly-developed FFQ yielded a reasonable validity in the tested population and provided a convenient means to estimate omega-3 PUFAs intake within healthy Malays and Chinese elderly individuals. Further study to evaluate its validity and reproducibility for different age groups is required.

Keywords
Elderly; Food frequency questionnaire; Food record; Omega-3 PUFAs; validity
An oral cancer biobank initiative: a platform for multidisciplinary research in a developing country


Identification of diagnostic markers for early detection and development of novel and therapeutic agents for effective patient management are the main motivation for cancer research. Biological specimens from large cohort and case-control studies which are crucial in providing successful research outcomes are often the limiting factor that hinders research efforts, especially in developing countries. Therefore, the Malaysian Oral Cancer Database and Tissue Bank System (MOCDTBS) were established to systematically collect large number of samples with comprehensive sociodemographic, clinicopathological, management strategies, quality of life and associated patient follow-up data to facilitate oral cancer research in Malaysia. The MOCDTBS also promotes sharing among researchers and the development of a multidisciplinary research team. The following article aims to describe the process of setting-up and managing the MOCDTBS.

Keywords
Oral cancer; Biobank; Malaysia; Multidisciplinary team
Correlates between risk perceptions of cervical cancer and screening practice

Wong, Y.L.; Chinna, K.; Mariapun, J.; Shuib, R.

Objectives:
To identify the correlates between risk perceptions and cervical cancer screening among urban Malaysian women.

Method:
A cross-sectional household survey was conducted among 231 women in Petaling Jaya city in 2007. The association of risk perceptions of cervical cancer and screening practice was analyzed using Poisson regression.

Results:
56% of the respondents ever had a Pap smear test. Knowledge of signs and symptoms (aPR=1.11, 95% CI=1.03-1.19), age (aPR=1.02, 95% CI=1.01-1.03), number of pregnancies (aPR=1.06, 95% CI=1.01-1.11), marital status, education level and religion were found to be significant correlates of Pap smear screening. Respondents who were never married were less likely to have had a Pap smear. Those who had no education or primary education were less likely to have had a Pap smear compared to those with degree qualification. The prevalence of screening was significantly higher among Christians and others (aPR=1.35; 95% CI=1.01-1.81) and Buddhists (aPR=1.38; 95% CI=1.03-1.84), compared to Muslims.

Conclusion:
Eliminating anecdotal beliefs as risks via targeted knowledge on established risk factors and culturally sensitive screening processes are strategic for increasing and sustaining uptake of Pap smear screening versus current opportunistic screening practices.

Keywords
Cervical cancer; Malaysia; Pap smear; Risk perception; Screening; Targeted knowledge
Battling malaria will be a persistent struggle without the proper means to diagnose the parasitic infection. However, the inherent limitations of microscopy, the conventional method of diagnosing malaria, affect the accuracy of diagnosis. The present study aimed to compare the accuracy of two different set of primers targeting the small subunit ribosomal RNA (ssRNA) and the dihydrofolate reductase-thymidylate synthase linker region (dhfr-ts) in detecting species specific malaria infections by nested PCR. The sensitivity and specificity of nested PCR assay using the two primers were calculated with reference to microscopy as the ‘gold standard’. The results show that 18S rRNA primers had 91.9% sensitivity and 100% specificity in detecting human Plasmodium species as opposed to dhfr-ts primers which had 51.4% sensitivity and 100% specificity. The higher sensitivity of 18S rRNA primers suggests that it may be a better diagnostic tool for detecting human malaria.
Drinking water is a significant predictor of Blastocystis infection among rural Malaysian primary schoolchildren


Blastocystis infection has a worldwide distribution especially among the disadvantaged population and immunocompromised subjects. This study was carried out to determine the prevalence and the association of Blastocystis infection with the socio-economic characteristics among 300 primary schoolchildren, living in rural communities in Lipis and Raub districts of Pahang state, Malaysia. Stool samples were collected and examined for the presence of Blastocystis using direct smear microscopy after in vitro cultivation in Jones’ medium. The overall prevalence of Blastocystis infection was found to be as high as 25.7%. The prevalence was significantly higher among children with gastrointestinal symptoms as compared to asymptomatic children (x^2 = 4.246; P=0.039). Univariate and multivariate analyses showed that absence of a piped water supply (OR=3.13; 95% CI=1.78, 5.46; P<0.001) and low levels of mothers’ education (OR=3.41; 95% CI=1.62, 7.18; P<0.01) were the significant predictors of Blastocystis infection. In conclusion, Blastocystis is prevalent among rural children and the important factors that determine the infection were the sources of drinking water and mothers’ educational level. Interventions with provision of clean water supply and health education especially to mothers are required.

Keywords

Blastocystis; Predictors; Drinking water; School children; Malaysia
High fluoride and low pH level have been detected in popular flavoured beverages in Malaysia

Rahim, Z.H.A.; Bakri, M.M.; Zakir, H.M.; Ahmed, I.A.; Zulkifli, N.A.

**Objective:** In children, excessive ingestion of fluoride from different sources including bottled drinking water and flavoured beverages or soft drinks can lead to the development of dental fluorosis. In addition, the pH level of beverages is important. Low pH can cause dental erosion. In this study we explore the fluoride content and pH level of certain popular beverages available in Malaysian supermarkets and hawkers’ stalls.

**Methods:** Bottled drinking water and selected popular flavoured packet drinks were purchased from a supermarket and the corresponding flavoured hawkers’ drinks, from a hawker’s stall in Kuala Lumpur. Fluoride and pH of the beverages were determined using digital fluoride meter and digital pH meter respectively.

**Results:** It was found that fluoride content and pH level vary among the beverages. The mean fluoride content in both packet and hawkers’ drinks (7.64±1.88 mg/L, 7.51±1.60 mg/L, respectively) was approximately 7 times higher than the bottled drinking water (1.05±0.35 mg/L). Among the beverages, the tea packet drink was found to contain the highest amount of fluoride (13.02±0.23 mg/L). The mean pH of bottled-drinking water was near neutral (6.96±0.17), but acidic for both supermarket (4.78.00±0.49) and hawkers’ drinks (5.73±0.24). The lychee packet drink had the lowest pH level (2.97±0.03).

**Conclusions:** Due to the wide variation of the fluoride content and pH level of the drinks tested in this study, it is recommended that steps should be taken to control the fluoride concentration and pH level in beverages if dental fluorosis and erosion are to be prevented.

**Keywords**

Beverages; Dental erosion; Dental fluorosis; Fluoride; pH
High diversity of cryptosporidium subgenotypes identified in Malaysian HIV/AIDS individuals targeting gp60 gene

Iqbal, A.; Lim, Y.A.L.; Surin, J.; Sim, B.L.H.

Background:
Currently, there is a lack of vital information in the genetic makeup of Cryptosporidium especially in developing countries. The present study aimed at determining the genotypes and subgenotypes of Cryptosporidium in hospitalized Malaysian human immunodeficiency virus (HIV) positive patients.

Methodology/Principal Findings:
In this study, 346 faecal samples collected from Malaysian HIV positive patients were genetically analysed via PCR targeting the 60 kDa glycoprotein (gp60) gene. Eighteen (5.2% of 346) isolates were determined as Cryptosporidium positive with 72.2% (of 18) identified as Cryptosporidium parvum whilst 27.7% as Cryptosporidium hominis. Further gp60 analysis revealed C. parvum belonging to subgenotypes IIaA13G1R1 (2 isolates), IIaA13G2R1 (2 isolates), IIaA14G2R1 (3 isolates), IIaA15G2R1 (5 isolates) and IIdA15G1R1 (1 isolate). C. hominis was represented by subgenotypes IaA14R1 (2 isolates), IaA18R1 (1 isolate) and IbA10G2R2 (2 isolates).

Conclusions/Significance:
These findings highlighted the presence of high diversity of Cryptosporidium subgenotypes among Malaysian HIV infected individuals. The predominance of the C. parvum subgenotypes signified the possibility of zoonotic as well as anthroponotic transmissions of cryptosporidiosis in HIV infected individuals.
Oncogenic human papillomavirus genital infection in southern Iranian women: population-based study versus clinic-based data


Background
Epidemiological studies on genital human papilloma viruses infection (HPVs) in general population are crucial for the implementation of health policy guidelines for developing the strategies to prevent the primary and secondary cervical cancer. In different parts of Iran, there is a lack of population-based studies to determine the prevalence of HPV in the general population. The aim of this population-based study is to compare the prevalence rate of genital HPV infection among reproductive women with our previous clinic-based data, which showed a prevalence rate of 5% in women in southern Iran.

Results
Using general primers for all genotypes of HPV, of 799 randomly selected women, five (0.63%, 95% CI 0.23-1.55%) tested positive for HPV DNA. Overall, seven different HPV genotypes were detected: six types (16, 18, 31, 33, 51 and 56) were carcinogenic, or “high risk genotypes” and one genotype (HPV-66) was “probably carcinogenic.”

Conclusions
In a population-based study, the prevalence of HPV infection among southern Iranian women was lower than that observed worldwide. However, our gynaecological clinic-based study on the prevalence of HPV infection showed results comparable with other studies in the Middle East and Persian Gulf countries. Since gynaecological clinic-based data may generally overestimate HPV prevalence, estimates of prevalence according to clinic-based data should be adjusted downward by the population-based survey estimates.

Keywords
Human papilloma virus; Bushehr; Cervical cancer; Iran; PCR
Diabetes has become a major health challenge affecting nearly 300 million people around the world. Complications of diabetes can be prevented by proper monitoring and regulation of glucose concentration in blood plasma. Continuous Glucose Monitoring Systems help to track the time course of blood glucose. These devices have the additional feature of giving threshold alert and predictive alert which is needed for an early warning of impending hypoglycemia. However, the accuracy of predictive alerts in currently available CGM devices is not very promising. Various algorithms have been developed in this regard by researchers. Still, a 100% accuracy has not been achieved. In our work, we have approached this prediction by training a simple neural network with the extracted features of continuous glucose monitoring sensor data time series. The data was obtained in three different ways, one set from the Self Monitoring Blood Glucose values, the second set from a diabetes resource and the third one from the patients using continuous glucose monitoring systems. A feed forward neural network with back propagation algorithm is trained with features of input patterns. The network is trained and validated to meet out the performance goal. The Root Mean Square Error between the actual glucose value and the predicted glucose value is used as the performance measure. It is observed that as the length of prediction horizon extends, the error increases. However, tracking of Hypoglycemic and Hyperglycemic trends are superior to the earlier approaches.

Keywords
CGM; Feature extraction; Hypo glycemia; Neural network; Prediction; RMSE
Safe zone for bone harvesting from the interforaminal region of the mandible

Al-Ani, O.; Nambiar, P.; Ha, K.O.; Ngeow, W.C.

Aims:
The mandibular incisive nerve can be subjected to iatrogenic injury during bone graft harvesting. Using cone beam computed tomography (CBCT), this study aims to determine a safe zone for bone graft harvesting that avoids injuring this nerve.

Methods:
Sixty CBCT examinations of patients were included in this study. The examinations were taken using the i-CAT CBCT imaging system, applying a standardized exposure protocol. Image reconstruction from the raw data was performed using the SimPlant dental implant software. The distances of mandibular incisive canal (MIC) to the inferior border and the labial and lingual cortices of the mandible were measured at 3, 5, 7 and 9 mm mesial to the mental foramen.

Results:
The MIC was visible in all (100%) CBCT images. The median distance and interquartile range from the lower border of the mandible was 9.86 (2.51) mm, curving downwards toward the inferior mandibular border at the symphysis menti. It was located closer to the buccal border of the mandible (3.15 [1.28] mm) than lingual cortex (4.78 [2.0] mm). The MIC curves toward the lingual side at the symphysis menti. There was gender difference in a number of these measurements. Current recommendation for chin bone graft harvesting can be applied to Asian subjects.

Conclusions:
While acknowledging that there is human variability, this study provides an accurate anatomic location of the MIC, which in turn helps to determine a safe zone for chin bone graft harvesting. This information can become a useful guide in centers where CBCT is not available.

Keywords: Clinical assessment; Diagnosis; Imaging; Morphometric analysis; Radiology
Larvae of *Aedes albopictus* obtained from dengue endemic areas in Selangor, Malaysia were evaluated for their susceptibility to operational dosage of temephos (1 mg/L). Larval bioassays were carried out in accordance to modified WHO standard methods. Biochemical microassay of enzymes in *Ae. albopictus* was conducted to detect the emergence of insecticide resistance and to define the mechanisms involved in temephos resistance. The 50% mortality lethal time (LT$_{50}$) for *Ae. albopictus* tested against temephos ranged between 58.65 to 112.50 minutes, with resistance ratio ranging from 0.75 - 1.45. This study addressed the fluctuation of time-related susceptibility status of *Ae. albopictus* towards insecticide. Significant difference on the weekly enzyme levels of non-specific esterases, mixed function oxidases and glutathione S-transferases was detected ($p \leq 0.05$). No significant correlation was found between temephos resistance and enzyme activity ($p > 0.05$). Only glutathione S-transferases displayed high level of activity, indicating that *Ae. albopictus* may be resistant to other groups of insecticide. The insensitive acetylcholinesterase was detected in some field collected *Ae. albopictus* populations, indicating the possibility of emergence of carbamate or other organophosphate resistance in the field populations. Continuous resistance monitoring should be conducted regularly to confirm the efficacy of insecticides for dengue control.
Towards an effective control programme of soil-transmitted helminth infections among Orang Asli in rural Malaysia. Part 2: knowledge, attitude, and practices

Nasr, N.A.; Al-Mekhlafi, H.M.; Ahmed, A.; Roslan, M.A.; Bulgiba, A.

Background

In the first part of this study, we investigated the prevalence and associated key factors of soil-transmitted helminth (STH) infections among Orang Asli children in rural Malaysia; an alarming high prevalence and five key factors significantly associated with infections were reported. Part 2 of this study aims to evaluate the knowledge, attitude and practices (KAP) on STH infections among Orang Asli in Peninsular Malaysia.

Methods

A cross-sectional study was carried out among 215 households from 13 villages in Lipis district, Pahang, Malaysia. Demographic and socioeconomic information of the participants and their KAP on STH were collected by using a pre-tested questionnaire.

Results

Overall, 61.4% of the participants had prior knowledge about intestinal helminths with a lack of knowledge on the transmission (28.8%), signs and symptoms (29.3%) as well as the prevention (16.3%). Half of the respondents considered STH as harmful, while their practices to prevent infections were still inadequate. Significant associations between the KAP and age, gender, educational and employment status, family size, and household monthly income were reported. Moreover, significantly lower prevalence of STH infections was reported among children of respondents who wear shoes/slippers when outside the house (72.8%; 95% CI= 62.6, 80.5 vs 87.0%; 95% CI= 81.4, 91.1), wash their hands before eating (32.4%; 95% CI= 24.3, 42.2 vs 51.4%; 95% CI= 44.7, 60.1), and wash their hands after defecation (47.8%; 95% CI= 35.7, 57.1 vs 69.2%; 95% CI= 63.7, 78.7) as compared to their counterparts. Multiple logistic regression analysis indicated that the educational level of the respondents was the most important factor significantly associated with the KAP on STH among this population.
Conclusion

This study reveals inadequate knowledge, attitude and practices on STH infections among Orang Asli in rural Malaysia. Hence, there is a great need for a proper health education programme and community mobilisation to enhance prevention and instil better knowledge on STH transmission and prevention. This is crucial for an effective and sustainable STH control programme to save the lives and future of the most vulnerable children in rural Malaysia.

Keywords

Knowledge; Attitude; Practice; Soil-transmitted helminths; Malaysia
Variable carbon catabolism among Salmonella enterica serovar typhi isolates.

Chai, L.C.; Kong, B.H.; Elemfareji, O.I.; Thong, K. L.

Background

Salmonella enterica serovar Typhi (S. Typhi) is strictly a human intracellular pathogen. It causes acute systemic (typhoid fever) and chronic infections that result in long-term asymptomatic human carriage. S. Typhi displays diverse disease manifestations in human infection and exhibits high clonality. The principal factors underlying the unique lifestyle of S. Typhi in its human host during acute and chronic infections remain largely unknown and are therefore the main objective of this study.

Methodology/Principal Findings

To obtain insight into the intracellular lifestyle of S. Typhi, a high-throughput phenotypic microarray was employed to characterise the catabolic capacity of 190 carbon sources in S. Typhi strains. The success of this study lies in the carefully selected library of S. Typhi strains, including strains from two geographically distinct areas of typhoid endemcity, an asymptomatic human carrier, clinical stools and blood samples and sewage-contaminated rivers. An extremely low carbon catabolic capacity (27% of 190 carbon substrates) was observed among the strains. The carbon catabolic profiles appeared to suggest that S. Typhi strains survived well on carbon substrates that are found abundantly in the human body but not in others. The strains could not utilise plant-associated carbon substrates. In addition, α-glycerolphosphate, glycerol, L-serine, pyruvate and lactate served as better carbon sources to monosaccharides in the S. Typhi strains tested.
Conclusion

The carbon catabolic profiles suggest that S. Typhi could survive and persist well in the nutrient depleted metabolic niches in the human host but not in the environment outside of the host. These findings serve as caveats for future studies to understand how carbon catabolism relates to the pathogenesis and transmission of this pathogen.
Comparative study on human and bovine AT-SC isolation methods

A.H. Reshak, M.M. Shahimin, F. Buang

Mammalian adipose tissue derived stem cells (AT-SC) have a tremendous potential in regenerative medicine for tissue engineering and somatic nuclear transfer (SNT). The isolation methods of human and bovine adipose tissue derived stem cells are compared in this paper to determine the feasibility and optimum method of isolation. The optimum isolation method will reduce the processing time, efforts and money as isolation is the first crucial and important step in stem cells research. Human abdominal subcutaneous adipose tissue and bovine abdominal subcutaneous adipose tissue are digested in three collagenase type 1 concentration 0.075%, 0.3% and 0.6% agitated at 1 h and 2 h under 37 °C in 5% CO₂ incubator. The cultures are then morphologically characterised. Human adipose tissue stem cells are found to be best isolated using abdominal subcutaneous depot, using 0.075% collagenase type 1 agitated at 1 h under 37 °C in CO₂ incubator. While bovine adipose tissue derived stem cells are best isolated using abdominal subcutaneous depot, using 0.6% collagenase type 1 agitated at 2 h under 37 °C in CO₂ incubator.

Keywords

Stem cell isolation; Human; Bovine; Abdominal subcutaneous adipose tissue
Surface electromyography for assessing triceps brachii muscle activities: A literature review

Asraf Ali, Kenneth Sundaraj, R. Badlishah Ahmad, Nizam Uddin Ahamed, Anamul Islam

The goal of this review was to summarise the scientific findings of research conducted on the triceps brachii muscle using surface electromyography. To achieve this goal, we searched through several articles available from the online databases ScienceDirect and SpringerLink published in the English language between January 2008 and June 2012. We specifically searched for the phrases “EMG” and “triceps brachii” in the title, abstract, keywords or methods sections. From a total of 569 articles we identified 77 potentially relevant studies where 42 studies have been examined triceps brachii muscle activity using surface electromyography that applied in the field of rehabilitation, physiological exercise, sports, and prosthesis control. Among the 42 articles found, 16 studies have been examined triceps brachii muscle activity in rehabilitation, 13 for physiological exercise, 9 for sports, and 4 for prosthesis control in this literature review. We therefore believe that the information contained in this review will greatly assist and guide the progress of studies that use surface electromyography to measure triceps brachii muscle activity in the context of rehabilitation, physiological exercise, sports, and prosthesis control.

Keywords
Triceps brachii muscle activity; Surface electromyography; Rehabilitation; Physiological exercise; Sports; Prosthesis control
The field of computer and robot-assisted rehabilitation system is rooted in the principle that software must be largely errorless, user-friendly, robust, accurate with respect to data, respond in a timely manner, and yet inexpensive, which lead to enhanced patient outcomes. In this digitized age, computerized and robotic rehabilitation systems act as a vital support for disabled individuals. Till today, different types of software for medical rehabilitation systems have been developed and applied to the rehabilitation process successfully, but improvement in quality and measurement of rehabilitation software is continuously in progress. Some ways of the software production have been established but further measurement process has always been a necessity. This paper presents the framework and recommends establishment of software quality measurement in computer- and robot-assisted automated medical rehabilitation system. Also, a brief discussion of rehabilitation technique and their software quality is also included. Lastly, we include its importance in medical technology and quality. To satisfy the end user, vendor satisfaction, software measurement and quality assurance are important components in software-based medical rehabilitation systems.
Analysis of right arm biceps brachii muscle activity with varying the electrode placement on three male age groups during isometric contractions using a wireless EMG sensor

Nizam Uddin Ahamed, Kenneth Sundaraj, R. Badlishah Ahmad, Matiur Rahman, Md. Anamul Islam

The purpose of this study was to quantify and analyze the muscle activity of the biceps brachii (BB) muscle from three different male age groups and varying the electrode placement on their muscles. Six subjects in three different age groups (adolescents, vicenarian and tricenarian) participated in this study. The electrodes were placed on one of three locations on the upper arm BB: muscle belly (M), upper muscle of the belly (U) and lower muscle of the belly (L). The current study shows some significant differences of muscle activeness among the three age groups and the electrode placement location. It indicates that there is difference in BB activity between adolescents and vicenarians, and between vicenarians and tricenarians ($p<0.05$), but no interaction between adolescents and tricenarians ($p>0.05$). According to statistical analysis, vicenarians' BBs are the most active, and then adolescents, and then tricenarians. The majority of the EMG results show that the muscle activity is highest in the lower portion of the muscle and decreases continuously up to the upper portion. Therefore, the present findings suggest that, EMG activity varies due to electrode placement and results are not similar for all age groups. Results are helpful for biceps rehabilitation, muscle coordination and other neuromuscular activities of the upper arms.

Keywords
Adolescent; Electromyography; Tricenarian; Vicenarian; Electrode placement
Modelling of PM$_{10}$ concentration for industrialized area in Malaysia: A case study in Shah Alam


In Malaysia, the predominant air pollutants are suspended particulate matter (SPM) and nitrogen dioxide (NO$_2$). This research is on PM$_{10}$ as they may trigger harm to human health as well as environment. Six distributions, namely Weibull, log-normal, gamma, Rayleigh, Gumbel and Frechet were chosen to model the PM$_{10}$ observations at the chosen industrial area i.e. Shah Alam. One-year period hourly average data for 2006 and 2007 were used for this research. For parameters estimation, method of maximum likelihood estimation (MLE) was selected. Four performance indicators that are mean absolute error (MAE), root mean squared error (RMSE), coefficient of determination ($R^2$) and prediction accuracy (PA), were applied to determine the goodness-of-fit criteria of the distributions. The best distribution that fits with the PM10 observations in Shah Alam was found to be log-normal distribution. The probabilities of the exceedences concentration were calculated and the return period for the coming year was predicted from the cumulative density function (cdf) obtained from the best-fit distributions. For the 2006 data, Shah Alam was predicted to exceed 150 μg/m$^3$ for 5.9 days in 2007 with a return period of one occurrence per 62 days. For 2007, the studied area does not exceed the MAAQG of 150 μg/m$^3$

**Keywords**

Particulate matter; Probability distributions; Performance indicators; Exceedences; Return period
Machine learning in lung sound analysis: A systematic review

Rajkumar Palaniappan, Kenneth Sundaraj, Nizam Uddin Ahamed

Machine learning has proven to be an effective technique in recent years and machine learning algorithms have been successfully used in a large number of applications. The development of computerized lung sound analysis has attracted many researchers in recent years, which has led to the implementation of machine learning algorithms for the diagnosis of lung sound. This paper highlights the importance of machine learning in computer-based lung sound analysis. Articles on computer-based lung sound analysis using machine learning techniques were identified through searches of electronic resources, such as the IEEE, Springer, Elsevier, PubMed and ACM digital library databases. A brief description of the types of lung sounds and their characteristics is provided. In this review, we examined specific lung sounds/disorders, the number of subjects, the signal processing and classification methods and the outcome of the analyses of lung sounds using machine learning methods that have been performed by previous researchers. A brief description on the previous works is thus included. In conclusion, the review provides recommendations for further improvements.

Keywords
Review; Lung sound; Lung disorder; Statistical; Machine learning
Early dementia questionnaire (EDQ): A new screening instrument for early dementia in primary care practice

Arabi Z., Aziz N.A., Abdul Aziz A.F., Razali R., Wan Puteh S.E.

Background:

Worldwide, the population is ageing, resulting in an associated increase in dementia prevalence. Forgetfulness in elderly people is often perceived as normal in some local cultures and thus, the early detection of dementia in primary care requires detection of symptoms other than memory complaints. This study was conducted to screen elderly patients for early dementia in primary care using a newly developed Early Dementia Questionnaire (EDQ) and comparing it with a standard assessment tool, the Mini Mental State Examination (MMSE).

Methods:

A cross-sectional study was conducted on a group of elderly patients using convenience sampling of consecutive patients. Elderly depression was excluded using the Geriatric Depression Scale (GDS). Exclusion criteria also included known cases of dementia. Inclusion criteria included a score of 5 or less in GDS and the presence of a reliable informant. A face-to-face interview was done using the EDQ with the patient and informant to elicit symptoms of early dementia. If the informant was not present, a telephone interview was used instead. The patient was then assessed with the Mini Mental State Examination (MMSE) using a cut-off point of 21.
Results:
Prevalence of dementia among 155 subjects was 52.3% by EDQ and 15.5% by MMSE. The EDQ demonstrated a sensitivity of 79.2% with specificity of 52.7%. Positive predictive value (PPV) of EDQ was 23.5% with the negative predictive value (NPV) of 93.2%. The strongest predictor of possible early dementia was complaints of memory problems (OR 26.22; 95% CI 2.03-338.14) followed by complaints of concentration problems (OR 14.33; 95% CI 5.53-37.12), emotional problems (OR 4.75; 95% CI 1.64-13.81) and sleep disturbances (OR 3.14; 95% CI 1.15-8.56). Socio-demographic factors, medical problems and smoking status were not associated with possible dementia (p>0.05), despite that 60-70% of the elderly had chronic illnesses.

Conclusion:
The EDQ is a promising alternative to MMSE for screening of early dementia in primary care.

Keywords
Dementia; Early dementia questionnaire; Mini mental state examination
Survey of atherosclerotic disease in Asian subjects with cardiovascular disease risk factors who were not receiving lipid-lowering agents


Background

Carotid intima media thickness (CIMT) is a surrogate marker for atherosclerosis, used to identify asymptomatic individuals at increased risk of cardiovascular events. The primary objective of this study was to obtain the distribution of CIMT measurements in Asian individuals with cardiovascular disease (CVD) risk factors who were not receiving lipid-lowering agents.

Methods

Mean CIMT based on ultrasonographic measurement of 12 sites within the common carotid artery was recorded for 2726 subjects across eight Asian countries who had two or more CVD risk factors but were not receiving lipid-lowering therapy. CVD risk factors and lipid and glucose profiles were analyzed with respect to distribution of CIMT and high-sensitivity C-reactive protein (hs-CRP) values.

Results

The overall mean (SD) of mean CIMT (mean–mean CIMT) was 0.662 (0.16) mm. There was a significant variation in mean–mean CIMT across countries (P < 0.0001). Mean–mean CIMT values (mm) by age were: 0.485, 0.527, 0.614, 0.665, 0.715 and 0.797 for ≤ 29, 30–39, 40–49, 50–59, 60–69 and ≥ 70 years, respectively. Multivariate analyses confirmed a significant association between increasing mean–mean CIMT and increasing age, male gender, low high-density lipoprotein-cholesterol (HDL-C) levels and elevated fasting blood glucose levels. Analysis of log-transformed hs-CRP levels showed significant association with increasing waist circumference, low-density lipoprotein-cholesterol, body-mass index, high blood glucose levels and low HDL-C.
Conclusions

Our data show normative mean–mean CIMT data for Asian subjects with two or more CVD risk factors who are not receiving lipid-lowering therapy, which may guide CVD risk-stratification of asymptomatic individuals in Asia.

Keywords

Carotid intima media thickness; Atherosclerosis; Cardiovascular disease risk factor; Ethnicity; Asia
The perception, level of safety satisfaction and safety feedback on occupational safety and health management among hospital staff nurses in Sabah state health department

Cheah W.L., Giloi N., Chang C.T., Lim J.F.

Background: This study aimed to determine the perception and level of safety satisfaction of staff nurses with regards to Occupational Safety and Health (OSH) management practice in the Sabah Health Department, and to associate the OSH management dimensions, to safety satisfaction and safety feedback.

Methods: A cross-sectional study using a validated self-administered questionnaire was conducted among randomly respondents.

Results: 135 nurses responded the survey. Mean (SD) score for each dimension ranged from 1.70 ± 0.68-4.04 ± 0.65, with training and competence dimension (mean [SD], 4.04 ± 0.65) had the highest while safety incidence was the least score (mean [SD], 1.70 ± 0.68). Both mean (SD) scores for safety satisfaction and safety feedback was high, 3.28 ± 0.51 and 3.57 ± 0.73, respectively. Pearson’s correlation analysis indicated that all OSH dimensions had significant correlation with safety feedback and satisfaction (r coefficient ranged from 0.176-0.512) except for safety incidence.

Conclusion: The overall perception of OSH management was rather low. Significant correlation between safety satisfaction and safety feedback and several dimensions, suggest that each organization to put in place the leaders who have appropriate leadership and supervisory skills and committed in providing staff training to improve staff’s competency in OSH practice. In addition, clear goals, rules, and reporting system will help the organization to implement proper OSH management practice.

Keywords: Hospital administration; Nurses; Occupational health; Safety management; Workplace
Perception of quality of life among people with diabetes


Diabetes is a chronic disease that affects a patient’s quality of life. This cross-sectional study aimed to determine the socio-demographic and disease profile factors associated with poor quality of life among patients with diabetes. The study was conducted at a primary health care clinic in Kuching between August to November 2010. Short Form -36 (SF - 36) questionnaire was used to assess the quality of life of diabetic patients aged ≥ 18. A total of 142 respondents participated in the survey. After adjusting for age, those with no education scored lower at vitality (p=0.043) and emotional health (p=0.033) compared with those who have tertiary education. Those working in the private sector scored better for physical functioning (p=0.042) compared with pensioners and the unemployed. Patients with uncontrolled diabetes scored lower in the role-emotional domain (p=0.003). Participants who were on <3 (p=0.014) and ≥3 (p=0.024) oral medications had better score for role-physical than those on insulin. Those on insulin had worse score for bodily pain than those on oral medication only (vs <3 oral drugs, p=0.026; vs ≥3 oral drugs, p=0.001). Various socio-demographic factors, uncontrolled diabetes and insulin usage were found to have negative impact on a diabetic patient’s quality of life. Programmes addressing the physical and emotional needs of diabetic patients at the primary health care setting are essential to help improve their quality of life.

Keywords
Diabetes mellitus; Medications; Primary health care; Quality of life; SF-36
Poor glycemic control in younger women attending Malaysian public primary care clinics: Findings from adults diabetes control and management registry

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Background: Women of reproductive age are a group of particular concern as diabetes may affect their pregnancy outcome as well as long-term morbidity and mortality. This study aimed to compare the clinical profiles and glycemic control of reproductive and non-reproductive age women with type 2 diabetes (T2D) in primary care settings, and to determine the associated factors of poor glycemic control in the reproductive age group women. Methods. This was a cross-sectional study using cases reported by public primary care clinics to the Adult Diabetes Control and Management registry from 1st January to 31st December 2009. All Malaysian women aged 18 years old and above and diagnosed with T2D for at least 1 year were included in the analysis. The target for glycemic control (HbA1c < 6.5%) is in accordance to the recommended national guidelines. Both univariate and multivariate approaches of logistic regression were applied to determine whether reproductive age women have an association with poor glycemic control. Results: Data from a total of 30,427 women were analyzed and 21.8% (6,622) were of reproductive age. There were 12.5% of reproductive age women and 18.0% of non-reproductive age women that achieved glycemic control. Reproductive age group women were associated with poorer glycemic control (OR = 1.5, 95% CI = 1.2-1.8). The risk factors associated with poor glycemic control in the reproductive age women were being of Malay and Indian race, longer duration of diabetes, patients on anti-diabetic agents, and those who had not achieved the target total cholesterol and triglycerides. Conclusion: Women with T2D have poor glycemic control, but being of reproductive age was associated with even poorer control. Health care providers need to pay more attention to this group of patients especially for those with risk factors. More aggressive therapeutic strategies to improve their cardiometabolic control and pregnancy outcome are warranted.

Keywords
Glycemic control; Registry; Reproductive age women; Type 2 diabetes mellitus
Diseases which are transmitted by vector mosquitoes are major health problems in many countries. Although many mathematical models for diseases had been formulated, they are customized. As these diseases are spread by a common vector, similarities in the disease transmission are notable hence it will be beneficial to construct a general model which encompasses the epidemiology aspects and transmission of mosquito-borne diseases. In this paper, a SI (Susceptible-Infectious) generic model for mosquito borne diseases is formulated. The model is made up of partial differential reaction-diffusion equations which incorporate both the human and mosquito populations. Numerical simulation of this model is presented.

Keywords

Diffusion; Mosquito-borne diseases; Spatial; Transmission model; Generic
Does ethnicity contribute to the control of cardiovascular risk factors among patients with type 2 diabetes?


This study aimed to examine the control of cardiovascular risk factors among the ethnic groups with type 2 diabetes in Malaysia. The authors analyzed the data of 70,092 adults from the Malaysian diabetes registry database. Malays had the worst achievement of target for most of the risk factors. Indians had poor achievement of control for waist circumference (odds ratio [OR] = 0.6, 95% confidence interval [CI] = 0.6-0.7) and high-density lipoprotein cholesterol (OR = 0.5, 95% CI = 0.4-0.5). As compared with the Malays, the Chinese had a better achievement of target control for the risk factors, including the following: body mass index (OR = 1.3, 95% CI = 1.2-1.4), blood pressure (OR = 1.3, 95% CI = 1.3-1.4), total cholesterol (OR = 1.7, 95% CI = 1.6-1.8), low-density lipoprotein cholesterol (OR = 1.7, 95% CI = 1.6-1.8), glycated hemoglobin A1c (OR = 1.4, 95% CI = 1.3-1.4) and fasting blood glucose (OR = 1.4, 95% CI = 1.3-1.5). Ethnicity, sociocultural factors, and psychobehavioral factors should be addressed in designing and management strategies for the control of cardiovascular risk factors among type 2 diabetes patients.

Keywords

Cardiovascular risk factors; Ethnic difference; Malaysia; Type 2 diabetes
Presence of Bacillus cereus s.l. from ready-to-eat cereals (RTE) products in Sarawak

Lesley M.B., Velnetti L., Yousr A.N., Kasing A., Samuel L.

Bacillus cereus is a soil inhabitant gram positive bacterium, and is known to cause severe food poisoning. The objective of this study was to isolate and identify the presence of Bacillus cereus s.l. from selected ready to eat cereals purchased randomly from local supermarkets in Kuching and Kota Samarahan, Sarawak. The result showed that four of the 30 food samples were detected to be contaminated by B. cereus s.l.. Our findings suggested that it is important for the public to be aware of the safety of RTE cereals consumption, as it is possible that B. cereus s.l. may be present in high count number and pose hazardous health effects to the consumers.

Keywords

Bacillus cereus s.l.; Ready-to-eat (RTE) cereals
Limb salvage in osteosarcoma using autoclaved tumor-bearing bone


Background:
Tumor prostheses currently give the best short- and medium-term results for limb-salvage reconstruction procedures in the treatment of bone tumors. However, in developing countries, the cost of a tumor prosthesis is beyond the reach of much of the population. We report the use of autoclaved tumor-bearing bone in 10 patients, as an affordable alternative to the use of prostheses.

Methods:
This is a case series of 10 patients (mean age 19 years) with osteosarcoma who were treated at our hospital from 1998 to 2008, and followed up for a mean of 35 months (range 14 to 8). The femur was involved in six cases, the humerus in three cases, and the ulna in one case. The mean length of the autoclaved bone was 150 mm (range 60-210).

Results:
Bone union occurred in seven patients over an mean duration of 12 months (range 8-17). Three patients had non-union. Two of these had associated implant failure, with one of them also developing chronic infection, and the third is still being followed up. Two other patients had local recurrence.

Conclusion:
The use of autoclaved tumor grafts provides an inexpensive limb-salvage option without sacrificing appropriate oncologic principles. A painless and stable limb is achievable, and the use of this technique can be further refined.
Genetic and phenotypic characterization of sylvatic dengue virus type 4 strains


Four serotypes of dengue virus (DENV 1–4) currently circulate between humans and domestic/peridomestic Aedes mosquitoes, resulting in 100 million infections per year. All four serotypes emerged, independently, from sylvatic progenitors transmitted among non-human primates by arboreal Aedes mosquitoes. This study investigated the genetic and phenotypic changes associated with emergence of human DENV-4 from its sylvatic ancestors. Analysis of complete genomes of 3 sylvatic and 4 human strains revealed high conservation of both the 5'- and 3'-untranslated regions but considerable divergence within the open reading frame. Additionally, the two ecotypes did not differ significantly in replication dynamics in cultured human liver (Huh-7), monkey kidney (Vero) or mosquito (C6/36) cells, although significant inter-strain variation within ecotypes was detected. These findings are in partial agreement with previous studies of DENV-2, where human strains produced a larger number of progeny than sylvatic strains in human liver cells but not in monkey or mosquito cells.

Keywords
Dengue virus (DENV); Sylvatic DENV; Human DENV; Phylogenetic and phenotypic analyses
Leptospirosis, an emerging zoonotic disease in Malaysia

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Leptospirosis is an endemic disease in Malaysia and recently has received increasing attention mainly due to several recent incidents that have resulted in human mortality which have alarmed health professionals in Malaysia. The increasing incidence of leptospirosis in forested regions is associated with the bacteria infecting small wild mammals other than rats. Infection in wildlife could result in the introduction of new serovars to humans and domesticated animals. More research on leptospirosis and the screening of wildlife and humans near wildlife habitats is required to have a better understanding of the involvement of wildlife in the disease.

Keywords

Infectious disease; Leptospirosis; Zoonotic disease; Wildlife
Systematic phylogenetic analysis of influenza A virus reveals many novel mosaic genome segments

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Recombination plays an important role in shaping the genetic diversity of a number of DNA and RNA viruses. Although some recent studies have reported bioinformatic evidence of mosaic sequences in a variety of influenza A viruses, it remains controversial as to whether these represent bona fide natural recombination events or laboratory artifacts. Importantly, mosaic genome structures can create significant topological incongruence during phylogenetic analyses, which can mislead additional phylogeny-based molecular evolutionary analyses such as molecular clock dating, the detection of selection pressures and phylogeographic inference. As a result, there is a strong need for systematic screenings for mosaic structures within the influenza virus genome database.

We used a combination of sequence-based and phylogeny-based methods to identify 388 mosaic influenza genomic segments, of which 332 are previously unreported and are significantly supported by phylogenetic methods. It is impossible, however, to ascertain whether these represent natural recombinants. To facilitate the future identification of recombinants, reference sets of non-recombinant sequences were selected for use in an automatic screening protocol for detecting mosaic sequences. Tests using real and simulated mosaic sequences indicate that our screening protocol is both sensitive (average >90%) and accurate (average >77%) enough to identify a range of different mosaic patterns. The relatively high prevalence of mosaic influenza virus sequences implies that efficient systematic screens, such as that proposed here, should be performed routinely to detect natural recombinant strains, potential laboratory artifacts, and sequencing contaminants either prior to sequences being deposited in GenBank or before they are used for phylogenetic analyses.

Keywords
Influenza A virus; Mosaic pattern; Recombination; Mosaic screening protocol
Determination of the required sample size with assurance for three-arm non-inferiority trials

Azmee N.A., Mohamed Z., Ahmad A.

The concept of assurance in the two-arm non-inferiority trials has been explored, expressing the noninferiority margin as a clinically meaningful treatment difference. This short paper focuses on developing an assurance formula in the three-arm non-inferiority trial, based on the ratio of means. The discussion starts with the simple case of known variances and then extends to the case of unknown but equal variances. To avoid complicated integration, assurance for the latter case was studied using Bayesian Clinical Trial Simulation (BCTS). The findings indicate that assurance allows the experimenter to formally take into account the uncertainty surrounding the parameter estimates by using the prior distributions. Furthermore, BCTS can be easily implemented to find the required sample size without having to resort to complex integration.

Keywords
Assurance, BCTS, Non-inferiority trial; Power, Three-arm design
Chitosan is a marine-derived product that has been widely used in clinical applications, especially in skin reconstruction. The mammalian scaffolds derived from bovine and porcine material have many limitations, for example, prion transmission and religious concerns. Therefore, we created a chitosan skin regenerating template (SRT) and investigated the behavior of fibroblast cell-scaffold constructs. Primary human dermal fibroblasts (HDF) were isolated and then characterized using vimentin and versican. HDF were seeded into chitosan SRT at a density of $3 \times 10^6$ cells/cm$^2$ for fourteen days. Histological analysis and live cells imaging revealed that the cell-chitosan constructs within interconnected porous chitosan showed significant interaction between the cells as well as between the cells and the chitosan. Scanning electron microscopy (SEM) analysis revealed cells spreading and covering the pores. As the pore sizes of the chitosan SRT range between 40-140 μm, an average porosity is about $93 \pm 12.57\%$ and water uptake ratio of chitosan SRT is $536.02 \pm 14.29\%$, it is a supportive template for fibroblast attachment and has potential in applications as a dermal substitute.

**Keywords**

Chitosan SRT; Human dermal fibroblasts; Interconnected pores; Three dimensional
Anti-tumour promoting activity and antioxidant properties of girinimbine isolated from the stem bark of *Murraya koenigii* S.

Kok Y.Y., Mooi L.Y., Ahmad K., Sukari M.A., Mat N., Rahmani M., Ali A.M.

Girinimbine, a carbazole alkaloid isolated from the stem bark of *Murraya koenigii* was tested for the *in vitro* anti-tumour promoting and antioxidant activities. Anti-tumour promoting activity was determined by assaying the capability of this compound to inhibit the expression of early antigen of Epstein-Barr virus (EA-EBV) in Raji cells that was induced by the tumour promoter, phorbol 12-myristate 13-acetate. The concentration of this compound that gave an inhibition rate at fifty percent was 6.0 µg/mL and was not cytotoxic to the cells. Immunoblotting analysis of the expression of EA-EBV showed that girinimbine was able to suppress restricted early antigen (EA-R). However, diffused early antigen (EA-D) was partially suppressed when used at 32.0 µg/mL. Girinimbine exhibited a very strong antioxidant activity as compared to α-tocopherol and was able to inhibit superoxide generation in the 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced differentiated premyelocytic HL-60 cells more than 95%, when treated with the compound at 5.3 and 26.3 µg/mL, respectively. However girinimbine failed to scavenge the stable diphenyl picryl hydrazyl (DPPH)-free radical.

**Keywords**

*Murraya koenigii*; Girinimbine; Anti-tumour promoting activity; Antioxidative; Superoxide
Identification of the major allergens of *Charybdis feriatus* (red crab) and its cross-reactivity with *Portunus pelagicus* (blue crab)

Misnun R., Murad S., Yadzir Z.H., Abdullah N.

**Background:**

Tropomyosin and arginine kinase have been identified as the major allergens in multiple species of crab. *Charybdis feriatus* is an important commercial crab in this country.

**Objective:**

To characterize the major allergens of *C. feriatus* using a proteomics approach and subsequently to identify the allergens involved in cross-reactivity with *Portunus pelagicus*.

**Methods:**

Raw and boiled extracts of the crabs were prepared from crab meat. The protein profile of the extracts was determined by SDS-PAGE and two-dimensional electrophoresis (2DE). Major allergens were identified by the immunoblotting test using sera from 50 patients with crab allergy. The major allergens were further identified by 2-DE immunoblotting. The major allergenic spots were then excised, digested by trypsin and identified by mass spectrometry analysis. The immunoblotting inhibition test was performed to study the crossreactivity between red crab and blue crab allergens using sera from 20 patients with allergy to both red and blue crabs.

**Results:**

At least 20 protein bands between 13 to 250 kDa were detected in the SDS-PAGE gel of raw extract, while boiled extract produced fewer protein bands. Proteins of 36 kDa and 41 kDa were recognized as the major allergens of the crab. The major allergenic spot sequences of the 36 and 41 kDa proteins were identified as crab tropomyosin and arginine kinase, respectively. All IgE-binding proteins, including both major allergens, were found to be cross-creative with *P. pelagicus* allergens.
Conclusions:

In addition to tropomyosin, arginine kinase was also identified as the major allergen of *C. feriatus* among our local crab-allergic patients. Cross-reactivity of this crab with *P. pelagicus* was demonstrated in this study.

Keywords

Arginine kinase; *Charybdis feriatus*; Cross-reactivity; Major allergen; *Portunus pelagicus*; Tropomyosin
The development of a computerized acoustical characterization system of medical phantoms is described in this paper. The system employs the insertion technique and it was developed using LabView 2011 where the ultrasound signal was acquired through the interfacing scheme of an oscilloscope to a personal computer. The system performance was validated by comparing measured acoustical properties with values obtained from the previous studies. Other than faster measurement time, the developed system carried percentage difference at less than 1.00% for all of the acoustical properties measurements at 23.0°C to 25.0°C respectively.

**Keywords**

Acoustical properties; Computerized acoustical characterization system; Insertion technique; Medical phantom
The use of the precautionary principle to the area of environmental management and sustainability is largely in response to the necessity of each individual state to protect rights and interests in order to safeguard the Mother Nature. Therefore, this study examines the use of the precautionary principle in the Malaysian food hygiene regulations in relation to the environmental management and sustainability from the legal perspectives; identify actions, which deal with the protection of the environment as well as a tool for the achievement of sustainable development.

Keywords

Environmental management and sustainability; Health and food hygiene safety; Precautionary principle
Identification of parvalbumin and two new thermolabile major allergens of *Thunnus tonggol* using a proteomics approach

Rosmilah M., Shahnaz M., Meinir J., Masita A., Noormalin A., Jamaluddin M.

**Background:**

The longtail tuna (*Thunnus tonggol*) is widely consumed in Asia. Parvalbumin, the main major allergen of fish, has been well identified in multiple fish species, yet little is known about the allergenic proteins in *T. tonggol*. Thus, the aim of this study was to characterize the major allergens of *T. tonggol* using a proteomics approach.

**Methods:**

Raw and boiled extracts of the fish were prepared. Fish proteins were separated by means of SDS-PAGE and two-dimensional (2-DE) electrophoresis. 1-DE immunoblotting of raw extract was performed with sera from fish-allergic patients. Ten sera were further analysed by 2-DE immunoblotting. Selected major allergenic protein spots were excised, trypsin digested and analysed by means of mass spectrometry.

**Results:**

SDS-PAGE of raw extract revealed 26 protein fractions, while boiled extract demonstrated fewer bands. The 2-DE gel profile of the raw extract further fractionated the protein bands to more than 100 distinct protein spots. 1-DE immunoblotting of raw extract exhibited two thermolabile protein fractions of 42 and 51 kDa as the major allergens, while the boiled extract only revealed a single IgE-binding band at 151 kDa. 2-DE immunoblotting of raw extract further detected numerous major IgE-reactive spots of 11-13, 42 and 51 kDa. Mass spectrometry analysis of the peptides generated from the 12, 42 and 51 kDa digested spots indicated that these spots were parvalbumin, creatine kinase and enolase, respectively.
Conclusions:

In addition to parvalbumin, two new thermolabile allergens were identified as major allergenic proteins of *T. tonggol*. This study proved that both thermostable and thermolabile proteins are important in local tuna allergy and should be included in diagnostic strategies.

**Keywords**

Fish allergy, Immunoblotting, Mass spectrometry, SDS-PAGE, *Thunnus tonggol*, Tuna, Two-dimensional electrophoresis
Identification of major and minor allergens of black tiger prawn (*Penaeus monodon*) and king prawn (*Penaeus latisulcatus*)

Sahabudin S., Misnan R., Yadzir Z.H.M., Mohamad J., Abdullah N., Bakhtiar F., Murad S.

**Background:** Prawns and shrimp are a frequent cause of seafood allergy mediated by IgE antibodies. *Penaeus monodon* and *Penaeus latisulcatus*, commonly known as black tiger prawn and king prawn, respectively, are among the most frequently consumed prawns in Malaysia. The aim of this study was to identify the IgE-binding proteins of these 2 prawn species.

**Methods:** Raw and boiled prawn extracts were prepared and then resolved by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE). IgE-immunoblotting was then performed using sera from patients with positive skin prick tests to the raw prawn extracts.

**Results:** SDS-PAGE analysis of the raw extracts of both prawn species revealed 23 protein bands; the boiled extracts yielded fewer protein bands. The bands in the range of 40 to 100 kDa were sensitive to heat and therefore were not found in the boiled extracts. Immunoblot of raw extracts of black tiger prawns and king prawns yielded 14 and 11 IgE-binding proteins, respectively, with molecular weights of between 15 and 200 kDa. Proteins at 36, 42, and 49 kDa were detected as the major allergens in both species of prawns. A protein of 75 kDa was also identified as a major allergen in black tiger prawns. Other potential allergens were also observed at various molecular masses.

**Conclusion:** Proteins of 36, 42, and 49 kDa were identified as the major allergens of both species of prawns. The 36 and 42 kDa proteins are hypothesised to be tropomyosin and arginine kinase, respectively. A high molecular weight protein of 75 kDa was found to be an additional major allergen in black tiger prawns.

**Keywords**

Allergens; Allergy and clinical immunology; Hypersensitivity; Immunoblotting; *Penaeus*; Tropomyosin
Dengue disease mapping in Malaysia based on stochastic SIR models in human populations

Samat N.A., Percy D.F.

Relative risk estimation is one of the most important issues in the study of geographical distributions of disease occurrence or disease mapping. For the case of dengue, there are only a few studies that use statistical methods to estimate the relative risk for disease mapping. Therefore this research will introduce an alternative method to estimate the relative risk of dengue occurrence based initially on discrete-time, discrete-space stochastic SIR models (Susceptible-Infective-Removed) in human populations for dengue disease transmission, to overcome the drawbacks of relative risk estimation in disease mapping using a classical method based on standardized morbidity ratio (SMR), and the earliest example of Bayesian mapping which involves a Poisson-Gamma model. The estimation of relative risk is applied to dengue data in Malaysia which will then be displayed in a map to represent the high and low risk areas of dengue occurrence.

Keywords

Dengue disease; Disease mapping; Relative risk; SIR models; Stochastic model
Vector-borne infectious disease mapping with stochastic difference equations: An analysis of dengue disease in Malaysia

Samat N.A., Percy D.F.

Few publications consider the estimation of relative risk for vector-borne infectious diseases. Most of these articles involve exploratory analysis that includes the study of covariates and their effects on disease distribution and the study of geographic information systems to integrate patient-related information. The aim of this paper is to introduce an alternative method of relative risk estimation based on discrete time-space stochastic SIR-SI models (susceptible-infective-recovered for human populations; susceptible-infective for vector populations) for the transmission of vector-borne infectious diseases, particularly dengue disease. First, we describe deterministic compartmental SIR-SI models that are suitable for dengue disease transmission. We then adapt these to develop corresponding discrete time-space stochastic SIR-SI models. Finally, we develop an alternative method of estimating the relative risk for dengue disease mapping based on these models and apply them to analyse dengue data from Malaysia. This new approach offers a better model for estimating the relative risk for dengue disease mapping compared with the other common approaches, because it takes into account the transmission process of the disease while allowing for covariates and spatial correlation between risks in adjacent regions.

Keywords
Dengue disease; Disease mapping; Relative risk; SIR-SI models; Tract-count data
Identification of major allergens of wildflower honey

Yadzir Z.H.M., Misnan R., Abdullah N., Arip M., Murad S.

The aim of this study was to identify the major allergens of wildflower honey in local patients with atopic disease. SDS-PAGE revealed ten protein bands of 25 to 110 kDa, with a heavy cluster in region of 40-75 kDa. Immunoblotting demonstrated seven IgE-binding bands of 39 to 110 kDa. The 60 kDa protein had the highest frequency of IgE-binding (100%) followed by 54 kDa protein (95%), thus identified as the major allergens of wildflower honey. Our findings indicate that the allergen extract used for diagnosis of honey allergy contains both the 54 kDa and 60 kDa proteins.

Keywords

Allergens; Atopic disease; SDS-PAGE; Wildflower honey
Hibiscus sabdariffa aqueous extracts prevents progression of acute liver injury induced by acetaminophen

Ahmad-Raus, R., Jamal, P. and Mohd-Isa, E. S.

Hibiscus sabdariffa (local name Roselle) is usually used as a beverage in Southeast Asia. It has been shown that this plant has benefits to the health in term of improving diabetes and hyperlipidemia conditions. In this study, the effect of H. sabdariffa aqueous extracts in preventing acute liver injury progression in rats induced by acetaminophen (or paracetamol, PCM) was investigated. Results of the current study showed that intravenous injection of PCM at 1000 mg/kg induced lipid peroxidation (malonaldehyde, MDA) and deteriorated liver marker enzymes (alanin transaminase, ALT and glutathione S-transferase, GST), as well as liver glutathione (GSH) and liver morphology. Feeding H. sabdariffa extract orally (500 or 1000 mg/kg) for three days after the PCM treatment was found to have significantly reduced lipid peroxidation. The depleted GSH observed in the affected liver returned to almost normal, while the liver marker enzyme, ALT and GST levels were improved by giving the extract. In histological examination, the H. sabdariffa extract was shown to have reduced the incidence of liver damage. However, a high dose of H. sabdariffa treatment to the untreated rats increased liver MDA and GST and serum ALT levels, although at a much lower level than the PCM-treated rats. Hence, the liver histology of these rats remains normal. In conclusion, the current study has shown that the post-treatment of H. sabdariffa prevents the progression of acute liver damage induced by PCM. However, the consumption of the plant at high dosage should be taken with caution.

Keywords
Hibiscus sabdariffa; Paracetamol; Liver toxicity; MDA; GSH; GST; ALT
An Audit of Type 2 Diabetes Care in a Malaysian Public Community Polyclinic


Adequate and proper diabetes care in any practice is paramount and deems to be the fundamental requirement for good diabetes control. This is an audit of type 2 diabetes care process in a public Polyclinic, with the objectives of studying the quality of diabetic care provided in terms of clinical and managerial performance and also to give recommendations on improving its diabetes care delivery. The audit was done on patients’ medical records selected via systematic random sampling. Patients who have been diagnosed with type 2 diabetes mellitus for more than 2 years, and those who have come for follow-up at least twice in between 1st October 2008 and 30th September 2009 by the medical officer and/or family medicine specialist. Patients with gestational diabetes mellitus and Type 1 diabetes mellitus were excluded. A total of 100 medical records were audited. 51% were female and 82% were in the 40-69 age group. Measurements of blood glucose and blood pressure were done at each follow-up at the polyclinic at 96% and 93% of the times, respectively. Within the past one year, HbA1c was performed in 46% of the patients, while renal profile was screened in 66% of the patients and urine protein was tested in 59% of the diabetics. Only 15% had their eyes screened by fundus camera. The diabetes care process at this public polyclinic was unsatisfactory, as many annual blood tests were not done and complications screening were also omitted. Thus, an urgent intervention is recommend in order to rectify these inadequacies.

Keywords
Type 2 diabetes mellitus; Health care deliveries; Medical audit; Community polyclinic
Mas Cotek (Ficus deltoidea): A Possible Supplement for Type II Diabetes: (A Pilot Study)

S. Draman, M. AM Aris, Razman1, Akter SFU, Azlina H., Nor Azlina A. R, Muzaffar , Norazlanshah H. and Azian

The aim of this research was to study the effect of the Ficus deltoidea (Mas Cotek) leaves on fasting bloodsugar, renal and lipid profile of Type II diabetic patients. This study was carried out at Polyclinic Balok, located in Kuantan, Pahang, Malaysia. Twenty patients participated in the study and they were divided intotwo (2) groups of ten (10) patients each. The inclusion criteria were registered as diabetic patients in the healthcentre, diagnosed as type II diabetes mellitus for more than one (1) year, age 18 years and above, HbA1c more than 6.5% and have contactable telephone number. The patients in the intervention group has been given F.deltoidea 350 mg twice daily orally and monitored every 20 days for two (2) months. In conclusion, the effectson fasting blood sugar, HbA1C, renal and lipid profiles were not significant. The patients in the intervention group felt energetic and fresh compared to the control.

Keywords
Diabetes mellitus; Energetic; Fasting blood sugar; Feeling fresh; Ficus deltoidea; Lipid profile; Renal profile
The Effects of Combined Training on Interleukin-6 and C Reactive Protein as Non-traditional Cardio Risk Factors in Inactive Students

Esmaelzadeh, M. R., Soh, K. G., Abdullah, M. N. H. and Bahaman, A. A.

Studies have shown a positive association between regular physical activity and reduction of cardio risk factors. The objective of this research was to examine the effects of combined training on some cardio risk factors in inactive students. Thirty healthy inactive men were assigned into two groups: 1) combined training (CTG) (n=15), 2) no-training (NTG) (n=15). The CTG performed 5 resistance exercises and this was followed by 30 minutes of endurance training with 60%-80% HRmax for 8 weeks (3 days per week). Meanwhile, the NT group continued the same activity routine that they had used prior to becoming a study participant. Pre- and post-measures included VO_2max, muscle strength, body composition, and blood cardio risk factors. The VO_2max and muscle strength significantly (P<0.05) increased in CTG. The percentage of body fat tended to slightly decrease (P>0.05) and skeletal muscle mass significantly increased in CTG (+0.85kg, P = 0.003). However, these parameters did not show any change in NTG. The concentrations of total cholesterol, TG and LDL in the blood did not significantly change during the study in the two groups (P> 0.05). HDL significantly improved after week 8 of combined training in the CTG. Furthermore, CRP did not change in the two groups (P> 0.05), while the level of interleukin-6 had decreased significantly in the CTG. The results of this study have shown that combined training improves some cardio risk factors, cardiorespiratory fitness, as well as muscle strength and body composition in inactive students.

**Keywords**

Body composition; Exercise training; Muscle strength; Inflammatory biomarkers; Lipid profiles and VO_2max
The study aimed to investigate family caregivers’ experiences of caring to a schizophrenia patient in the northern part of Malaysia. The family caregiving experiences from different ethnic groups in Malaysia were compared between urban and rural dwellers. Overall, there were 154 family caregivers who completed the questionnaires comprising standardized measures of the Experiences of Caregiving Inventory (ECI) and the Life Skills Profiles (LSP-39). Malay women were found to be the majority of the caregivers in this study who mostly came from the rural area. This study found that the majority of caregivers were Malay women who live in the rural area. Most of the caregivers identified themselves as parents aged 50 years and above. Predictors of negative appraisal for family caregivers were identified: (1) younger patient, (2) unemployed patient, (3) family with low income and (4) patient with low life skills. Meanwhile, predictors of positive appraisal include: (1) married patient, (2) patient with good life skills, (3) monthly income above RM800 and (4) dwelling in urban area. Interestingly, the life skills profile becomes a strong predictor for negative and positive appraisals. These predictors should assist community health workers when working with the family caregivers of schizophrenia patient.
Understanding the Perception Concerning Medication and Types of Adherence Behaviour in Hypertensive Patients

Lee, K., Halimatun, H. M., Steven, E. K. and Ong, B. K.

Hypertension is a significant public health problem. Despite the availability of effective treatment, non-adherence to treatment has been identified as the main cause of failure in controlling hypertension. The fragmented pattern of research related to adherence is unavoidable because it is a complex phenomenon and affects not only the health of patients but also their entire lives. The research gap in this field is the absence of the patients’ perspective and a dearth of qualitative research. The aim of this study was to understand the patients’ perception concerning medication and the extent that these perceptions are reflected in adherence behaviour. This is a qualitative exploratory study on hypertensive patients in a community health clinic in the state of Selangor, Malaysia. It was found that the participants perceive prescribed Western Medicine (WM) from the clinic as scientifically proven but has undesirable side effects. Therefore, Complementary and Alternative Medicine (CAM) are used to counteract the harmful effects of WM. The types of adherence behaviour found include faithful follower, self-regulator and intentional non-adherer. The reason to engage in particular adherence behaviour indicates a contextual relationship with the perception concerning the medication. Thus, it was concluded that patients acquire knowledge phenomenologically to cope with hypertension. Therefore, to improve self-management and self-efficacy in adherence with treatment, patient-tailored education and an empowerment approach should be introduced.

Keywords
Adherence; Hypertension; Medication; Perceptions; Qualitative research
Soil Factors Influencing Heavy Metal Concentrations in Medicinal Plants

Dayang S. N. and I. Che Fauziah

This study was conducted with the aim of finding soil factors which influence heavy metals uptake by medicinal plants. The heavy metal concentrations in medicinal plants at 3 different sites (different soil types) and the soils on which the plants grow were analysed. From the correlation analysis, soil properties affect all of the heavy metal concentrations in soils, meanwhile, only Cu and Se concentrations in soils affect their uptake by plants. However, this depends on plant parts (root and foliar), and the soil types. Principal component analysis (PCA) was also conducted to ascertain any patterns in the soil samples in relation to soil chemical characteristics and reinforce the findings from the correlation analysis. From the principal component analysis in this study, total Pb and As concentrations in medicinal plants were correlated with their concentrations in soils; however, they vary according to the soil types.

Keywords

Heavy metals; Medicinal plants; Soil properties; Agriculture input; Correlation analysis; Principal component analysis
Review on the Effects of Probiotics and Antibiotics towards *Clostridium difficile* Infections

Hazirah, A., Loong, Y. Y., Rushdan, A. A., Rukman, A. H. and Yazid, M. M.

*Clostridium difficile* can cause severe diseases with significant morbidity and mortality in infected patients. The rate of *Clostridium difficile* infection is high in North America and European countries. Metronidazole and vancomycin have been recommended as the treatments of choice since 1990s. Recurrent infection due to *Clostridium difficile* is common after several days of antibiotic administration. Probiotics have been used in these patients as an adjunct treatment with some successful findings. However, a detailed investigation on the use of probiotic for infected patients is still needed, particularly for its real efficacy.

**Keywords**

*Clostridium difficile*; Probiotic; Antibiotic
Effect of Breed on cis-9, trans-11 and trans-10, cis-12 Conjugated Linoleic Acids (CLA) Concentrations in Milk Fat of Dairy Cattle and the Relationship of These CLA with other Unsaturated C18 Fatty Acids


Much attention has been given to unsaturated carbon 18 fatty acids in milk, particularly conjugated linoleic acids (CLAs) which have a beneficial effect on human health. This study was undertaken to investigate the effect of breed on cis-9, trans-11 and trans-10, cis-12 CLA isomers in the milk fat of dairy cattle and their relationship with other unsaturated carbon 18 fatty acids. Mafriwal (n=15) and Jersey (n=15) cows were at mid-lactation period, grazed on pasture and given 5.5kg of concentrate per head daily. The composition of milk fatty acid was determined using gas chromatography after the extraction of milk fat using the modified Folch’s method. The results showed that breed had an effect on cis-9, trans-11 CLA deposition in milk fat. The level of cis-9, trans-11 CLA in milk fat of Mafriwal was significantly higher (P<0.05) than that of the Jersey cows, while the levels of trans-10, cis-12 CLA were not significantly different between the two breeds. The levels of cis-9, trans-11 CLA were positively correlated with the concentration of trans-11-octadecenoic (C18:1), cis-9-octadecenoic (C18:1) and octadecatrienoic (C18:3) acids. A positive correlation was also observed between the levels of trans-10, cis-12 CLA and octadecatrienoic (C18:3) acid in milk fat. These results indicated that breed selection could be used to improve the quality of milk for human consumption.

Keywords
Breed; Dairy cattle; Conjugated linoleic acids; Milk fat; Unsaturated carbon 18 fatty acids
The Use of Plants to Improve Indoor Air Quality in Small Office Space

Aini Jasmin, G., Noorizan, M., Suhardi, M., Murad, A. G. and Ina, K.

Exposure to volatile organic compounds (VOC) can cause a series of effects towards human health. VOC is also associated with Sick Building Syndrome and other building related illnesses. Common materials found in every home and place of business may cause elevated exposure to toxic chemicals. The aim of this study was to examine the best indoor plants that could be used to improve indoor air quality in a small office space. In this study, the concentration of VOC inside a room was monitored before and after the test, using Aeroquol Model S500 VOC Gas Detector and by using oil-based paint painted on a panel measuring 0.05 x 0.05 m in order to create a minimum of 3ppm of VOC. Three types of tropical indoor plants were used in this study; Nephrolepis exaltata, Rhapis excelsa and Dracaena fragrans. Data were monitored for eight hours at 10 minutes interval. The results showed no significant differences between the number of pots and the type of plants used in reducing VOC content in the real room environment. This was probably due to several factors, such as the interference of outside air and the condition of the experimental room. This experiment suggests that further experiments should be carried out in a controlled environment to improve our knowledge of how indoor plants can improve indoor air quality, and thus improve human health and well-being.

Keywords

Human health; Indoor air quality; Tropical indoor plants; Volatile organic compounds (VOC)
The outbreak of food poisoning due to *Staphylococcus aureus* has been reported with a significant level of morbidity worldwide. In this study, 128 samples taken from nasal swabs of 64 food handlers and 64 food items were collected and analyzed for the presence of *S. aureus*. The antibiotic susceptibility profiles of the isolates were also determined. Cross-sectional was used as a study design in this research. The isolates were identified as *S. aureus* based on colonial morphology, gram stain, mannitol salt agar fermentation, catalase and coagulase test. Fifteen (23.4%) of food handlers were positive for *S. aureus* nasal carriage and 24 (37.5%) of food items were contaminated with an average of 8.4 x 10^6 CFU/g of *S. aureus*. All isolates were susceptible to oxacillin and mupirocin respectively. However, 74.4% and 5.1% isolates were resistant to penicillin and erythromycin. Our findings suggest that the prevalence of *S. aureus* carriage is high among our food handlers and food items. Thus, we believed that there is a need for proper training on food safety among food handlers and quality improvement in the food premises.

**Keywords**

Food poisoning; Food handlers; Nasal carriers; *Staphylococcus aureus*
Consumption of the aqueous leaf extract of Nauclea latifolia as anti-malaria concoction without any recourse or regard for its safety is a common practice in the Northern Nigeria. The aim of this study was to evaluate the safety efficacies of the ingestion of the methanolic leaf extract of this plant on the liver and kidney functions in wistar albino rats. Acute toxicity tests were carried out to determine LD$_{50}$, while sub-chronic toxicity study was carried out by oral administration of graded doses (200, 400, 800, 1600 and 3200mg/ Kg) of the extract to different groups of rats for 30 days. Both the liver and kidney functions assessed biochemically using standard methods revealed the LD$_{50}$ of N. latifolia at 3200mg/Kg body weight as being non-lethal. Meanwhile, biochemical and histological results obtained for the liver and kidney function parameters indicated that ingestion of N. latifolia leaf extract has no observable toxic effects on these organs at the tested doses. It was therefore suggested that these results could form the basis for clinical trial in human.

**Keywords**

Hepatotoxicity; *Nauclea latifolia* nephrotoxicity; Wistar albino rats
Contribution of Attachment in Children’s Separation Anxiety

Sakineh Mofrad, Rohani Abdullah and Ikechukwu Uba

Literature suggests that child attachment and anxiety symptoms are related. The purpose of the present study was to assess whether attachment patterns related differently to separation anxiety symptoms (fear of being alone, and fear of abandonment). Three attachment patterns assessed were secure, avoidant and ambivalent attachment. The findings indicated that ambivalent attachment was related with higher separation anxiety symptoms (r=.57) compared to avoidant attachment (r=.53). More so, ambivalent attachment was also related to the fear of abandonment (r=.52), while avoidant attachment was related with the fear of being alone (r=.63). In conclusion, consistently responsive mothers are always receptive and supportive of their children’s mental health.

Keywords
Attachment; Separation anxiety; Avoidance; Ambivalence
Relationship between defense mechanisms and coping styles among relapsing addicts

Abd Halim, M. H.; Sabri, Farhana

Defense mechanisms and coping styles are dissimilar in terms of the cognitive operations involved. This study aims to determine the pattern of defense mechanisms and coping styles and its association among relapsing addicts. A descriptive-correlational research design and a multi-stage sampling method were applied in the sample selection process. A total of 120 respondents, randomly selected from four centers in the central zone of Peninsular Malaysia, were involved in this study. The findings of the study indicate that neurotic defense mechanisms (M=12.46, S.D=2.14) and task-oriented coping style (M=58.67, S.D=10.06) are the most used by relapsing addicts. The neurotic and maturity defense mechanisms are significantly correlated to all three types of coping styles, while the immaturity defense mechanisms were found to be correlated with emotion-oriented coping style. These findings demonstrate that relapsing addicts employ multiple defense mechanism styles and all these styles confirm the existence and nature of sub-cultures in addiction. Associations found between these two variables indicate a need to incorporate the elements of defense mechanisms and coping styles in relapse prevention counseling.

Keywords

Defense mechanisms; Coping styles; Relapsing addicts
The anthelmintic efficacy of papaya latex in a rodent-nematode model is not dependent on fasting before treatment

Luoga, W.; Mansur, F.; Buttle, D. J.; et al.

In earlier studies of the anthelmintic activity of plant cysteine proteinases (CPs), a period of food deprivation was routinely employed before administration of CPs, but there has been no systematic evaluation as to whether this does actually benefit the anthelmintic efficacy. Therefore, we assessed the effect of fasting on the efficacy of CPs from papaya latex (PL) against *Heligmosomoides bakeri* in C3H mice. We used a refined, supernatant extract of papaya latex (PLS) with known active enzyme content. The animals were divided into three groups (fasted prior to treatment with PLS, not fasted but treated with PLS and fasted but given only water). The study demonstrated clearly that although food deprivation had been routinely employed in much of the earlier work on CPs in mice infected with nematodes, fasting has no beneficial effect on the efficacy of PLS against *H. bakeri* infections. Administration of CPs to fed animals will also reduce the stress associated with fasting.
Systematic review of safety in paediatric drug trials published in 2007

Aripin, Khairun Nain Bin Nor; Choonara, Imti; Sammons, Helen M.

There is now greater involvement of children in drug trials to ensure that paediatric medicines are supported by sound scientific evidence. The safety of the participating children is of paramount importance. Previous research shows that these children can suffer moderate and severe adverse drug reactions (ADRs) in clinical trials, yet very few of the trials designated a data safety monitoring board (DSMB) to oversee the trial.

Safety data from a systematic review of paediatric drug randomised controlled trials (RCTs) published in 2007 were analysed. All reported adverse events (AEs) were classified and assessed to determine whether an ADR had been experienced. ADRs were then categorised according to severity. Each trial report was examined as to whether an independent DSMB was in place.

Of the 582 paediatric drug RCTs analysed, 210 (36%) reported that a serious AE had occurred, and in 15% mortality was reported. ADRs were detected in more than half of the RCTs (305); 66 (11%) were severe, and 79 (14%) were moderate. Severe ADRs involved a wide range of organ systems and were frequently associated with cytotoxic drugs, antiparasitics, anticonvulsants and psychotropic drugs. Two RCTs reported significantly higher mortality rates in the treatment group. Only 69 (12%) of the RCTs stated there was a DSMB. DSMBs terminated five RCTs and changed the protocol in one.

Children participating in drug RCTs experience a significant amount and a wide range of ADRs. DSMBs are needed to ensure the safety of paediatric participants in clinical drug trials.

Keywords
Paediatric clinical trials; Adverse drug reactions (ADRs); Drug safety; Data safety monitoring boards (DSMBs); Systematic review
Organotypic culture of human amnion cells in air-liquid interface as a potential substitute for skin regeneration


**Background aims:** The aim of the present study was to evaluate the effects of air-liquid interface on the differentiation potential of human amnion epithelial cells (HAECs) to skin-like substitute in organotypic culture.

**Methods:** HAECs at passage 1-2 were seeded onto a fibrin layer populated with human amnion mesenchymal cells to form the organotypic cultures. The organotypic HAECs were then cultured for 7, 14 and 21 d in two types of culture system: the submerged culture and the airliquid interface culture. Cell morphogenesis was examined under the light and electron microscopes (transmission and scanning) and analyzed by immunohistochemistry.

**Results:** Organotypic HAECs formed a single layer epithelium after 3 wk in submerged as well as air-liquid interface cultures. Ultrastructurally, desmosomes were observed in organotypic HAECs cultured in the air-liquid interface but not in the submerged culture. The presence of desmosomes marked the onset of early epidermal differentiation. Organotypic HAECs were positive against anti-CK18 and anti-CK14 in both the submerged and the air-liquid interface cultures. The co-expression of CK14 and CK18 suggested that differentiation of HAECs into skin may follow the process of embryonic skin development. However, weak expression of CK14 was observed after 2 and 3 wk of culture in air-liquid interface. CK10, involucrin, type IV collagen and laminin-5 expression was absent in organotypic HAECs. This observation reflects the initial process of embryonic epidermal differentiation and stratification.

**Conclusions:** Results from the present study suggest that the air-liquid interface could stimulate early differentiation of organotypic HAECs to epidermal cells, with a potential use for skin regeneration.

**Keywords**
- Air-liquid interface
- Epithelial stem cells
- Fibrin
- Human amnion–derived stem cells
- Organotypic culture
- Skin regeneration
Porphyromonas gingivalis peptidylarginine deiminase substrate specificity


While a group of oral commensals have been implicated in the aetiology of chronic periodontitis; the asaccharolytic Gram negative anaerobe Porphyromonas gingivalis is most commonly reported to be associated with severe forms of the disease. Although a variety of human tissues can produce a number of peptidylarginine deiminase (PAD), enzymes that convert peptide bound arginine residues to citrulline, *P. gingivalis* is one of the few prokaryotes known to express PAD. Protein and peptide citrullination are important in the development of rheumatoid arthritis and in recent years a number of authors have suggested a possible link between periodontitis and rheumatoid arthritis (RA). Indeed, some have linked *P. gingivalis* directly to RA via the action of PAD. Accordingly, the prime purpose of this study was to further characterise PAD in *P. gingivalis* cells particular emphasis on substrate specificity, using arginine containing peptides and RA relevant proteins.

**Methods:** *P. gingivalis* W50 was anaerobically cultured in BHI broth, cells harvested and resuspended in assay buffer. A colourimetric assay was developed to measure citrulline and employed to determine enzyme activity using the substrate BAEE. The assay was employed to investigate the effects of environmental pH and temperature on activity. Citrullination of BAEE by sonicated cells allowed the proportion of intracellular enzyme to be estimated. Enzyme specificity and substrate preference were investigated by using various arginine containing peptides, proteins and arginine analogues, as substrates and measuring the rate of citrullination. The influence of gingipains on citrullination was assessed by measuring the rates of citrullination of bovine serum albumin in the presence of protease inhibitors.

**Results:** Enzyme activity decreased by 13% following exposure of cells to 60°C for 10min. A comparison of intact and disrupted cells indicated that 90% of PAD activity is cell surface associated and the remainder cytoplasmic. Optimal pH for enzyme activity was between pH 7.5 and 8. All small arginine-containing peptides were citrullinated with reaction rates faster than that for free arginine with rates that varied with arginine residue position and number. Arginine analogues exhibited minimal effect and influence when tested as either substrates or competitive inhibitors. Cells were able to citrullinate yeast enolase,
human vimentin and fibrin at varying rates. All proteins were modified at slower rates than those for peptide substrates. Inhibition of gingipains had no influence on the rate of protein citrullination.

**Conclusions:** P.gingivalis PAD is a primarily cell surface associated, heat stable, enzyme that exhibits optimal activity under alkaline conditions similar to those present in the inflammatory environment. The enzyme displays high specificity for arginine residues in peptides and modified arginine in all positions and the gingipains did not influence the rate of protein citrullination. The ability of the enzyme to convert arginine residues in all proteins tested would indicate that its presence in inflamed tissue may promote autoimmune reactions by creation of altered host epitopes.

**Keywords**

Citrullination; *Porphyromonas gingivalis*; Peptidylarginine deiminase; Periodontitis; Rheumatoid arthritis
Factors influencing insulin acceptance among type 2 diabetes mellitus patients in a primary care clinic: A qualitative exploration

Abu Hassan, H., Tohid, H., Mohd Amin, R., Long Bidin, M.B., Muthupalaniappen, L., Omar, K.

Background: Many Type 2 Diabetes Mellitus (T2DM) patients refuse insulin therapy even when they require this modality of treatment. However, some eventually accept insulin. This study aimed to explore the T2DM patients’ reasons for accepting insulin therapy and their initial barriers to use insulin.

Methods: This qualitative study interviewed twenty-one T2DM patients at a primary care clinic who had been on insulin for more than a year through three in-depth interviews and three focus group discussions. A semi-structured interview protocol was used and the sessions were audio-recorded. Subsequently, thematic analysis was conducted to identify major themes.

Results: The participants’ acceptance of insulin was influenced by their concerns and beliefs about diabetes and insulin. Concerns about complications of poorly controlled diabetes and side effects of other treatment regimes had resulted in insulin acceptance among the participants. They also had a strong belief in insulin benefits and effectiveness. These concerns and beliefs were the result of having good knowledge about the diabetes and insulin, experiential learning, as well as doctors’ practical and emotional support that helped them to accept insulin therapy and become efficient in self-care management. These factors also allayed their negative concerns and beliefs toward diabetes and insulin, which were their barriers for insulin acceptance as it caused fear to use insulin. These negative concerns were related to injection (self-injection, needle phobia, injection pain), and insulin use (inconvenience, embarrassment, lifestyle restriction, negative social stigma, and poor self-efficacy), whereas the negative beliefs were ‘insulin could cause organ damage’, ‘their diabetes was not serious enough’, ‘insulin is for life-long’, and ‘insulin is for more severe disease only’.

Conclusions: Exploring patients’ concerns and beliefs about diabetes and insulin is crucial to assist physicians in delivering patient-centered care. By understanding this, physicians could address their concerns with aim to modify their patients’ misconceptions towards insulin therapy. In addition, continuous educations as well as practical and emotional support from others were found to be valuable for insulin acceptance.

Keywords: Type 2 diabetes mellitus; Insulin; Insulin resistance; Qualitative research
The improvement of in vivo model (Balb/c mice) for cervical carcinogenesis using diethylstilbestrol (DES)

Zulfahmi, S., Yazan, L.S., Ithnin, H., Armania, N.

Cervical cancer is the most common gynecological cancer and one of the major causes of female cancer-related death worldwide particularly in developing countries. Thus far, there are a few in vivo models have been developed in investigating this type of cancer. In this study, we induced cervical cancer in Balb/c mice by exploiting the carcinogenic property of diethylstilbestrol (DES). The Balb/c pregnant mice were given subcutaneous (SC) injection of 67 µg/kg body weight of DES on GD 13, and the mice gave birth approximately at gestation day 19-22. Female offspring were reared and the body weight was recorded once weekly. The female offspring were sacrificed at age of 5 months. Upon termination, blood was collected in a plain tube via cardiac puncture and the reproductive tracts were collected and weighed. The reproductive tract sections were stained using H&E for observation of pathological changes. The progression of disease state was monitored by measuring the level of serum interleukin (IL-6) using the Mouse IL-6 ELISA Assay Kit (BD OptEIA™, USA). All parameters were compared with Not-induced group. The outcome of this study demonstrated a significant difference in body weight gain, reproductive organ weight, diameter of cervix and the level of serum IL-6 in the Induced group as compared to the Not-induced group (P<0.05). Histopathological findings revealed the presence of adenosis only in the Induced group. It shows that DES could be employed as an agent to induce cervical carcinogenesis in animal model. In addition to that, new potential anti-cancer agents from various sources could be further evaluated using this technique.

Keywords

In vivo model; Balb/c mice; Diethylstilbestrol; Carcinogenesis; Adenosis; Interleukin-6
Cloning, expression, and purification of the hemolysin/cytolysin (HlyE antigen) from Salmonella enterica serovar Typhi: Potential application for immunoassay development

Ong, E.B.B., Anthony, A.A., Ismail, A., Ismail, A., Lim, T.S.

The hemolysin (HlyE) protein of Salmonella enterica serovar Typhi was reported to be antigenic. This work describes the cloning, expression, and purification of a hexahistidine-tagged HlyE protein under native conditions. Immunoblot analysis and a competitive enzyme-linked immunosorbent assay using sera from typhoid patients showed the presence of HlyE-specific antibodies in circulation.

Keywords

Antigen; ELISA; HlyE; Immunoblot; Salmonella; Typhi
Risk factors associated with unconjugated neonatal hyperbilirubinemia in Malaysian Neonates

Wong, F., Boo, N.Y., Othman, A.

Objective: To investigate the risk factors associated with neonatal hyperbilirubinemia in Malaysian neonates.

Methods: A prospective study was conducted to investigate the effects of glucose-6-phosphate dehydrogenase (G6PD) mutation, variant uridine diphosphate glucuronosyltransferase UGT1A1 gene and hepatic organic anion transporter protein (OATP2) gene on a group of neonates. Hyperbilirubinemia was defined as a total serum bilirubin level of ≥250 µmol/l.

Results: Of 318 neonates, 52 (16.4%) had hyperbilirubinemia. The incidence of G6PD mutation was 5.4% (15/280) among these infants. The incidence of G6PD mutation was significantly higher in the male neonates with hyperbilirubinemia (7.8%) when compared with the normal male neonates without hyperbilirubinemia (1.8%; p=0.03). Logistic regression analysis showed that the significant risk factors for neonatal hyperbilirubinemia were Malay ethnicity (adjusted odds ratio (OR), 2.77; 95% confidence interval (CI): 1.31-5.86; p=0.007) and G6PD mutation (adjusted OR, 3.29; 95% CI: 1.06-10.1820; p=0.039). The gender, birth weight and gestation age of neonates, variant c.211G>A and variant of OATP2 gene were not significant.

Conclusions: Neonates with Malay ethnicity and G6PD mutation were at risk for hyperbilirubinemia.

Keywords: G6PD mutation; OATP2; UGT1A1 c.211G > A; Neonatal hyperbilirubinemia
Effects of keratinocyte growth factor on skin epithelial differentiation of human amnion epithelial cells


The aim of the present study was to determine the effects of KGF on the differentiation of cultured human amnion epithelial cells (HAECs) towards skin keratinocyte. HAECs at passage 1 were cultured in medium HAM’s F12: Dulbecco’s Modified Eagles Medium (1:1) supplemented with different concentrations of KGF (0, 5, 10, 20, 30 and 50 ng/ml KGF). Dose-response of KGF on HAECs was determined by morphological assessment; growth kinetic evaluation; immunocytochemical analysis; stemness and epithelial gene expression quantification with two step real time RT-PCR. KGF promotes the proliferation of HAECs with maximal effect observed at 10 ng/ml KGF. However, KGF decreased the stemness genes expression: Oct-3/4, Sox-2, Nanog3, Rex-1, FGF-4, FZD-9 and BST-1. KGF also down-regulates epithelial genes expression: CK3, CK18, CK19, Integrin-β1, p63 and involucrin in cultured HAECs. No significant difference on the gene expression was detected for each Nestin, ABCG-2, CK1 and CK14 in KGF-treated HAECs. Immunocytochemical analysis for both control and KGF-treated HAECs demonstrated positive staining against CK14 and CK18 but negative staining against involucrin. The results suggested that KGF stimulates an early differentiation of HAECs towards epidermal cells. Differentiation of KGF-treated HAECs to corneal lineage is unfavourable. Therefore, further studies are needed to elucidate the roles of KGF in the differentiation of HAECs towards skin keratinocytes.

Keywords

Amnion cells; Differentiation; Epithelial; Keratin; Keratinocyte growth factor; Stemness; Skin
A neurophysiological insight into the potential link between transcranial magnetic stimulation, thalamocortical dysrhythmia and neuropsychiatric disorders

Fuggetta, G., Noh, N.A.

Altered neural oscillations and their abnormal synchronization are crucial factors in the pathophysiology of several neuropsychiatric disorders. There is increasing evidence that the perturbation with an abnormal increase of spontaneous thalamocortical neural oscillations lead to a phenomenon termed Thalamocortical dysrhythmia (TCD) which underlies the symptomatology of a variety of neurological and psychiatric disorders including Parkinson’s disease, schizophrenia, epilepsy, neuropathic pain, tinnitus, major depression and obsessive-compulsive disorder. In addition, repetitive transcranial magnetic stimulation (rTMS) is a non-invasive neurophysiological tool that has been shown to both induce a modulation of neural oscillations and alleviate a wide range of human neuropsychiatric pathologies. However, little is known about the precise electrophysiological mechanisms behind the therapeutic effect of rTMS and its potential to improve abnormal oscillations across diverse neuropsychiatric disorders. Here we show, using combined rTMS and surface electroencephalography (EEG), a short lasting frequency-dependent rTMS after-effect on thalamocortical rhythmic interplay of low-frequency oscillations in healthy humans at rest. In particular, high-frequency rTMS (10 Hz) induces a transient synchronised activity for delta (δ) and theta (θ) rhythms thus mimicking the pathological TCD-like oscillations. In contrast, rTMS 1 and 5 Hz have the opposite outcome of de-synchronising low-frequency brain rhythms. These results lead to a new neurophysiological insight of basic mechanisms underlying neurological and psychiatric disorders and a probable electrophysiological mechanism underlying the therapeutic effects of rTMS. Thus, we propose the use of rTMS and EEG as a platform to test possible treatments of TCD phenotypes by restoring proper neural oscillations across various neuropsychiatric disorders.

Keywords

Resting-state neural oscillations; Brain stimulation; Oscillatory brain activity; Pathophysiology; Frequency-dependent effects of rTMS; Cortical excitability
Phage display antibodies for diagnostic applications

Hairul Bahara, N.H., Tye, G.J., Choong, Y.S., Ong, E.B.B., Ismail, A., Lim, T.S.

With major developments in molecular biology, numerous display technologies have been successfully introduced for recombinant antibody production. Even so, phage display still remains the gold standard for recombinant antibody production. Its success is mainly attributed to the robust nature of phage particles allowing for automation and adaptation to modifications. The generation of monospecific binders provides a vital tool for diagnostics at a lower cost and higher efficiency. The flexibility to modify recombinant antibodies allows great applicability to various platforms for use. This review presents phage display technology, application and modifications of recombinant antibodies for diagnostics.

Keywords
Antibodies; Diagnostics; Phage display; scFv
Virgin coconut oil prevents blood pressure elevation and improves endothelial functions in rats fed with repeatedly heated palm oil

Nurul-Iman, B.S., Kamisah, Y., Jaarin, K., Qodriyah, H.M.S.

This study was performed to explore the effects of virgin coconut oil (VCO) in male rats that were fed with repeatedly heated palm oil on blood pressure, plasma nitric oxide level, and vascular reactivity. Thirty-two male Sprague-Dawley rats were divided into four groups: (i) control (basal diet), (ii) VCO (1.42 mL/kg, oral), (iii) five-times-heated palm oil (15%) (5HPO), and (iv) five-times-heated palm oil (15%) and VCO (1.42 mL/kg, oral) (5HPO + VCO). Blood pressure was significantly increased in the group that was given the 5HPO diet compared to the control group. Blood pressure in the 5HPO + VCO group was significantly lower than the 5HPO group. Plasma nitric oxide (NO) level in the 5HPO group was significantly lower compared to the control group, whereas in the 5HPO + VCO group, the plasma NO level was significantly higher compared to the 5HPO group. Aortic rings from the 5HPO group exhibited attenuated relaxation in response to acetylcholine and sodium nitroprusside as well as increased vasoconstriction to phenylephrine compared to the control group. Aortic rings from the 5HPO + VCO group showed only attenuated vasoconstriction to phenylephrine compared to the 5HPO group. In conclusion, VCO prevents blood pressure elevation and improves endothelial functions in rats fed with repeatedly heated palm oil.
Pro-angiogenic potential of human chorion-derived stem cells: In vitro and in vivo evaluation

Fariha, M.-M.N., Chua, K.-H., Tan, G.-C., Lim, Y.-H., Hayati, A.-R.

Human chorion-derived stem cells (hCDSC) were previously shown to demonstrate multipotent properties with promising angiogenic characteristics in monolayer-cell culture system. In our study, we investigated the angiogenic capability of hCDSC in 3-dimensional (3D) in vitro and in vivo angiogenic models for the purpose of future application in the treatment of ischaemic diseases. Human CDSC were evaluated for angiogenic and endogenic genes expressions by quantitative PCR. Growth factors secretions were quantified using ELISA. In vitro and in vivo vascular formations were evaluated by histological analysis and confocal microscopic imaging. PECAM-1⁺ and vWF⁺ vascular-like structures were observed in both in vitro and in vivo angiogenesis models. High secretions of VEGF and bFGF by hCDSC with increased expressions of angiogenic and endogenic genes suggested the possible angiogenic promoting mechanisms by hCDSC. The cooperation of hCDSC with HUVECS to generate vessel-like structures in our systems is an indication that there will be positive interactions of hCDSC with existing endothelial cells when injected into ischaemic tissues. Hence, hCDSC is suggested as the novel approach in the future treatment of ischaemic diseases.

Keywords
Fetal stem cells; Pro-angiogenic; Quantitative PCR; Vascular; Ischemic disease
**Introduction**: Posterior reversible encephalopathy syndrome (PRES) is a rare neurological disorder which is increasingly recognized to occur in systemic lupus erythematosus (SLE).

**Objective**: The purpose of this study was to identify the characteristics of SLE patients with PRES and the associated factors of the poor outcome among them.

**Methods**: We investigated SLE patients who developed PRES between 2005-2011 at the Universiti Kebangsaan Malaysia Medical Centre. A comprehensive literature search was done to find all published cases of PRES in SLE. Pooled analysis was conducted to identify the factors associated with poor outcome.

**Results**: There were 103 cases of PRES in SLE published in the literature but only 87 cases were included in the analysis in view of incomplete individual data in the remaining cases. The majority of the cases were Asians (74.2%), female (95.4%) with mean age of 26.3±8.8 years. PRES was highly associated with active disease (97.5%), hypertension (91.7%) and renal involvement (85.1%). We found that 79 patients had a full recovery (90.8%) with a mean onset of full clinical recovery in 5.6±4.1 days. On univariate analysis and logistic regression analysis the predictors of poor outcome, defined as incomplete clinical recovery or death, were intracranial hemorrhage, odds ratio (OR) 14 (1.1-187.2), p=0.04 and brainstem involvement in PRES, OR 10.9 (1.3-90.6), p=0.003.

**Conclusion**: Intracranial hemorrhage and brainstem involvement were the two important predictors of poor outcome of PRES. Larger prospective studies are needed to further delineate the risk of poor outcome among them.

**Keywords**

Hemorrhage; Lupus; Posterior reversible encephalopathy syndrome; renal
Oro-Pharyngeal Carriage and Antimicrobial Susceptibility of Streptococcus Pneumoniae From Healthy Children


Objectives: Streptococcus pneumoniae causes acute otitis media, pneumonia, meningitis and bacteraemia. This study aimed to determine the prevalence of Streptococcus pneumoniae oropharyngeal carriage in healthy children and the antimicrobial susceptibility in a daycare nursery and a government-managed orphanage in Kuala Lumpur during 2010.

Methods: Throat swabs were obtained from 36 children of daycare nursery (open community) and from 84 orphans from orphanage (closed community) those did not receive any pneumococcal vaccine. Children were between births to 6 years of age. Antibiotic susceptibility of isolated strains was determined using disk diffusion method and Etest® (minimum inhibitory concentration).

Results: Overall prevalence of Streptococcus pneumoniae of the children was 1.7% (2 out of 120). Prevalence of the bacteria in open community was 5.6% (2 out of 36) and no positive cases were recorded in orphanage (closed community, p=0.161). Prevalence was 15.4% (2 out of 13) in children aged below 2 years in the open community. There was no association was found to exist between Streptococcus pneumoniae carriage with age (p=0.432) and gender (p=0.418). Serotyping showed serotype 11F for one isolate, while the other was non-typable. Both isolates were susceptible to penicillin, azithromycin, ceftriaxone and vancomycin. The serotype 11F isolate was susceptible while the non-typable isolate was resistant to erythromycin.

Conclusions: The results demonstrated low prevalence of Streptococcus pneumoniae in healthy children. These findings may complement other studies to explore further risk factors for colonisation, antimicrobial susceptibility and serotype distribution of Streptococcus pneumoniae to help for the planning of immunization strategies.

Keywords: Antimicrobial susceptibility; Children; Colonisation; Oropharyngeal carriage; serotype; Streptococcus pneumoniae
Stemness and angiogenic gene expression changes of serial-passage human amnion mesenchymal cells


**Background:** Particular attention has been directed towards human amnion mesenchymal stem cells (HAMCs) due to their accessibility, availability and immunomodulatory properties. Therefore, the aim of the present study was to determine the temporal changes of stemness and angiogenic gene expressions of serial-passage HAMCs.

**Methods:** HAMCs were isolated from human term placenta and cultured in serial passages in culture medium supplemented with 10% fetal bovine serum. Morphological analysis, growth kinetic and CFU-F assay of HAMCs were assessed. In vitro differentiation and the immunophenotype of HAMCs at P5 were also analyzed. Quantitative PCR was used to determine the stemness, angiogenic and endothelial gene expression of cultured HAMCs after serial passage.

**Results:** Cultured HAMCs displayed intermediate epitheloid-fibroblastoid morphology at an initial culture and the fibroblastoid features became more pronounced in later passages. They showed high clonogenic activity and faster proliferation at later passages with colony forming efficiency of 0.88%. HAMCs were successfully differentiated into adipocytes, osteocytes and neuron-like cells. Most HAMCs expressed CD9, CD44, CD73, CD90 and HLA-A,B,C but negligibly expressed CD31, CD34, CD45, CD117 and HLA-DR,DP,DQ. After serial passage, stemness genes Oct-3/4, Sox-2, Nanog3, Rex-1, FGF-4 and FZD-9 expressions significantly decreased. Of the angiogenic genes PECAM-1, bFGF, eNOS, VEGFR-2, VEGF, and vWF expressions also decreased significantly except angiopoietin-1 which significantly increased. No significant differences were observed in ABCG-2, BST-1, nestin, PGF and HGF expressions after serial passage.

**Conclusion:** These results suggested that cultured HAMCs could be an alternative source of stem cells and may have the potential for angiogenesis and hence its use in stem-cell based therapy.
Isolation of *Acanthamoeba* spp. from contact lens paraphernalia


**Introduction:** *Acanthamoeba* spp. are ubiquitous free-living protozoa that are widely distributed in all types of environment throughout the world. *Acanthamoeba* sp. is the causative agent of two diseases; keratitis and granulomatous amoebic encephalitis. Contaminated contact lenses and corneal lesions are the major risk factors in causing *Acanthamoeba* keratitis.

**Objective:** The main objective of this study is to isolate *Acanthamoeba* sp. from contact lens paraphernalia.

**Materials and Methods:** One hundred and seventy five swabs from contact lens paraphernalia were obtained, consisting of 66 swabs of contact lenses, 52 swabs of contact lens storage cases and 57 samples of contact lens disinfecting solutions. Filtration and culture techniques were used to isolate the organism using standard methods.

**Results:** This study successfully isolated *Acanthamoeba* sp. from contact lenses and contact lens storage cases at 10.6% and 13.5% respectively. However no *Acanthamoeba* sp. was isolated from the contact lens disinfecting solution. Many of those contact lens wearers whose contact lens paraphernalia were positive for *Acanthamoeba* showed a deviation from contact lens wear and care procedures recommended by the lens manufacturer and health professionals.

**Conclusion:** The findings that contact lens paraphernalia harbours *Acanthamoeba* is particularly worrying as the number of cases is increasing. Contact lens wearers should be educated regarding proper hygienic care of their contact lenses.
An in vitro study of fracture resistance of weakened tooth roots reinforced with two types of adhesive restorative materials

Ahmad, A.M., Bakar, W.Z.W., Husein, A., Alam, M.K.

Introduction: Composite resin (CR) is among the commonly used material for intraradicular reinforcement of weakened tooth roots.

Purpose: This study was to compare the fracture resistance of experimentally weakened tooth roots reinforced using auto-polymerized composite resin and light-polymerized composite resin.

Materials and Methods: Fifty-six extracted human maxillary incisors were divided into 2 groups (n = 28) and the root canals were over prepared to weaken it. The samples in Group A were restored using light-cured CR Z100 and light-transmitting polymerizing post (Luminex), whereas Group B using auto-cured CR Alpha-dent. Both groups were placed with metal parapost cemented with a resin luting cement (Nexus 2). Specimens were subjected to compressive load (N) using Instron machine until fracture. Data were submitted to independent t test analysis of variance (p < 0.05).

Results: There was no significant difference (p = 0.233) in fracture resistance between the teeth reinforced with light-polymerizing and auto-polymerizing CR are 549.3 (± 95.44) and 490.7 (± 110.37) respectively.

Conclusion: The use of less technique sensitive auto-polymerizing CR give equivalent benefit effect on reinforcing weakened roots, as the more commonly light-polymerized composite resin.

Keywords: Fracture resistance; Weakened tooth roots; Reinforcement; Adhesive materials
Endogenous and induced angiogenic characteristics of human chorion-derived stem cells

Nur Fariha, M.-M., Chua, K.-H., Tan, G.-C., Lim, Y.-H., Hayati, A.-R.

Cell-based therapy using stem cells has emerged as one of the pro-angiogenic methods to enhance blood vessel growth and sprouting in ischaemic conditions. This study investigated the endogenous and induced angiogenic characteristics of hCDSC (human chorion-derived stem cell) using QPCR (quantitative PCR) method, immunocytochemistry and fibrin-matrigel migration assay. The results showed that cultured hCDSC endogenously expressed angiogenic-endogenic associated genes (VEGF, bFGF, PGF, HGF, Ang-1, PECAM-1, eNOS, Ve-cad, CD34, VEGFR-2 and vWF), with significant increase in mRNA levels of PGF, HGF, Ang-1, eNOS, VEGFR-2 and vWF following induction by bFGF (basic fibroblast growth factor) and VEGF (vascular endothelial growth factor). These enhanced angiogenic properties suggest that induced hCDSC provides a stronger angiogenic effect for the treatment of ischaemia. After angiogenic induction, hCDSC showed no reduction in the expression of the stemness genes, but had significantly higher levels of mRNA of Oct-4, Nanog (3), FZD9, ABCG-2 and BST-1. The induced cells were positive for PECAM-1 (platelet/endothelial cell adhesion molecule 1) and vWF (von Willebrand factor) with immunocytochemistry staining. hCDSC also showed endothelial migration behaviour when cultured in fibrin-matrigel construct and were capable of forming vessels in vivo after implanting into nude mice. These data suggest that hCDSC could be the cells of choice in the cell-based therapy for pro-angiogenic purpose. © The Author(s) Journal compilation.

Keywords

Angiogenesis; Cell-based therapy; Fetal stem cells; Growth factors; Ischaemia; placenta
In Malaysia, private health insurance coverage is usually limited to inpatient treatment or hospitalisation. With private health insurance, there is a possibility that individuals will use health care services more frequently or spend more on health care (known as moral hazard effects) because they know they are protected. This study estimates the importance of factors affecting the demand for private health insurance and how it affects health care utilisation. This paper also provides an empirical test for the existence of moral hazard effects in health care utilisation. The analysis uses the second and third National Health and Morbidity Surveys (NHMS), which were conducted in 1996 and 2006. The analysis applies a bivariate probit model to estimate the demand for private insurance and its effect on the utilisation of health care. Utilisation of health care is defined as being admitted to either a public or private hospital. The results show that taking up private health insurance is lower among disadvantaged individuals, such as those with lower income, a lower level of education, those living in less developed regions and the unemployed. The findings also show that health conditions have a very strong effect on the hospitalisation decision. Furthermore, the results demonstrate that evidence of moral hazard existed in the 1996 but not in the 2006 data. From the results, policy makers can target an appropriate population for providing health subsidies if the National Health Insurance Scheme is implemented.

Keywords
Private health insurance; Health care financing; Moral hazard; Health care utilisation
Pyogenic granuloma of the nasal septum: A rare cause of epistaxis

Hassan, N.E., Goh, B.S.

Pyogenic granuloma (PG) is a benign hyperplastic, vascular proliferation either on the skin or mucosal membranes. It commonly occurs following traumatic or hormonal changes, particularly in pregnancy. While the lesions occur frequently in the oral cavity in the head and neck region, occurrence in the nasal septum is rarely reported. We report a case of a 23-year-old male with unilateral pyogenic granuloma of the anterior nasal septum, who presented with epistaxis and nasal blockage. Although intra nasal PG is rare, we advocate that PG be considered in any anterior nasal septum mass with epistaxis.

Keywords

Pyogenic granuloma; Lobular capillary haemangioma; Epistaxis; Nasal obstruction; Nasal septum
Prevalence of iron deficiency anaemia and thalassaemia trait among undergraduate medical students


**Background.** Anaemia is a global health problem including Malaysia. In adults, anaemia may affect work productivity. Iron deficiency anaemia and thalassaemia are common causes of anaemia in Malaysia. However, there is scarcity of data on national prevalence of iron deficiency anaemia and thalassaemia, especially in young adults. This cross-sectional study was performed to determine the prevalence of iron deficiency anaemia and thalassaemia among medical students of Universiti Kebangsaan Malaysia Medical Centre (UKMMC).

**Materials and Methods.** Blood samples collected in EDTA tubes were analyzed for haemoglobin level and red cell parameters such as MCV, MCH and red cell counts. Samples with abnormal red cell indices were sent for analysis of RBC morphology, iron status, haemoglobin analysis and DNA analysis.

**Results.** A total of 400 samples were available for this study. Fiftyeight (14.5%) students had hypochromic microcytic red cell indices in which 44 (11%) showed thalassaemia red cell indices while 14 (3.5%) had iron deficiency red cell indices which were finally confirmed by serum iron/TIBC analysis. Amongst those suspected to have thalassaemia, 12 (27.3%) were confirmed as alpha thalassaemia trait (α/αSEA), 11 (25%) as Haemoglobin-E trait, 8 (18.2%) as beta thalassaemia trait and 2 (4.5%) as Haemoglobin Constant Spring (α/αCSa). However, eleven students (25%) with thalassaemia red cell indices could not be confirmed with the common thalassaemia primers available, thus causes have yet to be established.

**Conclusion.** Our prevalence of thalassaemia was high and thus we opine that better screening methods should be adopted.
Enzyme Hydrolysates from *Stichopus horrens* as a New Source for Angiotensin-Converting Enzyme Inhibitory Peptides.

Forghani, B., Ebrahimpour, A., Bakar, J., Abdul Hamid, A., Hassan, Z., Saari, N.

*Stichopus horrens* flesh was explored as a potential source for generating peptides with angiotensin-converting enzyme (ACE) inhibitory capacity using 6 proteases, namely alcalase, flavourzyme, trypsin, papain, bromelain, and protamex. Degree of hydrolysis (DH) and peptide profiling (SDS-PAGE) of *Stichopus horrens* hydrolysates (SHHs) was also assessed. Alcalase hydrolysate showed the highest DH value (39.8) followed by flavourzyme hydrolysate (32.7). Overall, alcalase hydrolysate exhibited the highest ACE inhibitory activity (IC$_{50}$ value of 0.41 mg/mL) followed by flavourzyme hydrolysate (IC$_{50}$ value of 2.24 mg/mL), trypsin hydrolysate (IC$_{50}$ value of 2.28 mg/mL), papain hydrolysate (IC$_{50}$ value of 2.48 mg/mL), bromelain hydrolysate (IC$_{50}$ value of 4.21 mg/mL), and protamex hydrolysate (IC$_{50}$ value of 6.38 mg/mL). The SDS-PAGE results showed that alcalase hydrolysate represented a unique pattern compared to others, which yielded potent ACE inhibitory peptides with molecular weight distribution lower than 20 kDa. The evaluation of the relationship between DH and IC$_{50}$ values of alcalase and flavourzyme hydrolysates revealed that the trend between those parameters was related to the type of the protease used. We concluded that the tested SHHs would be used as a potential source of functional ACE inhibitory peptides for physiological benefits.

**Keywords**

Enzymatic hydrolysis; Sea cucumber hydrolysates; Angiotensin converting enzyme; Bioactive peptides; IC50; Amino acids, HPLC
Human cortical theta reactivity to high-frequency repetitive transcranial magnetic stimulation

Azila Noh, N., Fuggetta, G.

Electroencephalography (EEG) can directly monitor the temporal progression of cortical changes induced by repetitive Transcranial Magnetic Stimulation (rTMS) and facilitate the understanding of cortical and subcortical influences in the genesis of oscillations. In this combined rTMS/EEG study, we aimed to investigate changes in oscillatory activity after high-frequency (~11 Hz) rTMS relative to the number of applied pulses. Twenty intermittent trains of 20 or 60 rTMS pulses were delivered over the human primary motor cortex at rest and tuned to individual mu frequency. The regional and interregional oscillatory neural activity after stimulation were evaluated using event-related power (ERPow) and event-related coherence (ERCoh) transformations. The most prominent changes for ERPow were observed in the theta band (4-7 Hz), as an increase in ERPow up to 20 s following 60 rTMS pulses, whereas ERPow increases were smaller in mu (10-12 Hz) and beta (13-30 Hz). ERCoh revealed that rTMS 60 modulated the connectivity in the theta band for up to 20 s. The topography of mu and theta changes were not identical; mu was more focal and theta was more global. Our data suggested the presence of independent cortical theta and mu generators with different reactivity to rTMS but could not rule out possible thalamocortical contributions in generating theta and mu over the motor network.

Keywords
EEG-TMS combination; Event-related power; Event-related coherence; Motor cortex; Oscillations; Synaptic plasticity
GC-MS analysis of various extracts from leaf of Plantago major used as traditional medicine

Jamilah, J., Sharifa, A.A., Sharifah, N.R.S.A.

Plantago major L. leaves have been used as a wound healing remedy for centuries in the treatment of a number of diseases. The objective of this study is to analyse the chemical composition in the leaf extract of P. major. The chemical composition of various extract (petroleum ether, methanol, ethyl acetate, n-butanol and aqueous) from leaf of Plantago major have been examined by Triple Quadrupole GC-MS. Results have showed the main constituents in petroleum ether extract were phytol 13.22%, benzofuranone 10.48%, penthynediol 10.26% and benzene propanoic acid 10.18%; methanol extract were group of diglycerol 30.31% and glycol 18.91%; ethyl acetate extract were glycerine 30.70%, benzene 21.81% and dibuthyl phthalate 16.22%; n-butanol were phtalic acid 24.62%, benzene propanoic acid 16.83% and group of phenol 10.20%; and aqueous extract were phenol 27.47%, diathiapentene 14.53%, napthalenone 14.13% and glycerine 12.02%. Chemical composition identified in all five extracts has showed that all of them have phenol’s group in their extract while having different variation of organic acid groups, flavonoids and terpenoids. These data would be constructive for future ethno-pharmacological studies in P. major.

Keywords
Plantago major; Soxhlet extraction; GC-MS; Chemical composition; Halal traditional medicine
Human mesenchymal stromal cells could deliver erythropoietin and migrate to the basal layer of hair shaft when subcutaneously implanted in a murine model

Mok, P.L., Cheong, S.K., Leong, C.F., Chua, K.H., Ainoon, O.

Mesenchymal stromal cells (MSC) are an attractive cell-targeting vehicle for gene delivery. MiDGE (an acronym for Minimalistic, Immunologically Defined Gene Expression) construct is relatively safer than the viral or plasmid expression system as the detrimental eukaryotic and prokaryotic gene and sequences have been eliminated. The objective of this study was to test the ability of the human MSC (hMSC) to deliver the erythropoietin (EPO) gene in a nude mice model following nucleofection using a MiDGE construct. hMSC nucleofected with MiDGE encoding the EPO gene was injected subcutaneously in Matrigel at the dorsal flank of nude mice. Subcutaneous implantation of nucleofected hMSC resulted in increased hemoglobin level with presence of human EPO in the peripheral blood of the injected nude mice in the first two weeks post-implantation compared with the control groups. The basal layer of the hair shaft in the dermal layer was found to be significantly positive for immunohistochemical staining of a human EPO antibody. However, only a few basal layers of the hair shaft were found to be positively stained for CD105. In conclusion, hMSC harboring MiDGE-EPO could deliver and transiently express the EPO gene in the nude mice model. These cells could be localized to the hair follicle and secreted EPO protein might have possible role in hair regeneration.
Extended and stable gene expression via nucleofection of MIDGE construct into adult human marrow mesenchymal stromal cells

Mok, P.L., Cheong, S.K., Leong, C.F., Chua, K.H., Ainoon, O.

Human mesenchymal stromal cell (hMSC) is a potential target for cell and gene therapy-based approaches against a variety of different diseases. Whilst cationic lipofection has been widely experimented, the Nucleofector technology is a relatively new non-viral transfection method designed for primary cells and hard-to-transfect cell lines. Herein, we compared the efficiency and viability of nucleofection with cationic lipofection, and used the more efficient transfection method, nucleofection, to deliver a construct of minimalistic, immunologically defined gene expression encoding the erythropoietin (MIDGE-EPO) into hMSC. MIDGE construct is relatively safer than the viral and plasmid expression systems as the detrimental eukaryotic and prokaryotic gene and sequences have been eliminated. Using a plasmid encoding the luciferase gene, we demonstrated a high transfection efficiency using the U-23 (21.79 \pm 1.09\%) and C-17 (5.62 \pm 1.09\%) pulsing program in nucleofection. The cell viabilities were (44.93 \pm 10.10\%) and (21.93 \pm 5.72\%), respectively 24 h post-nucleofection. On the other hand, lipofection treatment only yielded less than 0.6\% efficiencies despite showing higher viabilities. Nucleofection did not affect hMSC renewability, immunophenotype and differentiation potentials. Subsequently, we nucleofected MIDGE-EPO using the U-23 pulsing program into hMSC. The results showed that, despite a low nucleofection efficiency with this construct, the EPO protein was stably expressed in the nucleofected cells up to 55 days when determined by ELISA or immunocytochemical staining. In conclusion, nucleofection is an efficient non-viral transfection approach for hMSC, which when used in conjunction with a MIDGE construct, could result in extended and stable transgene expression in hMSC.
Anti-urolithiatic terpenoid compound from *Plantago major* Linn. (Ekor Anjing)

Sharifa, A.A., Jamaludin, J., Kiong, L.S., Chia, L.A., Osman, K.

The aim of this study was to determine the inhibition effects of the terpenoid of *Plantago major* on calcium oxalate crystals in vitro and to compare the effects of *Plantago major* with clinically used drugs like zyloric and potassium citrate for the treatment of urinary stone. Modified Schneider slide gel method was used for in vitro study and crystals formed were measured by Image Analyser System (Leica) after 24 h of treatment. The active compound in the methanol extract of *Plantago major* was isolated by bioassay-guided fractionation & isolation method. Dimethylsulphoxide (DMSO) was used as the negative control and zyloric and potassium citrate were used as positive controls. The results showed that crude methanol extract of *Plantago major* contained the active compound terpenoid. Terpenoid, zyloric and potassium citrate at concentrations in the range of (100 µg/mL - 250 µg/mL) significantly inhibited the area of crystal formation in comparison to the negative control after 24 h (p<0.001). The Zyloric and terpenoid of *Plantago major* in the concentrations of (100 µg/mL - 250 µg/mL) inhibited the sizes of crystals significantly (p<0.05). Potassium citrate was more effective, than terpenoid of *Plantago major* in inhibiting the size of crystals at two concentrations i.e., 100 µg/mL and 150 µg/mL respectively (p<0.05). However the IC50 values for terpenoid of *Plantago major*, potassium citrate and zyloric were 250 µg/mL, 300 µg/mL and 550 µg/mL, respectively. The inhibition effect of the terpenoid of *Plantago major* extract on crystal size was much better than Zyloric and potassium citrate.

**Keywords**
Calcium oxalate crystals; Inhibition effects; *Plantago Major*; Terpenoid
The effectiveness of gentamicin against *Acanthamoeba* cysts *in vitro*


*Acanthamoeba* is a free-living protozoa which causes serious ocular problem. *Acanthamoeba* keratitis is becoming more prevalent amongst contact lens wearers and it can cause loss of vision and blindness if not treated properly. The objective of this research is to determine the effectiveness of gentamicin against six *Acanthamoeba* spp. isolates, of which three were clinical isolates (HS 6, HKL 95, HTH 73) and three environmental isolates (SMAL 7, SMAL 8, TTT 9). Cyst suspension from the chosen isolates were exposed to gentamicin. After 48 hours of incubation at temperature of 30°C and 37°C, each mixture was filtered and filtration membrane was put onto non-nutrient agar laid with *Escherichia coli*. The agar plates were incubated for three days at 30°C and 37°C and the plates were examined daily until day 14 to look for the presence of *Acanthamoeba* trophozoites under inverted microscope. The presence of trophozoites indicated the ineffectiveness of gentamicin. Gentamicin was found to be effective against *Acanthamoeba* cysts from all the test strains at both incubation temperatures. The minimum cysticidal concentration (MCC) mean value of gentamicin was 0.193 mg/mL at 30°C and 0.229 mg/mL at 37°C. So, we concluded that gentamicin has cysticidal potential towards *Acanthamoeba*.

**Keywords**

*Acanthamoeba*; Sensitivity; Gentamicin
In vitro sensitivity testing of Acanthamoeba clinical isolates from patients with keratitis against polyhexamethylene biguanide (PHMB) and chlorhexidine

Abdullah, N.S., Ghani, M.K.A., Nordin, A., Suboh, Y., Rahim, N.A., Ahmad, N.

Acanthamoeba keratitis is a serious infection of the eye which can result in permanent visual impairment. Therefore this study was performed to evaluate the effectiveness of antimicrobial agents on three Acanthamoeba clinical isolates (HS 6, HKL 95 and HTH 73). Antimicrobial agents used in this study were polyhexamethylene biguanide (PHMB) and chlorhexidine and both were serially diluted. Cyst suspensions from all three strains were tested against the antimicrobial agents, respectively. After 48 h of incubation at 37°C, the suspension was filtered and the filter membrane was placed onto non-nutrient agar plate lawned with heat-killed Escherichia coli. The plates were examined daily under the inverted microscope until day 14 but were negative for Acanthamoeba trophozoites. The presence of trophozoites indicated ineffectiveness of the antimicrobial agents. Both antimicrobial agents used were found to be effective against Acanthamoeba cysts for all the strains tested. PHMB gave minimum cysticidal concentration (MCC) mean value of 4.232 µg/mL and chlorhexidine showed MCC mean value of 3.906 µg/mL. So, from this study, it can be concluded that PHMB and chlorhexidine were effective in killing the tested Acanthamoeba cysts.

Keywords
Acanthamoeba; In vitro; Sensitivity; Polyhexamethylene biguanide; Chlorhexidine
Review of stem cell deregulation and breast cancer: An emerging hypothesis

Kumar, D., Kutty, M.

Cancer is fundamentally a cellular genetic disease capable of transferring the “disease” to the next generation of mutated cells. Similar proliferative and information transferring capacity exists in the stem cells of various organ systems in the human body. Understanding the bio-mechanism of stem cell metabolism and its regulation by signaling molecules and extracellular micro-environment is an important step toward successful prevention and treatment of cancer. According to the cancer stem cell hypothesis, both hereditary and sporadic cancers can arise from deregulation of these cancer stem cells (CSCs), triggered by genetic and environmental factors. It is shown that deregulation of normal self-renewal pathways in undifferentiated breast stem cells or progenitor cells had altered mammary system or progenitor cells, resulting in abnormally differentiated cells in human and rodent breast cancer cell lines. Breakthroughs in molecular pathways have important therapeutic implications. Hence, significant stress is laid on targeting signaling molecules and their micromilieu in breast cancer therapy.
Effects of epidermal growth factor on the proliferation and cell cycle regulation of cultured human amnion epithelial cells

Fatimah, S.S., Tan, G.C., Chua, K.H., Tan, A.E., Hayati, A.R.

Human amnion epithelial cells (HAECs) hold great promise in tissue engineering for regenerative medicine. Large numbers of HAECs are required for this purpose. Hence, exogenous growth factor is added to the culture medium to improve epithelial cells proliferation. The aim of the present study was to determine the effects of epidermal growth factor (EGF) on the proliferation and cell cycle regulation of cultured HAECs. HAECs at P1 were cultured for 7 days in medium containing an equal volume mix of HAM’s F12: Dulbecco’s Modified Eagles Medium (1:1) supplemented with different concentrations of EGF (0, 5, 10, 20, 30 and 50 ng/ml EGF) in reduced serum. Morphology, growth kinetics and cell cycle analysis using flow cytometry were assessed. Quantitative gene expression for cell cycle control genes, pluripotent transcription factors, epithelial genes and neuronal genes were also determined. EGF enhanced HAECs proliferation with optimal concentration at 10 ng/ml EGF. EGF significantly increased the proportion of HAECs at S- and G2/M-phase of the cell cycle compared to the control. At the end of culture, HAECs remained as diploid cells under cell cycle analysis. EGF significantly decreased the mRNA expression of p21, pRb, p53 and GADD45 in cultured HAECs. EGF also significantly decreased the pluripotent genes expression: Oct-3/4, Sox2 and Nanog; epithelial genes expression: CK14, p63, CK1 and Involucrin; and neuronal gene expression: NSE, NF-M and MAP 2. The results suggested that EGF is a strong mitogen that promotes the proliferation of HAECs through cell cycle regulation. EGF did not promote HAECs differentiation or pluripotent genes expression.

Keywords

Epidermal growth factor; Human amnion; Epithelial; Pluripotent; Cell cycle; Tissue engineering
Organotypic culture of human amnion cells in air-liquid interface as a potential substitute for skin regeneration.

Simat Siti Fatimah, Kienhui Chua, Geok Chin Tan, Tengku Ibrahim Azmi, Ay Eeng Tan, Hayati Abdul Rahman

The aim of the present study was to evaluate the effects of air-liquid interface on the differentiation potential of human amnion epithelial cells (HAECs) to skin-like substitute in organotypic culture. HAECs at passage 1–2 were seeded onto a fibrin layer populated with human amnion mesenchymal cells to form the organotypic cultures. The organotypic HAECs were then cultured for 7, 14 and 21 d in two types of culture system: the submerged culture and the air-liquid interface culture. Cell morphogenesis was examined under the light and electron microscopes (transmission and scanning) and analyzed by immunohistochemistry. Organotypic HAECs formed a single layer epithelium after 3 wk in submerged as well as air-liquid interface cultures. Ultrastructurally, desmosomes were observed in organotypic HAECs cultured in the air-liquid interface but not in the submerged culture. The presence of desmosomes marked the onset of early epidermal differentiation. Organotypic HAECs were positive against anti-CK18 and anti-CK14 in both the submerged and the air-liquid interface cultures. The co-expression of CK14 and CK18 suggested that differentiation of HAECs into skin may follow the process of embryonic skin development. However, weak expression of CK14 was observed after 2 and 3 wk of culture in air-liquid interface. CK10, involucrin, type IV collagen and laminin-5 expression was absent in organotypic HAECs. This observation reflects the initial process of embryonic epidermal differentiation and stratification. Results from the present study suggest that the air-liquid interface could stimulate early differentiation of organotypic HAECs to epidermal cells, with a potential use for skin regeneration.

Keywords
Air-liquid interface; Epithelial stem cells; Fibrin; Human amnion-derived stem cells; Organotypic culture; Skin regeneration
Cloning, expression, and purification of the hemolysin/cytolysin (HlyE antigen) from Salmonella enterica serovar Typhi: potential application for immunoassay development

Eugene Boon Beng Ong, Amy Amilda Anthony, Aziah Ismail, Asma Ismail, Theam Soon Lim

The hemolysin (HlyE) protein of Salmonella enterica serovar Typhi was reported to be antigenic. This work describes the cloning, expression, and purification of a hexahistidine-tagged HlyE protein under native conditions. Immunoblot analysis and a competitive enzyme-linked immunosorbent assay using sera from typhoid patients showed the presence of HlyE-specific antibodies in circulation.

Keywords
Antigen; ELISA; HlyE; Immunoblot; Salmonella; Typhi
Phage display antibodies for diagnostic applications

Nur Hidayah Hairul Bahara, Gee Jun Tye, Yee Siew Choong, Eugene Boon Beng Ong, Asma Ismail, Theam Soon Lim

With major developments in molecular biology, numerous display technologies have been successfully introduced for recombinant antibody production. Even so, phage display still remains the gold standard for recombinant antibody production. Its success is mainly attributed to the robust nature of phage particles allowing for automation and adaptation to modifications. The generation of monospecific binders provides a vital tool for diagnostics at a lower cost and higher efficiency. The flexibility to modify recombinant antibodies allows great applicability to various platforms for use. This review presents phage display technology, application and modifications of recombinant antibodies for diagnostics.

Keywords

Antibodies; Diagnostics; Phage display; ScFv
Previous studies have found out that educational applications using the Augmented Reality (AR) technology have provided immersion, motivation, fun and high level of engagement. However, designing and developing of the AR courseware with these characteristics while ensuring the effectiveness in teaching and learning process can be quite challenging. The increasingly use of AR has called for the creation of more usable products of high quality, which in turn, makes the Usability Evaluation testing an essential process. Previous researchers stressed that until very recently, where the Usability Evaluation of AR interfaces had not been systematically examined. Furthermore, nowadays usability is a fundamental factor to consider when developing educational courseware. Therefore, a good design for the usability evaluation methodology is needed which is best suited for Down Syndrome (DS) learners in early reading. This paper describes the review of usability evaluation in learning courseware and presenting the usability evaluation that has been successfully applied to previous AR applications. Next, we will present several existing usability evaluation methods as a guideline in conducting the usability evaluation for AR BACA SindD. Lastly, this paper proposed a Design of Usability Evaluation Methodology Framework for AR BACA SindD, especially for the DS children in this case study. Hopefully, the methods that were used for the evaluation as well as the suitable usability evaluation methodology proposed, can be deployed to evaluate the effectiveness of the courseware to disabled children as general and primarily to the DS children.
A cross-sectional survey was conducted with the objective to explore a community’s knowledge and practices towards prevention of Influenza A (H1N1) in three residential areas in Tampin. Respondents were randomly selected from a list of residences and interviewed face-to-face using a structured questionnaire. A total of 221 respondents (80.9%) were involved with the majority (64.7%) comprising female and who had attained secondary level of education (86.0%). The main source of information was from television/radio. The total score for knowledge questions was 15 and practice questions were 25. A total of 60.2% attained “adequate knowledge” and 52.0% “good practice”. Mean (SD) for knowledge score was 11.6(2.3) and practice was 18.1(4.1). Ethnicity, education, income and practice score were identified as predictors for knowledge score. Income and knowledge scores were predictors for practice score. There was positive correlation between knowledge and practice scores.
A case report of classical chikungunya fever

Ali, U., Isahak, I., Rahman, M.M.

The present case discusses about an elderly gentleman who contracted the disease following a visit to area reported to have chikungunya outbreak in Malaysia. He had severe, incapacitating arthralgia and swelling of both hands and elbow joint as well as rash and high grade fever. His serum was tested for both dengue and chikungunya fevers as the symptoms of both the cases were overlapping. In the present case some classical clinical features such as fever, arthralgia and rash were noted. Laboratory result revealed positive for chikungunya IgM on day 5 of illness. Laboratory confirmation is essential to ensure correct diagnosis of chikungunya.

Keywords
Chikungunya fever; Arthropod borne; Arthralgia; Myalgia; IgM
The use of enzymatically synthesized medium- and long-chain triacylglycerols (MLCT) oil blends in food application


The potential use of medium- and long-chain triacylglycerols (MLCT) oil blends in food applications such as frying oil and salad dressings were investigated. The frying strength of palm-based MLCT oil with different antioxidants under deep frying conditions was assessed. Palm-based MLCT oil showed better thermal resistant oxidative strength than refined, bleached and deodorized (RBD) palm olein throughout the five consecutive days of frying. Sensory evaluation and rancidity assessment on fried chips showed no significant differences (P > 0.05) between chips fried in RBD palm olein and palm-based MLCT oil. MLCT-based salad dressings treated with different antioxidants showed similar rheological behaviors as compared to soybean-based salad dressings. The overall quality of the physical appearance and organoleptic acceptability based on quantitative descriptive analysis showed no significant differences (P > 0.05) in all salad dressings. These findings indicated that MLCT-based oil blends can be used as healthy functional oil for daily consumption.
Dillenia suffruticosa exhibited antioxidant and cytotoxic activity through induction of apoptosis and G_2/M cell cycle arrest

Nurdin Armania, Latifah Saiful Yazan, Siti Noorhidayah Musa, Intan Safinar Ismail, Jhi Biau Foo, Kim Wei Chan, Husain Noreen, Abdul Hamid Hisyam, Said Zulfahmi, Maznah Ismail

Dillenia suffruticosa (Family: Dilleniaceae) locally known as Simpoh air has been reported to be used traditionally to treat cancerous growth. Therefore, the present study was attempted to investigate the antioxidant and cytotoxic properties of different parts (root, flower, fruit and leaf) of *D. suffruticosa* extracts. In this study, direct solvent extraction (aqueous and methanol) from different parts of *D. suffruticosa* (root, flower, fruit and leaf) were carried out. Antioxidant activities of *D. suffruticosa* extract were determined by using DPPH, ABTS FRAP and β-carotene bleaching assays. Cytotoxicity and cell cycle arrest of the active extract were determined using MTT assay and flow cytometer, respectively. Sequential solvent extraction (hexane, DCM, EtOAc, and MeOH) were also carried out in root of *D. suffruticosa* to further evaluate the antioxidant and cytotoxic activity of the different solvent extracts. Methanol (MeOH) root extract showed the highest TPC, antioxidant and cytotoxic activities (especially towards HeLa) compared to others (*P*<0.05). Based on the results, sequential solvent extraction (hexane, DCM, EtOAc and MeOH) was carried out in the roots of *D. suffruticosa*. MeOH extract exhibited the highest antioxidant activities among others and significantly correlated (*P*<0.05) with TPC, suggesting the important contribution of phenolic compounds to its antioxidant activity. On the other hand, the DCM and EtOAc exhibited higher cytotoxic activity to selected cancer cells (HeLa, MCF-7, MDA-MB-231, A549 and HT29) compared to others. In short, there is no established correlation between antioxidant and cytotoxic activities of *D. suffruticosa* extracts indicating that an agent with high antioxidant activities will not necessarily possesses good cytotoxic activities in return. Qualitative phytochemical screening of *D. suffruticosa* extracts suggested the presence of saponins, triterpenes, sterols, and polyphenolic compounds which are believed to contribute to the cytotoxic activities. It is suggested that the cytotoxicity of the active extracts in HeLa was due to the induction of apoptosis and cell cycle arrest at G_2/M.
Effects of keratinocyte growth factor on skin epithelial differentiation of human amnion epithelial cells

Simat Siti Fatimah, Geok Chin Tan, Kienhui Chua, Ay Eeng Tan, Abdul Ghani Nur Azurah, Abdul Rahman Hayati

The aim of the present study was to determine the effects of KGF on the differentiation of cultured human amnion epithelial cells (HAECs) towards skin keratinocyte. HAECs at passage 1 were cultured in medium HAM’s F12: Dulbecco’s Modified Eagles Medium (1:1) supplemented with different concentrations of KGF (0, 5, 10, 20, 30 and 50 ng/ml KGF). Dose–response of KGF on HAECs was determined by morphological assessment; growth kinetic evaluation; immunocytochemical analysis; stemness and epithelial gene expression quantification with two step real time RT-PCR. KGF promotes the proliferation of HAECs with maximal effect observed at 10 ng/ml KGF. However, KGF decreased the stemness genes expression: Oct-3/4, Sox-2, Nanog3, Rex-1, FGF-4, FZD-9 and BST-1. KGF also down-regulates epithelial genes expression: CK3, CK18, CK19, Integrin-β1, p63 and involucrin in cultured HAECs. No significant difference on the gene expression was detected for each Nestin, ABCG-2, CK1 and CK14 in KGF-treated HAECs. Immunocytochemical analysis for both control and KGF-treated HAECs demonstrated positive staining against CK14 and CK18 but negative staining against involucrin. The results suggested that KGF stimulates an early differentiation of HAECs towards epidermal cells. Differentiation of KGF-treated HAECs to corneal lineage is unfavourable. Therefore, further studies are needed to elucidate the roles of KGF in the differentiation of HAECs towards skin keratinocytes.

Keywords
Amnion cells; Differentiation; Epithelial; Keratin; Keratinocyte growth factor; Stemness; Skin
The anthelmintic efficacy of natural plant cysteine proteinases against two rodent cestodes *Hymenolepis diminuta* and *Hymenolepis microstoma* in vitro

F. Mansur, W. Luoga, D.J. Buttle, I.R. Duce, Ann Lowe, J.M. Behnke

Little is known about the efficacy of cysteine proteinases (CP) as anthelmintics for cestode infections. We examined the effects of CPs on two rodent cestodes, *Hymenolepis diminuta* and *H. microstoma* in vitro. Our data showed that naturally occurring mixtures of CPs, such as those found in papaya latex, and relatively pure preparations of fruit bromelain, papain and stem bromelain, were active in vitro against both juvenile, artificially excysted scoleces, as well as against adult worms of both rodent cestodes. Significant dose-dependent reduction in motility, ultimately leading to death of the worms, was observed with both species, and against both freshly excysted scoleces and 14-day old pre-adult worms. The most effective was fruit bromelain (after 30 min of incubation of juvenile *H. diminuta* and *H. microstoma* IC50 = 63 and 74 μM, respectively, and for pre-adult worms = 199 and 260 μM, respectively). The least effective was stem bromelain (after 30 min of incubation of juvenile *H. diminuta* and *H. microstoma* IC50 = 2855 and 2772 μM, respectively, and for pre-adult worms = 1374 and 1332 μM, respectively) and the efficacies of papaya latex supernatant and papain were between these extremes. In all cases these values are higher than those reported previously for efficacy of CPs against intestinal nematodes, and in contrast to nematodes, all CPs were effective against cestodes in the absence of exogenous cysteine in incubation media. The CPs appeared to attack the tegument resulting in generalised erosion mainly on the strobila. The scolex was more resistant to CP attack but nevertheless some damage to the tegument on the scolex was detected.

**Keywords**

Anthelmintics; Cysteine proteinases; *Hymenolepis diminuta*; *Hymenolepis microstoma*; Papaya latex
Organotypic culture of human amnion cells in air-liquid interface as a potential substitute for skin regeneration.

Fatimah SS, Chua K, Tan GC, Azmi TI, Tan AE, Abdul Rahman H.

Background Aims:
The aim of the present study was to evaluate the effects of air-liquid interface on the differentiation potential of human amnion epithelial cells (HAECs) to skin-like substitute in organotypic culture.

Methods:
HAECs at passage 1-2 were seeded onto a fibrin layer populated with human amnion mesenchymal cells to form the organotypic cultures. The organotypic HAECs were then cultured for 7, 14 and 21 d in two types of culture system: the submerged culture and the air-liquid interface culture. Cell morphogenesis was examined under the light and electron microscopes (transmission and scanning) and analyzed by immunohistochemistry.

Results:
Organotypic HAECs formed a single layer epithelium after 3 wk in submerged as well as air-liquid interface cultures. Ultrastructurally, desmosomes were observed in organotypic HAECs cultured in the air-liquid interface but not in the submerged culture. The presence of desmosomes marked the onset of early epidermal differentiation. Organotypic HAECs were positive against anti-CK18 and anti-CK14 in both the submerged and the air-liquid interface cultures. The co-expression of CK14 and CK18 suggested that differentiation of HAECs into skin may follow the process of embryonic skin development. However, weak expression of CK14 was observed after 2 and 3 wk of culture in air-liquid interface. CK10, involucrin, type IV collagen and laminin-5 expression was absent in organotypic HAECs. This observation reflects the initial process of embryonic epidermal differentiation and stratification.
Conclusions:

Results from the present study suggest that the air-liquid interface could stimulate early differentiation of organotypic HAECs to epidermal cells, with a potential use for skin regeneration.

Keywords

Air-liquid interface; Epithelial stem cells; Fibrin; Human amnion-derived stem cells; Organotypic culture; Skin regeneration
Factors Associated with Preferences for Safe Drinking Water among Outpatients at Hospital Universiti Sains Malaysia (HUSM), Kelantan, Malaysia

Azlina A., Nik Rosmawati N.H., Zaliha I.

Food and water borne diseases are resulted from consuming unsafe drinking water. However, a few states in Malaysia including Kelantan were reported to have low accessibility to treated water. The aim of this study was to assess the preference for safe drinking water and its associated factors among Hospital Universiti Sains Malaysia (HUSM) outpatient clinic attendees. A cross-sectional study was conducted from 1st February 2011 to 30th April 2011. A convenient sampling was applied and face to face interview was conducted by using a structured questionnaire. Those 18 years and above and literate were included as subjects. Results show that the proportion towards safe drinking water preferences was 30.4% (95% CI: 0.22, 0.39). Two significant associated factors for safe drinking water preferences were current used of drinking water source and household income status. People who currently used municipal water has 14.32 times odds to prefer safe drinking water than person who used other sources (95% CI: 4.08, 50.30, p <0.001). Those at low and middle income level were 0.23 (95% CI: 0.06, 0.84, p=0.027) and 0.11 (95% CI: 0.03, 0.47, p=0.003) times odds to prefer safe drinking water than those below poverty line consecutively. In conclusion, the proportion of safe drinking water preference among HUSM outpatient clinic attendees was low and associated with current drinking water source and income level. An effective public awareness campaign is needed to convince public toward municipal water supply in order to help reducing the incidence of food and water borne diseases.

Keywords

Associated factors; Drinking water preferences; Safe drinking water
The aim of present study was to assess nutritional knowledge and behaviour in relationship with demographic variations in a group of normal pregnant women. Participants were in their second or third trimester of gestation and were selected randomly while they attended in Obstetrics and Gynecology clinic for antenatal follow-up. Information about demography, knowledge, attitude and practices on food and nutrition were assessed using the developed and validated questionnaire. Multivariate analyses showed that there was a significant linear relationship between nutritional knowledge and occupation, educational level and monthly income while there was no significant relationship between demographic characteristics and nutritional belief. The findings also showed significant relationship between nutritional practices and monthly income and educational level after they were entered into the multiple regression model. It can be concluded that more educated people with higher economic status had better nutritional knowledge and dietary behavior. Participants’ occupation was related significantly only to their nutritional knowledge. For improvement of diet quality among all levels of society, educational interventions during health programs should target different segments of people to reduce the inequalities in health due to diversities in education and occupation.

Keywords
Pregnancy; Lifestyle; Dietary practices
Quality of life in relationship with Nutritional Attitude and Practices during Pregnancy

Mitra Ossadat Mirsanjari, Wan Abdul Manan Wan Muda, Affizal Ahmad, Mohd Shukri Othman and Mir Mehrdad Mirsanjari

Health and nutritional related problems during pregnancy impact not only on women’s quality of life, but consequently on her newborn’s well-being after delivery, her family members and community as well. The aim of this study was to investigate the contribution of quality of life indices and nutritional knowledge, attitude and practices among normal pregnant women during second and third trimester of gestation. A cross-sectional study was conducted among pregnant women who attended Obstetrics and Gynaecology clinic during their antenatal care visits. Demographic questions and the short form-36 questionnaire of quality of life (SF-36) were utilized. The findings of this study showed significantly higher vitality for pregnant women with healthy choice of breakfast, consumption of bean and vegetables every day, doing exercise every day or 2-3 times/week and first priority when buying foods on nutrient content. Subdomain of general health was significantly higher in subjects with higher nutritional knowledge and those who consumed bean and products every day. However, healthy choice of dinner had negative relationship with general health. Consumption of fast foods never or 2-3 times/month was significantly related with higher level of physical and social functioning. Sub domain of role physical was shown to have negative relationship with healthy choices of breakfast, lunch and type of drink. Social functioning had significant relationship with, healthy choice of breakfast and positive attitude about changing dietary pattern. Consumption of chicken/duck every day had significant relationship with role emotion. Sub domain of mental health was in positive and significant relationship with eating breakfast every day and positive attitude of changing dietary pattern. The findings of this study indicate that aspects of health related quality of life during normal pregnancy are predicted by some healthy attitude and practice factors on food and nutrition.

Keywords: Quality of life; Pregnancy; Nutritional practices; Health
Diversity of Nutrient Intake in Pregnant Women with Different Nutritional Behaviors

Mitra Mirsanjari, Wan Abdul Manan Wan Muda, Affizal Ahmad 1, Mohd Shukri Othman and Mir Mehrdad Mirsanjari

A healthy and varied diet during pregnancy is important as it provides improvement of maternal health and birth outcomes. The aim of this study is to investigate pregnant women nutritional intake and comparison with recommended dietary allowances (RDA), and also to understand whether healthy and unhealthy food practices influence on nutrient intake of pregnant women. A cross-sectional study was carried out among pregnant women attended Obstetrics and Gynaecology clinic during their antenatal care visits. Questionnaire KAP and 24 diet recall were used for obtaining data. The findings of this study showed that mean differences of some essential vitamins and minerals was significantly different between two groups of healthy and unhealthy food practices. This study showed that protein, carbohydrate, vit B₁, vit B₂, Niacin, folate, vit B₁₂, phosphorous and zinc, were higher than RDA. Whereas, intake of some other nutrients e.g. fiber, magnesium, potassium were lower than RDA. Pregnant women in this study had higher percentage of positive attitude on food and nutrition (65.1%) versus (27.4% and 7.5%) for moderate and poor attitude respectively. Also, the participants with moderate food practices had highest percentage (77.3%) among 21.7% and 1% for poor and good practices respectively. Knowledge score for poor, moderate and good categories were 18%, 45.6% and 36.4% respectively. It is concluded that pregnant women need to increase their food intakes with rich sources of fibre, magnesium and potassium. The findings recommend that pregnant women need continuous guidance to choose nutrient dense food items. Additionally, the results of this study highlight the importance of healthy nutritional practices of pregnant women with respect to nutritional knowledge. Therefore appropriate nutrition counselling and education could be performed in different stages of women’s childbearing age to be reflected on adequate dietary intake before and during the pregnancy.

Keywords
Nutrient intake; Pregnancy; Nutritional practices; Health
Socio-Demographic, Dietary and Physical Activity Determinants of Adolescents Overweight and Obesity in Kelantan

Sakinah H., Seong-Ting C., Rosniza R. and Jayah K.P.

The increasing prevalence of overweight and obesity among adolescents in Malaysia has become a serious epidemic. The objective of this study was to determine the association between socio-demographic, dietary habits and physical activity risk factors with overweight and obesity prevalence. A cross-sectional study was conducted among 178 secondary school students aged 13 to 16 years old in Bachok district (n=88) and Kota Bharu district (n=90). A self-administered questionnaire on demographic, socio-economic status, dietary habits and physical activity information was used; standard anthropometric measurements: body weight, height and body mass index (BMI) were obtained. Results show that the mean BMI of the respondents was 21.04 ± 4.87 kg/m². The prevalence of overweight and obesity (30%) was greater among respondents from Kota Bharu district as compared to Bachok district. The mean household income of the respondents from Kota Bharu district was significantly greater than that of Bachok (p<0.05). Data also showed a significant association between students’ residence, household income, frequency of fast food consumption, breakfast skipping and physical activity with overweight and obesity prevalence (p<0.05). In conclusion these findings demonstrated the contributing factors towards body weight problems among the adolescents. This information is useful for the planning of health and nutrition programmes as well as intervention strategies to combat adolescent obesity.

Keywords

Adolescent; Overweight; Obesity
Validity of a local nutritional screening tool in hospitalized Malaysian elderly patients

Sakinah H. and Tan S.L.

Nutritional screening is a process used to identify characteristics associated with the nutritional problems. A local Malnutrition Risk Screening Tool–Hospital (MRST-H) has been developed to assess the risk of poor nutrition among elderly patients in Malaysia. The aim of this study was to evaluate the validity of MRST-H as a screening tool for malnutrition in elderly patients in Kuala Lumpur Hospital, Malaysia. A cross-sectional study was carried out at the Medical and Oncology Wards of Kuala Lumpur Hospital, Malaysia from July to August 2004. Face-to-face interviews were conducted using a structure questionnaire followed by anthropometry measurements. The MRST-H was validated against the Global Indicator of Malnutrition (GIM), combined-measures of nutritional assessment. A total of 100 respondents (37.0% men and 63.0% women) aged 65 years and above (mean age = 73.11 ± 6.03 years) were recruited. Our results showed that MRST-H was valid with 66.7% sensitivity, 96.2% specificity and 82.4% positive predictive value. The magnitude of malnutrition among the elderly patients was 21.0% according to the GIM. MRST-H is a valid nutritional screening tool for hospitalized Malaysian elderly patients. It can be used to identify patients in need of nutrition care plan.

Keywords
Nutritional screening; Validation; MRST-H; Elderly patients
Knowledge, Attitude and Dietary and Lifestyle Practices on Bone Health Status among Undergraduate University Students in Health Campus, Universiti Sains Malaysia, Kelantan

Wan Arfah Nadiah Wan Jamil, Mohd Ezane Aziz, Foo Leng Huat

Dietary and environmental lifestyle factors play an important role in the development and maintenance of bone health throughout lifecycle. This study aims to assess the knowledge, attitude and dietary and lifestyle practices of osteoporosis among 70 healthy undergraduate male and female students aged 18-21 years chosen by a simple random sampling at Health Campus, University Science Malaysia (USM). Several research protocols were used namely, a validated questionnaire on general characteristics, socio-demographic, questions pertaining to the knowledge, attitude and dietary and lifestyle practices towards bone health status, anthropometric profile measurements and dietary intakes intake assessment. Mean age of the subjects was 19.8 ± 0.9 years with 67% were females. The present finding indicates that mean score of knowledge pertaining to risk factors of bone health was low with majority of the subjects (82.6%) were scored below 80%. In contrast, three-quarters of subjects (77.1%) understood the importance of positive attitude of high calcium foods and physically active lifestyle towards positive bone health status and osteoporosis prevention. Dietary and lifestyle practices revealed that only 1.4% subjects met the daily recommended level of calcium intake and only 7.2% subjects were engaged in active (vigorous) physical activity of at least 2 hours weekly. Thus, the present findings highlight the need of formulating health education programs on bone health status and osteoporosis prevention among young adults in order to increase awareness of maintaining positive lifestyle behaviors associated with higher bone mass accretion and at the same time promote specific preventive behavior among collegiate students in Malaysia.

Keywords
Knowledge; Attitude; Dietary and lifestyle practices; Bone status; Health
Environmental Degradation and Human Disease

Haliza Abdul Rahman, Rapeah Suppian

Human health is strongly linked to the health of ecosystems. However, destruction of natural resources such as soil, water and the atmosphere not only affect the terrestrial fauna and flora, but also resulted in unprecedented levels of disease emergence which potentially cause severe future impacts on human health. Many important human diseases have originated in micro- and macro-organisms, thus, changes in the habitats of these populations may affect the mode of action as well as their pathogenicity. In addition, the continuous degradation of ecosystems is leading to increased susceptibility to disease caused by these organisms. The adverse health impacts will be much greater in low-income populations than in richer nations. Thus, there is a great need for collective action to prevent environmental degradation.

Keywords

Environmental degradation; Human disease; Health; Ecosystems
Stimulating Urban Environment Sustainability through Edible Garden Plants

Main R., Fatimah H.

This article discusses the role of gardens, small plots or areas surrounding a house designated for edible plants or flowers and its contribution towards environment sustainability. A study on transpiration was done on chilly plant (Capsicum frutescens). Its popularity as an edible garden plant in urban residences is due to lower planting cost but higher economic revenue to the planters. The finding shows that for an average surface area of 7.02 square centimetres, every chilli leaf has the potential of evaporating 0.045 millilitres of water in 24 hours. For this reason, neither chilly nor other plants in edible gardens that are capable in producing water have the potential to become sustainable source in lowering the temperature and hence creating a sustainable urban environment.

Keywords

Environment sustainability; Urban; Temperature; Economic
Assessment of Indoor Radon Concentration in Dwellings in Iraqi Kurdistan Using CR-39 Dosimeters

Najeba F.S. and Mohamad S.J.

The effect of indoor radon radiation on the fertility of women living in 30 spatial dwellings in three governorates in Iraqi Kurdistan was investigated. The radon concentrations in kitchens were measured using 60 CR-39 detectors. The level of radiation of alpha particles was evaluated depending on the track density of the particles. Also, the indoor radon progeny and concentration of radon varied depending on the type of dwelling, ventilation, and geological formation. The results show that radon concentration was high in Sedakan city and low in Dukan city. The levels of radon in the kitchen of the dwellings ranged between 99.947 Bq m\(^{-3}\) and 360.112 Bq m\(^{-3}\), with an average activity of 187.215 Bq m\(^{-3}\). The radon progeny concentration WL varied between 10.805 Bq m\(^{-3}\) and 38.931 Bq m\(^{-3}\). The indoor radon levels in few dwellings were above the recommended limits of the US Environmental Protection Agency. The distribution of indoor radon concentration in Iraqi Kurdistan was high in many houses and this could pose a health risk or affect women fertility.

Keywords

CR-39 NTDs; Dwelling; Fertility of women; Indoor radon; Kitchen; Radon Concentration
Metabolic Syndrome and Occupational Risk Factors among Healthcare Workers in Kelantan

Ahmad Faris A., Mohd. Nazri S., Wan Mohd Zahiruddin W.M.

Occupational factors such as stress and shift work are found to be risk factors for Coronary Heart Disease (CHD). Several studies have documented increase risk of CHD among individuals with metabolic syndrome. This study was designed to determine the prevalence of metabolic syndrome using the definition by the Third Report of the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) and to describe the characteristics of nurses with metabolic syndrome including work related factors. A cross-sectional study was conducted between January to April 2009 among 404 nurses in Hospital Universiti Sains Malaysia (HUSM), Kelantan, Malaysia. All the respondents were female nurses aged 30–56 years. Data was collected using a questionnaire consists of sociodemographic, occupational history and physical activity as well as DASS 42 questions (translated to Malay language and validated). Waist circumference, blood pressure measurement and fasting venous blood for lipid profile and fasting blood sugar were taken from each subject. Data entry and analysis were done using SPSS Version 12.0.1. The prevalence of metabolic syndrome was determined, and factors associated with the metabolic syndrome were analyzed by multiple logistic regression. Majority of the respondents were Malay with mean (SD) age of 42.1 (7.19) years old. The mean (SD) duration of employment was 17.8 (6.33) years. Majority (91.1%) of nurses was physically inactive and 14.1% were having stress. The prevalence of metabolic syndrome was 24.3% (95%CI: 20.1, 28.4). The significant factors associated with metabolic syndrome after statistical adjustments for the confounding factors were total duration of employment (years) and one way commuting time to work (minutes). High prevalence of metabolic syndrome indicates that nurses are occupational risk group for CHD. Further multicentres cross sectional studies or better, a cohort study are needed to plan for an effective intervention programme.

Keywords
Metabolic syndrome; Nurses; Shift work; Occupational
Objective: This study aims to evaluate the association of neurotic personality traits and coping styles with depression amongst first year medical and dental students.

Methods: A total of 167 students consisting of 133 medical and 34 dental students in their first year were recruited. All the subjects were assessed using BDI, NEO PI-R (N) and Brief COPE for depression, neurotic personality traits and coping styles respectively.

Result: First year dental students were 3 times more likely to have depression than first year medical students. Students who scored high and very high on the total Neuroticism factor and the Depression facet of NEO PI-R (N) were 3.6 times and 7 times more likely to have depression than students who scored very low, low or average for the above scales. All coping styles and other socio-demographic factors showed no association with depression.

Conclusion: Neurotic personality traits are significantly associated with depression. NEO PI-R (N) proved to be a useful tool to evaluate the neurotic traits among medical and dental students allowing early interventional measures to those who need it.

Keywords
Neurotic personality traits; Depression; Coping style; Medical student; Dental student
Offenders with Schizophrenia: Relationship to Psychopathology

Surina Z.H., Zahiruddin O., Mohd Azhar M.Y., Rabaiah M.S.

Objective: To study the relationship between psychopathology and characteristics of offenders with schizophrenia.

Methods: In this cross-sectional study, 70 consecutive offenders with schizophrenia (aged 18-65) admitted to Hospital Bahagia Ulu Kinta within a six-month period were studied. Subjects’ psychopathology was assessed using Positive and Negative Syndrome Scale (PANSS).

Results: Offenders against person group received treatment at later age ($p=0.043$) compared to against property and drug or firearm-related offenders groups. Offenders in drug or firearm-related group had significantly higher PANSS negative scores ($p=0.015$). Unsound mind at the time of offense was significantly associated with high PANSS positive scores ($p=0.011$) and offenders against person or property groups ($p=0.004$).

Conclusion: Offenders against person had a significantly later age of treatment and probably onset of illness. Unsoundness of mind was significantly associated with positive symptoms and more frequently reported among offenders against person or property. Offenders in drug or firearm-related group were significantly associated with negative symptoms.

Keywords

Mentally ill offender; Schizophrenia; Positive symptoms; Negative symptoms; Unsound Mind
Biodegradation of microbial polyesters P(3HB) and P(3HB-co-3HV) under the tropical climate environment

Akmal D., Azizan M.N., Majid M.I.A.

The biodegradation of poly(3-hydroxybutyrate), P(3HB), and its copolymer poly(3 hydroxybutyrate-co-3-hydroxyvalerate), P(3HB-co-3HV) produced by a locally isolated bacteria identified as Erwinia sp. USMI-20 were carried out by using soil burial test and immersion test method at various places under the tropical environment in West Sumatra, Indonesia. The isolation of P(3HA)-degrading microorganisms was done by the in vitro rapid plate test method and was further characterized by using biochemical reactions. Our results showed that P(3HB) biodegraded at a rate of 3.6% per week in activated sludge, 1.9% per week in soil, 1.5% per week in lake water and 0.8% per week in Indian Ocean sea water. The degradation rates for P(3HB-co-3HV) were 17.8% per week in activated sludge, 6.7% per week in soil, 3.2% per week in lake water and 2.7% per week in Indian Ocean sea water. The biodegradation of both polymers were highest after burial into activated sludge with a half-life ($T_{1/2}$) of 14 weeks and the time for 100% degradation ($T_{100%}$) of 28 weeks for P(3HB), and a $T_{1/2}$ of 3 weeks and $T_{100%}$ at 6 weeks for P(3HB-co-3HV). In this study, 10 bacteria which were responsible for the biodegradation of P(3HB) and P(3HB-co-3HV) film were isolated and identified from the various places studied under the tropical environment. They were Bacillus sp. FAAC-2202, Enterobacter sp. FAAC-2207, Bacillus sp. FAAC-2209 and Proteus sp. FAAC-2203 obtained from activated sludge, Bacillus sp. FAAC-2201 and Alcaligenes sp. FAAC-2210 from soil, Alcaligenes sp. FAAC-2205, Micrococcus sp. FAAC-2206 and Pseudomonas sp. FAAC-2208 from lake water and Proteus sp. FAAC-2204 from Indian Ocean sea water.

Keywords

Biodegradation; Microbial polyesters; Tropical climate; Poly(3 hydroxybutyrate); Poly(3-hydroxybutyrate-co-valerate)
YB-1 and CTCF Differentially Regulate the 5-HTT Polymorphic Intron 2 Enhancer Which Predisposes to a Variety of Neurological Disorders

Elena Klenova, Alison C. Scott, Julian Roberts, Shaharum Shamsuddin, Elizabeth A. Lovejoy, Stephan Bergmann, Vivien J. Bubb, Hans-Dieter Royer, and John P. Quinn

The serotonin transporter (5-HTT) gene contains a variable number tandem repeat (VNTR) domain within intron 2 that is often associated with a number of neurological conditions, including affective disorders. The implications of this polymorphism are not yet understood, however, we have previously demonstrated that the 5-HTT VNTR is a transcriptional regulatory domain, and the allelic variation supports differential reporter gene expression in vivo and in vitro. The aim of this study was to identify transcription factors responsible for the regulation of this VNTR. Using a yeast one-hybrid screen, we found the transcription factor Y box binding protein 1 (YB-1) interacts with the 5-HTT VNTR. Consistent with this, we demonstrate in a reporter gene assay that the polymorphic VNTR domains differentially respond to exogenous YB-1 and that YB-1 will bind to the VNTR in vitro in a sequence-specific manner. Interestingly, the transcription factor CCTC-binding factor (CTCF), previously shown to interact with YB-1, interferes with the ability of the VNTR to support YB-1-directed reporter gene expression. In addition, CTCF blocks the binding of YB-1 to its DNA recognition sequences in vitro, thus providing a possible mechanism of regulation of YB-1 activation of the VNTR by CTCF. Therefore, we have identified YB-1 and CTCF as transcription factors responsible, at least in part, for modulation of VNTR function as a transcriptional regulatory domain. Our data suggest a novel mechanism that explains, in part, the ability of the distinct VNTR copy numbers to support differential reporter gene expression based on YB-1 binding sites.

Keywords

CTCF; YB-1; 5-HTT; VNTR; Affective disorders; Transcription
In vitro cytotoxicity evaluation of dental porcelain using human cell lines

Hazem Yousef Abu Sharbeh, Thirumulu Ponnuraj Kannana, Raja Azman Raja Awang, Adam Husein

The in vitro cytotoxic potential of locally produced dental porcelain was evaluated in this study. The cellular response of human osteoblast and fibroblast cell lines were assessed using MTT assay by incubating with the fluid extract of dental porcelain powder and dental porcelain discs (direct test). Aging process was carried out by submerging the discs into 3% bovine serum albumin (BSA) solution. Tests on extracts showed that dental porcelain was significantly different from the control at a concentration of 250 mg/ml. Direct test showed that dental porcelain after aging was not significantly different from the control with a mean (SD) of 89.2 (13.4)%, whereas, it was significantly different from the control before conditioning of BSA with a mean (SD) of 88.5 (12.1)%. However, the dental porcelain caused mild suppression of succinate dehydrogenase activity (<25%), which is considered to be accepted clinically and hence can be ranked as being non-cytotoxic.

Keywords
Dental porcelain; Cell line; Cytotoxicity; MTT assay
**In vitro evaluation of novel chitosan derivatives sheet and paste cytocompatibility on human dermal fibroblasts**

Mohammad Syaiful Bahari Abdull Rasad, Ahmad Sukari Halim, Kamaruddin Hashim, Ahmad Hazri Abdul Rashid, Norimah Yusof, Shaharum Shamsuddin

The cytocompatibility of novel chitosan derivative sheets and pastes were evaluated *in vitro* for possible utilization in wound dressing applications for wound healing. In this study, the cytotoxicity of oligochitosan (O-C), N,O-carboxymethyl-chitosan (NO-CMC) and N-carboxymethyl-chitosan (N-CMC) derivatives in sheet-like and paste forms were evaluated using primary normal human dermal fibroblast cultures and hypertrophic scars; a fibrotic conditions representing a model of altered wound healing with overproduction of extracellular matrix and fibroblast hyperproliferative activity. Cytotoxicities of these chitosan derivatives were assessed using 3-[4,5-dimethyl-2-thiazolyl]-2,5-diphenyl tetrazolium bromide (MTT) assay. The results indicate that both chitosan derivative sheets and pastes have appropriate cytocompatibility and appear promising as safe biomaterials with potential wound healing applications. The SH120 (NO-CMC) derivatives sheet exhibited highest cytocompatibility property and may be regulated by MMP-13 in controlling the cell growth and its expression level.

**Keywords**

Cytocompatibility; Chitosan derivatives; Sheet; Paste; Primary human fibroblasts; Hypertrophic scars; Matrix metalloproteinase-13
Generating temporal model using climate variables for the prediction of dengue cases in Subang Jaya, Malaysia

Nazri Che Dom, A. Abu Hassan, Z. Abd Latif, Rodziah Ismail

Objective: To develop a forecasting model for the incidence of dengue cases in Subang Jaya using time series analysis.

Methods: The model was performed using the Autoregressive Integrated Moving Average (ARIMA) based on data collected from 2005 to 2010. The fitted model was then used to predict dengue incidence for the year 2010 by extrapolating dengue patterns using three different approaches (i.e. 52, 13 and 4 weeks ahead). Finally, cross correlation between dengue incidence and climate variable was computed over a range of lags order to identify significant variables to be included as external regressor.

Results: The result of this study revealed that the ARIMA (2,0,0) (0,0,1) model developed, closely described the trends of dengue incidence and confirmed the existence of dengue fever cases in Subang Jaya for the year 2005 to 2010. The prediction per period of 4 weeks ahead for ARIMA (2,0,0) (0,0,1) was found to be best fit and consistent with the observed dengue incidence based on the training data from 2005 to 2010 (Root Mean Square Error=0.61). The predictive power of ARIMA (2,0,0)(0,0,1) is enhanced by the inclusion of climate variables as external regressor to forecast the dengue cases for the year 2010.

Conclusions: The ARIMA model with weekly variation is a useful tool for disease control and prevention program as it is able to effectively predict the number of dengue cases in Malaysia.

Keywords: Dengue; Forecasting; ARIMA model; Climate; Malaysia
Enhanced Recovery and Purification of P(3HB-co-3HHx) from Recombinant Cupriavidus necator Using Alkaline Digestion Method

Siti Nor Syairah Anis, M. I. Nurhezreen, K. Sudesh, A. A. Amirul

A simple, efficient and economical method for the recovery of P(3HB-co-3HHx) was developed using various chemicals and parameters. The initial content of P(3HB-co-3HHx) in bacterial cells was 50–60 wt%, whereas the monomer composition of 3HHx used in this experiment was 3–5 mol%. It was found that sodium hydroxide (NaOH) was the most effective chemical for the recovery of biodegradable polymer. High polyhydroxyalkanoate purity and recovery yield both in the range of 80–90 wt% were obtained when 10–30 mg/ml of cells were incubated in NaOH at the concentration of 0.1 M for 60–180 min at 30 °C and polished using 20 % (v/v) of ethanol.

Keywords
Polyhydroxyalkanoates; Cupriavidus; Alkaline digestion; Recovery; 3HHx
Structural characterization of nanoparticles from thermoresponsive poly(N-isopropylacrylamide)-DNA conjugate

Wei-Yang Ooi, Masahiro Fujita, Pengju Pan, Hui-Ying Tang, Kumar Sudesh, Kazuki Ito, Naoki Kanayama, Tohru Takarada, Mizuo Maeda

Poly(N-isopropylacrylamide) (PNIPAAm) grafted with single-stranded (ss) DNA conjugate (PNIPAAm-g-DNA) self-assembles above its lower critical solution temperature to form colloidal particles. When the ssDNA within the particle hybridizes with its complementary DNA, the particles aggregate above a certain threshold of salt concentration with drastically increased turbidity in solution. Detailed structural information of the particle was obtained mainly by small-angle X-ray scattering. The influence of copolymer composition on the morphology of particle and non-crosslinking aggregation was examined. The particle consists of hydrophobic PNIPAAm core surrounded by hydrophilic DNA strands. The increase in DNA fraction brought about a significant decrease in core size, whereas the shell thickness little changed and corresponded to the length of DNA. A structural model with a sticky potential was applied to the analysis of particle aggregate. This analysis provided that the particles aggregate while the coronal layers interpenetrate each other. The interaction between the particles was quantified in terms of the sticky potential and showed a trend to be influenced by the particle size rather than the graft density of DNA strands on the particle.

Keywords
PNIPAAm; DNA; Soft interface; SAXS
Bringing change to the housing industry requires multiple efforts from various angles especially to overcome any resistances in the form of technology, human aspects, financial and resources. The transition from conventional to sustainable approach consumes time as it requires changes from different facets in the industry ranging from individual, organisational to industry level. In Malaysia, there are various efforts to bring green into the industry but the progress is low-moderate. Will the current efforts bear larger fruits in the near future? This study examines the perceptions of the developers in Malaysia on the future of the green housing sector for the next 5 years. The introduction of GBI rating system, improvement of awareness and knowledge among the stakeholders, support from the government and local industry and the effect of competitive advantage would support brighter future. Meanwhile, the status quo in rules and regulation, lack of public interest and demand, organization disinterest, local authority enforcement and project cost escalation would hinder a faster progress.

Keywords
Developers; Green concept; Housing industry; Sustainable construction
Many people have turned away from conventional medicines, with the belief that ‘natural’ substances like herbs are safer than synthetic substances. This belief is augmented by many other unwarranted claims such as herbal products do not contain chemicals while conventional medicines do, thus contributing to the latter’s side effects. The increasing use of herbal medicines has resulted in concern about the efficacy and safety of these products. Herbs can be hazardous in many ways. They may be intrinsically toxic or toxic when taken in combination with other preparations. Because herbal preparations are usually not evaluated for purity and consistency of active compounds, they often contain contaminants. Inclusion of incorrect but toxic species, allergens, pollen, insect parts, heavy metals such as lead, mercury and arsenic and scheduled poisons (drugs), whether intentional or unintentional, have been cited as the causes of herbal adverse reactions or toxicities. The increasing use of herbal medicines means that there is potential for more drug interactions, particularly between herbal products and conventional ‘Western’ medicines. Toxicity and drug-local herb interaction studies are scarcely conducted and therefore should be encouraged. Proper documentation of adverse effects of herbs should be initiated and patients should be asked about their use of herbal products in order to evaluate the potential of these products to interact with concurrent prescription medications. The public should be made aware of the adverse effects of herbal products.

Keywords
Herbs; Adverse effects; Safety; Herbal toxicities; Drug-herbal interactions
Antioxidant activity and phytochemical screening of the methanol extracts of *Euphorbia hirta* L

Abu Arra Basma, Zuraini Zakaria, Lacimanan Yoga Latha, Sreenivasan Sasidharan

Objective:
To assess antioxidant activities of different parts of *Euphorbia hirta* (E. hirta), and to search for new sources of safe and inexpensive antioxidants.

Methods:
Samples of leaves, stems, flowers and roots from *E. hirta* were tested for total phenolic content, and flavonoids content and *in vitro* antioxidant activity by diphenyl-1-picrylhydrazyl (DPPH) assay and reducing power was measured using cyanoferrate method.

Results:
The leaves extract exhibited a maximum DPPH scavenging activity of (72.96±0.78)%, followed by the flowers, roots and stems whose scavenging activities were (52.45±0.66)%, (48.59±0.97)%, and (44.42±0.94)%, respectively. The standard butylated hydroxytoluene (BHT) was (75.13±0.75)%. The IC$_{50}$ for leaves, flowers, roots, stems and BHT were 0.803, 0.972, 0.989, 1.358 and 0.794 mg/mL, respectively. The reducing power of the leaves extract was comparable with that of ascorbic acid and found to be dose dependent. Leaves extract had the highest total phenolic content [(206.17±1.95) mg GAE/g], followed by flowers, roots and stems extracts which were (117.08±3.10) mg GAE/g, (83.15±1.19) mg GAE/g, and (65.70±1.72) mg GAE/g, respectively. On the other hand, total flavonoids content also from leave had the highest value [(37.970±0.003) mg CEQ/g], followed by flowers, roots and stems extracts which were (35.200±0.002) mg CEQ/g, (24.350±0.006) mg CEQ/g, and (24.120±0.004) mg CEQ/g, respectively. HPTLC bioautography analysis of phenolic and antioxidant substance revealed phenolic compounds. Phytochemical screening of *E. hirta* leaf extract revealed the presence of reducing sugars, terpenoids, alkaloids, steroids, tannins, flavanoids and phenolic compounds.
Conclusions:

These results suggested that *E. hirta* have strong antioxidant potential. Further study is necessary for isolation and characterization of the active antioxidant agents, which can be used to treat various oxidative stress-related diseases.

Keywords

Antioxidant; *Euphorbia hirta* L; DPPH scavenging; Reducing power; Total phenolics content; Total flavonoids content; Phytochemical screening
In Vitro Antioxidant Activity Potential of Lantadene A, a Pentacyclic Triterpenoid of Lantana Plants

Chong Grace-Lynn, Ibrahim Darah, Yeng Chen, Lachimanman Yoga Latha, Subramanian L. Jothy and Sreenivasan Sasidharan

Lantadenes are pentacyclic triterpenoids present in the leaves of the plant *Lantana camara*. In the present study, *in vitro* antioxidant activity and free radical scavenging capacity of lantadene A was evaluated using established *in vitro* models such as ferric reducing antioxidant power (FRAP), 2,2-diphenyl-1-picryl-hydrazyl (DPPH•), hydroxyl radical (OH•), nitric oxide radical (NO•), superoxide anion scavenging activities and ferrous ion chelating assay. Interestingly, lantadene A showed considerable *in vitro* antioxidant, free radical scavenging capacity activities in a dose dependant manner when compared with the standard antioxidant in nitric oxide scavenging, superoxide anion radical scavenging and ferrous ion chelating assay. These findings show that the lantadene A possesses antioxidant activity with different mechanism of actions towards the different free radicals tested. Since lantadene A is a very popular drug in modern medicine, it is a promising candidate for use as an antioxidant and hepatoprotective agent.

Keywords

Antioxidant activity; Free radical; Lantadene A; Triterpenes
The Improvement of Hypertension by Probiotics: Effects on Cholesterol, Diabetes, Renin, and Phytoestrogens

Huey-Shi Lye, Chiu-Yin Kuan, Joo-Ann Ewe, Wai-Yee Fung, and Min-Tze Liong

Probiotics are live organisms that are primarily used to improve gastrointestinal disorders such as diarrhea, irritable bowel syndrome, constipation, lactose intolerance, and to inhibit the excessive proliferation of pathogenic intestinal bacteria. However, recent studies have suggested that probiotics could have beneficial effects beyond gastrointestinal health, as they were found to improve certain metabolic disorders such as hypertension. Hypertension is caused by various factors and the predominant causes include an increase in cholesterol levels, incidence of diabetes, inconsistent modulation of renin and imbalanced sexual hormones. This review discusses the antihypertensive roles of probiotics via the improvement and/or treatment of lipid profiles, modulation of insulin resistance and sensitivity, the modulation of renin levels and also the conversion of bioactive phytoestrogens as an alternative replacement of sexual hormones such as estrogen and progesterone.

Keywords
Probiotic; Antihypertension; Cholesterol; Diabetes; Renin; Phytoestrogen
Genotoxicity of Euphorbia hirta: An Allium cepa Assay

Kwan Yuet Ping, Ibrahim Darah, Umi Kalsom Yusuf, Chen Yeng and Sreenivasan Sasidharan

The potential genotoxic effects of methanolic extracts of Euphorbia hirta which is commonly used in traditional medicine to treat a variety of diseased conditions including asthma, coughs, diarrhea and dysentery was investigated using Allium cepa assay. The extracts of 125, 250, 500 and 1,000 µg/mL were tested on root meristems of A. cepa. Ethylmethanesulfonate was used as positive control and distilled water was used as negative control. The result showed that mitotic index decreased as the concentrations of E. hirta extract increased. A dose-dependent increase of chromosome aberrations was also observed. Abnormalities scored were stickiness, c-mitosis, bridges and vagrant chromosomes. Micronucleated cells were also observed at interphase. Result of this study confirmed that the methanol extracts of E. hirta exerted significant genotoxic and mitodepressive effects at 1,000 µg/mL.

Keywords
Genotoxicity; Allium cepa; Ethylmethane sulfonate; Mitotic index; Chromosome aberrations
Ultrastructural Findings of *Anastatica hierochuntica* L. (Sanggul Fatimah) towards explaining its Medicinal Properties


‘Sanggul Fatimah’ or *Anastatica hierochuntica* L. is popular traditional herbal remedy consumed minutes prior to labor by Kelantanese Malay women to help ease childbirth. Scanning electron microscopic characterization of *Anastatica hierochuntica* L. is virtually a research lacunae and information on this herb is lacking but it is utmost importance as it will affect women’s attitudes and practices. The supra variable pressure scanning electron microscope (VPSEM) study of *Anastatica hierochuntica* L. revealed a surface characterization built-up of pebbles-like structures, asinus rings with thick tunica, an overwhelming soft lamellated surface and spiky corallike or torn-like structures closely associated with the raised pedunculated putative shoots of spikelike feature highly prominent in the stem. Micro diffraction analysis (EDX) revealed significant presence of carbon, oxygen, silica, calcium, magnesium, aluminium, potassium, zinc and iron varying with location. Although silica is quite significant in most probe areas, the topographical distributions of these periodic elements are non-homogenous. The combination silica and calcium may be associated with bone repair and possible help formation of collagen. The use of *Anastatica hierochuntica* L. in labor and post labor may be intended to achieve good tissue and organ repair but this hypothesis needs further scientific exploration.

**Keywords**

Ultrastructure; Elemental analysis; Scanning electron microscope; *Anastatica hierochuntica* L. (Sanggul Fatimah)
Assessment of Anticandidal Activity and Cytotoxicity of Root Extract from *Curculigo latifolia* on Pathogenic *Candida albicans*

Lim Sheh-Hong and I. Darah

*Curculigo latifolia* Dryand has been widely used as a traditional medicine, with beneficial effects in various diseases, including to ease joint pains and prevention of diabetes, obesity and cardiovascular. In this study, we demonstrated anticandidal activity and cytotoxicity activities of the methanolic root extract of *C. latifolia* Dryand. The solvent used for the process of extraction was methanol. The crude extract from *C. latifolia* Dryand root showed a favourable anti-*Candida* activity against different strains of pathogenic *C. albicans* cell by using disc diffusion method and broth dilution method. Brine shrimps assay was used to determine the cytotoxicity of methanolic root extract of *C. latifolia* Dryand. The Minimum Inhibitory Concentration (MIC) for the extract against *C. albicans* had determined. Time-kill assay demonstrated that *C. latifolia* Dryand root extract had inhibited the growth profile of *C. albicans*. The microscopic studies showed the extract acts by caused the alterations in morphology and complete collapse of the yeast cells after 36 h of exposure time. The result of *in vivo* cytotoxicity test revealed that the value of LC$_{50}$ of the root extract from *C. latifolia* Dryand was 2.25 mg mL$^{-1}$. Our data indicate that methanolic root extract of *C. latifolia* Dryand exerts significant anticandidal activity. Thus, the findings are demonstrating its relevant therapeutic potential in clinical treatment of candidiasis.

**Keywords**

*Curculigo latifolia*; Antimicrobial activity; *Candida albicans*; Minimum inhibition concentration; Cytotoxicity
Antioxidant Properties of Honey and Its Role in Preventing Health Disorder

M.I. Khalil, S.A. Sulaiman and L. Boukraa

Honey is being used since long time both in medical and domestic needs, but only recently its antioxidant property has come to limelight. With increasing demand for antioxidant supply in the food, honey is becoming popular as a source of antioxidant since it is rich in phenolic acids and flavonoids and other antioxidants including glucose oxidase, catalase, ascorbic acid, carotenoid derivatives, organic acids, amino acids and proteins. The antioxidants have several preventative effects against different diseases like cancer, cardiovascular diseases, inflammatory disorders, neurological degeneration, wound healing, infectious diseases and aging, which led to search for foods rich in antioxidants. Various studies on antioxidant properties of honey have been done. The present article is a short review on the antioxidant properties of honey and its role against health disorder.

Keywords
Honey; Antioxidant; Phytochemicals; Health disorder
Determination of total phenol, condensed tannin and flavonoid contents and antioxidant activity of *Uncaria gambir* extracts

M. Jain Kassim, M. Hazwan Hussin, A. Achmad, N. Hazwani Dahon, T. Kim Suan and H. Safley Hamdan

*Uncaria gambir*, a well-known Southeast Asia plant have been previously used as an alternative medicine for treatment such as diarrheal, sore throat and spongy gums. Due to its useful properties, in this study we have analysed the total phenol, condensed tannin, flavonoid content and antioxidant activity of *Uncaria gambir* in three different solvent extracts. Characterization and quantification analysis using Fourier Transform Infrared (FTIR) spectroscopy and reverse phase-high performance liquid chromatography (RP-HPLC) has confirmed that the major chemical constituents of *Uncaria gambir* are mainly catechins. It was revealed that the ethyl acetate gambir extract gives the highest catechin content and antioxidant activity compared with other solvent extracts.

**Keywords**

*Uncaria gambir*; Antioxidant activity; Condensed tannin; Flavonoid
Antiproliferative effect of methanolic extraction of tualang honey on human keloid fibroblasts

Mohamad Shah Nurul Syazana, Ahmad Sukari Halim, Siew Hua Gan and Shaharum Shamsuddin

Background: Keloid is a type of scar which extends beyond the boundaries of the original wound. It can spread to the surrounding skin by invasion. The use of Tualang honey is a possible approach for keloid treatment. The objective of this study was to determine the antiproliferative effect of methanolic extraction of Tualang honey to primary human keloid fibroblasts and to identify the volatile compounds in methanol extraction of Tualang honey.

Methods: Crude Tualang honey was extracted with methanol and then dried using rota vapor to remove remaining methanol from honey. Normal and keloid fibroblasts were verified and treated with the extracted honey. Cell proliferation was tested with [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt] (MTS) assay. Extraction of Tualang honey using methanol was carried out and the extracted samples were analysed using gas chromatography-mass spectrometry (GC-MS). The result was analysed using SPSS and tested with Kruskal-Wallis and Mann-Whitney tests.

Results: Methanolic extraction of honey has positive anti proliferative effect on keloid fibroblasts in a dosedependent manner. The presence of fatty acids such as palmitic acid, stearic acid, oleic acid, linoleic acid and octadecanoic acid may contribute to the anti-proliferative effect in keloid fibroblasts.

Conclusions: The methanolic honey extraction has an antiproliferative effect on keloid fibroblasts and a range of volatile compounds has been identified from Tualang honey. The antiproliferative effect of keloid fibroblasts towards Tualang honey may involve cell signaling pathway. Identifying other volatile compounds from different organic solvents should be carried out in future.
Randomized Controlled Trial on the Effects of Tualang Honey and Hormonal Replacement Therapy (HRT) on Cardiovascular Risk Factors, Hormonal Profiles and Bone Density Among Postmenopausal Women: A Pilot Study

Nik Hazlina Nik Hussain, Siti Amrah Sulaiman, Intan Idiana Hassan, Azidah Abdul Kadir, Norhayati Mohd Nor, Shaiful Bahari Ismail, Lili Husniati Yaacob, Rahimah Zakaria, Nazlah Shaniza Shafie, Juhara Haron, Kamarul Imran Musa

Results of recent trial have shown some negative effects of HRT on postmenopausal women. Therefore, there has been a need to search for an alternative treatment and honey is one of the well-known traditional remedies used in minimizing postmenopausal problems. The objectives of the study were to investigate the effects of Tualang honey on the cardiovascular risk factors, changes in hormonal profiles and also effect on the bone. A randomized controlled trial comparing the effects of Tualang honey 20 g/day and HRT for a 4-month intervention period among healthy postmenopausal Malay women aged 45-60 years old was conducted. The primary outcome measures were changes from baseline on the cardiovascular risk profiles, hormonal profiles and effect on bone. Tualang honey compared with low dose HRT, consumed for 4 months by postmenopausal women had no demonstrable effects on the parameters examined such as blood pressure measurement, body mass index and waist circumference. There was no significant difference in the lipid profile, blood sugar profile and bone density between the two groups at the end of the study period.
Forensic Drug Profiling of Erimin-5 Using TLC and GC-MS

Ahmad Fahmi Lim Abdullah, Abigail Asha Abraham, Maimonah Sulaiman and Vanitha Kunalan

Sixty-four groups of Erimin-5 tablets from 23 sources were profiled based on their dye and active ingredients. Dye of the tablets was extracted using 5% acetic acid and subjected to TLC separation using isopropanol/ammonia (4:1) as the solvent system while the active ingredients were analysed using GCMS and diluents were analysed using FTIR. All tablets were of peach-like or green in colour. The dye components were identified as tartrazine, sunset yellow, erythrosine, ponceau 4R and brilliant blue. The active ingredients were identified as nimetazepam and diazepam with glucose, sorbitol, mannitol and lactose as diluents. The combination of dye information and chemical contents allowed a quick classification of these 23 sources into six different profiles. This drug profiling method can provide useful information for narcotic enforcement and intelligence purposes. Forensic drug laboratories receiving tablet-form Erimin-5 should perform forensic profiling a profile database of the drug.

Keywords
Erimin-5; Nimetazepam; Dye; Active ingredients; Forensic chemistry
Residues at Clandestine Methamphetamine Laboratories and Their Health Effects

Ahmad Fahmi Lim Abdullah, Gordon Miskelly

There has been a sharp increase in the existence of methamphetamine related clandestine laboratories in Malaysia. When a clandestine laboratory is discovered, the law enforcement personnel normally remove the bulk of the chemicals. However, contamination remaining in the structure (ranging from visible stains to invisible residues) is still a concern. It is therefore important to identify the chemicals that could have been present, used and/or generated in a clandestine laboratory, and the health risks posed by them to law enforcement personnel as well as the future occupants of the structure. This article reviews the scientific literature and reports on clandestine laboratories, with particular focus on the residues present at clandestine laboratory sites, and current knowledge of the health risk associated with these.

Keywords

Clandestine laboratory; Methamphetamine; Residues; Exposure; Health
Challenges in the Management of Nasopharyngeal Carcinoma: A Review

Baharudin Abdullah, Azila Alias, Shahid Hassan

Nasopharyngeal carcinoma (NPC) is a non-lymphomatous, squamous cell carcinoma that occurs in the epithelial lining of the nasopharynx, an area that shows varying degrees of differentiation. Although relatively rare worldwide, NPC has substantial incidence and mortality in populations in Southeast Asia and in people with Southern Chinese ancestry. In Malaysia, NPC is a leading cancer type. In the clinic, NPC presents on a very wide spectrum. Therefore, a high degree of suspicion on the part of the clinician and an increased awareness by the patient is essential for the recognition of an early lesion. Early detection of the cancer is important as it affects the patient’s prognosis and the mode of treatment. Managing patients with NPC is very challenging as patients usually present late when the cancer is already in an advanced stage. Here, we review the challenges in the management of NPC.

Keywords
Nasopharyngeal carcinoma; Management; Challenges; Medical sciences
Health Concern on Lead Encountered during Firing Practices: A Review

Chang Kah Haw, P. T. Jayaprakash, Yew Chong Hooi, Ahmad Fahmi Lim Abdullah

Firing a gunshot leads to the expulsion of vapours and particulate materials termed gunshot residues (GSR) which includes particles of primer residue i.e. oxides of lead, antimony and barium as principle components. A fired bullet itself may contribute to lead particles or the particles of its jacket. Metallic lead or its oxide either airborne or deposited in soil and water followed by inhalation or ingestion by human beings would lead to chronic lead poisoning. Such poisoning has been shown to cause adverse effects in hematopoietic, nervous, endocrine, cardiovascular, reproductive and renal systems. Thus, airborne lead encountered during the routine firing practices is an increasing health concern for our security personnel. A number of reports and studies have been conducted emphasizing the risk of airborne lead exposure to the personnel at firing range. The effects of lead poisoning on the shooter depend on the dose and duration of exposure. The acute and chronic adverse health impacts due to lead exposure have been documented in the past. This paper emphasizes the measures that should be taken, especially by the police and army personnel involved in frequent firing practices including the introduction of lead free ammunition, proper ventilation system at firing range, wearing suitable personal protective equipments, proper personal and occupational hygiene and behaviours. Issues regarding the environment at firing range to minimize the exposure potential and the importance of contaminated site remediation are also emphasized.

Keywords

Airborne lead or lead oxide; Heavy metal; Gunshot residues; Firing range; Protection of security personnel
Prognostic Factors of Severe Traumatic Brain Injury Outcome in Children Aged 2-16 Years at A Major Neurosurgical Referral Centre

Choon Hong Kan, Mohd Saffari, Teik Hooi Khoo

Background:
Traumatic Brain Injury (TBI) in children has been poorly studied, and the literature is limited. We evaluated 146 children with severe TBI (coma score less than 8) in an attempt to establish the prognostic factors of severe TBI in children.

Methods:
The severity of TBI was assessed via modified Glasgow Coma Score for those more than 3 years old and via Children Coma Score for those under 3 years old. Clinical presentations, laboratory parameters and features of Computerised Tomography brain scans were analyzed. Outcomes were assessed at 6 months with the Pediatric Cerebral Performance Categories Scale; the outcomes were categorised as good or poor outcomes. Correlations with outcome were evaluated using univariate and multivariate logistic models.

Results:
A low coma score upon admission was independently associated with poor outcome. The presence of diabetes insipidus within 3 days post-TBI (OR: 1.9), hyperglycaemia (OR: 1.2), prolonged PT ratio (OR: 2.3) and leukocytosis (OR: 1.1) were associated with poorer outcome.

Conclusion:
Knowledge of these prognostic factors helps neurosurgeons and neurocritical care specialists to manage and improve outcome in severe TBI in children.

Keywords
Severe traumatic brain injury (TBI); Children; Prognostic factors; Pediatric cerebral performance categories score; Neurosciences
Occupational Safety and Health (OSH) issues are increasingly receiving attention and found as important in Malaysian Industrial Relations. In an operational analysis report of the OSH Regulations (2000) has found that 80 percent of workplace investigated failed to adhere fully to regulations (Abdul Rahman, 2007). Mass medias are also continuously reporting various accidents at the workplace which results in deaths. As a developing nation, improvements to its workers safety and health issues should go hand in hand with Malaysia economic booming. With the increased number of its small and medium enterprises (SMEs), Malaysia is facing greater challenges to monitor OSH requirements are adhered to in spite of trying to stay competitive and survive with its limited capital or financial resources. After making a comparison of implementation models of OSH of two developed nations namely United States and the United Kingdom, it is concluded that the involvement of various parties including the public in policy making, the development of appropriate infrastructure and human resources, enforcement autonomy, focused job scope within department, appropriate language usage, training inclusive of all forms of diversity at work and appropriate penalty are key success factors at reducing death rates, accidents and lost work days at the workplace for these two countries (Khoo, Kh’ng, Chee et al., 2007). Survey was distributed to SMEs in Malaysia, results were analyzed and findings with regard to the implementation of OSH in workplace are discussed.

Keywords

Occupational safety and health; Management commitment; External support
Retrospective Review of Outcomes of a Multimodal Chronic Pain Service in a Major Teaching Hospital: A Preliminary Experience in Universiti Sains Malaysia

Nizar Abdul Jalil, Zaharah Sulaiman, Mohamed Saufi Awang, Mohamarowi Omar

Abstract

Chronic pain is a common medical issue. Beside chronic devastating pain, patients also suffer dysfunction more generally, including in the physical, emotional, social, recreational, vocational, financial, and legal spheres. Integrate multidisciplinary and multimodal chronic pain management programmes offer clear evidence for relief of suffering and return to functional lifestyles.

Materials and Methods:

This retrospective review was performed in order to evaluate one-year outcomes among all newly referred patients of the multimodal chronic pain service at Hospital Universiti Sains Malaysia (HUSM). All patients received multimodal pain therapy, including pharmacological, physical, and psychological therapy, exercise, and pain intervention. The variables evaluated were based on a patient’s global pain assessments, which were made using the Visual Analogue Scale (VAS) and Oswestry Disability Index (ODI), modified by patient self-report, and were taken within days to months of commencing our multimodal pain regime.

Results:

A total of 169 patients were enrolled in this study. Out of this number, 102 (60.4%) were seen at the pain clinic, and 67 (39.6%) were referred while they were inpatients. About one-third of the patients had chronic pain due to cancer. Our data showed that 128 (75.7%) of our chronic pain patients were successfully managed when ≥50% of pain relief (as measured by their VAS score) was achieved at any point during the course of the study period. In addition, 104 patients (61.5%) showed improvement in their modified ODI by 50% or more.
Conclusion:

A multimodal chronic pain service plays a significant role in managing chronic pain patients in a major hospital, as it is capable of delivering comprehensive and attainable care to manage refractory and intractable chronic pain.

Keywords

Chronic pain service; Visual analogue scale; Modified Oswestry Disability Index; Multimodal pain therapy; Multidisciplinary pain management; Medical sciences
Risk Factors for Breast Cancer among Women in Klang Valley, Malaysia

Rabeta Mohd Salleh, Suzana Shahar, Ahmad Rohi Ghazali, Normah Haron, Poh Bee Koon

There has been an explosion in the incidence of breast cancer throughout the world. A case-control study was done to identify the lifestyle risk factors for breast cancer among women in Klang Valley. This study was carried out among 70 newly diagnosed breast cancer patients and 138 controls, aged 29-65 years old in Klang Valley. The inclusion criteria for cases were (i) newly diagnosed breast cancer (stage I to III) (ii) not undergone any therapy for cancer (iii) no other chronic diseases such as hypertension and diabetic (iv) not pregnant and lactating (v) not in menstruation for those who are not menopause yet. The control group comprised women, who were healthy, not diagnosed with cancer and other chronic disease, not pregnant, not lactating and not menstruating. Demographic data were obtained through standardized pre-tested questionnaire by trained interviewers. Smoking, alcohol consumption, family history, age at menarche, usage of oral contraceptive pill and hormone-replacement therapy, breast-feeding, chi-square test did not show any significant differences between cases and control. Women who got her first pregnancy at the age of more than 30 years old were at five time higher risk of getting breast cancer \([\text{adjusted OR}=4.5 (95\% \ CI=1.8-11.1)]\) \((p<0.05)\) compared to those who got her first pregnancy at the age less than 30 years old. In conclusion, certain lifestyle factors were associated with risk of getting breast cancer. Effort should be taken to increase awareness and understanding of the importance of healthy lifestyle to prevent breast cancer occurrence.

Keywords
Risk factor; Breast cancer; Women
Assessment of muscle fatigue associated with prolonged standing in the workplace

Halim I., Omar A.R., Saman A.M., Othman I.

**Objectives:** The objectives of this study were to determine the psychological fatigue and analyze muscle activity of production workers who are performing processes jobs while standing for prolonged time periods.

**Methods:** The psychological fatigue experienced by the workers was obtained through questionnaire surveys. Meanwhile, muscle activity has been analyzed using surface electromyography (sEMG) measurement. Lower extremities muscles include: erector spinae, tibialis anterior, and gastrocnemius were concurrently measured for more than five hours of standing. Twenty male production workers in a metal stamping company participated as subjects in this study. The subjects were required to undergo questionnaire surveys and sEMG measurement.

**Results:** Results of the questionnaire surveys found that all subjects experienced psychological fatigue due to prolonged standing jobs. Similarly, muscle fatigue has been identified through sEMG measurement. Based on the non-parametric statistical test using the Spearman’s rank order correlation, the left erector spinae obtained a moderate positive correlation and statistically significant ($r_s = 0.552$, $p < 0.05$) between the results of questionnaire surveys and sEMG measurement.

**Conclusion:** Based on this study, the authors concluded that prolonged standing was contributed to psychological fatigue and to muscle fatigue among the production workers.

**Keywords**

Prolonged standing; Muscle fatigue; Questionnaire survey; Surface electromyography; Metal stamping industry
Development of optimal photosensors based heart pulse detector


The development of heart pulse instruments rapidly fast in market since 21st century. However, the heart pulse detector is expensive due to the complicated system and it is used widely only in hospitals and clinics. The project is targeting to develop a significant photosensor to the medical fields that is easy to use and monitor their health by the user everywhere. The other target is to develop a comfortable instrument, reliable, accurate result to develop of heart pulse using low cost photosensors. This project involved both hardware and software with related to signal processing, mathematical, computational, formalisms, modeling techniques for transforming, transmitting and also for analog or digital signal. This project also used Peripheral Interface Controller (PIC) 16F877A microcontroller as the main function to control other elements. Result showed this project functioned smoothly and successfully with overall objectives were achieved. Apart from that, this project give good services for people to monitor their heart condition form time to time. In the future, wireless connection e.g. Global System for Mobile Communications (GSM) and Zigbee would be developed to make the system more reliable to the current world. Furthermore, the system should be compatible to various environments such as Android based OS so that it can be controlled away from the original location.

Keywords

Colour wavelength; Heart rate; Photosensor; PIC 16F877A microcontroller; Sensor
Autism cannot run away from their triangle deficits: social, communication and stereotyped behaviour. There is no cure for autism or any definitive treatment to treat the core symptoms of this developmental disorder. However, the deficits can be minimized by maximize their learning through behavioural therapy and educational intervention. Nowadays, the methods in the rehabilitation of autism have been upgraded by the innovation of humanoid robots, in particular the humanoid robot NAO. In this study, NAO has being programmed using Choregraphe as programming tool to develop lesson modules for children with autism to practice their social interaction skill. This paper focuses specifically on social interaction subscale to observe the behaviour of the autistic children during interaction with the humanoid robot NAO. The observation is based on six items referenced from the Gilliam Autism Rating Scale-second edition (GARS-2). The use of humanoid robot NAO in the rehabilitation of autistic children is expected to help them to interact and practice their social traits just like normal children. The results evidently showed that children with autism are positively affected by NAO by giving encouraging responses in social interaction when interacting with the robot. Two-way communication between the child and robot in real time significantly give positive impact in the responses towards the robot.

**Keywords**

Human-robot interaction (HRI); Autism; Humanoid robot NAO
Discovering pattern in medical audiology data with FP-growth algorithm

Noma N.G., Abd Ghani M.K.

There is potential knowledge inherent in vast amounts of untapped and possibly valuable data generated by healthcare providers. So often, clinicians rely in their skills and experience and that of other medical experts as their source of information. The healthcare sector is now capturing more data in the form of digital and non digital format that may potentially be mined to generate valuable insights. In this paper we propose a five step knowledge discovery model to discover patterns in medical audiology records. We use frequent pattern growth (FP-Growth) algorithm in the data processing step to build the FP-tree data structure and mine it for frequent itemsets. Our aim is to discover interesting itemsets that shows connection between hearing thresholds in pure-tone audiometric data and symptoms from diagnosis and other attributes in the medical records. The experimental results are summaries of frequent structures in the data that contains symptoms of tinnitus, vertigo and giddiness with threshold values and other information like gender.

Keywords

FP-Growth; Audiometry; Giddiness; Threshold; Tinnitus; Vertigo
Non-contact and non-invasive heartbeat detection is one of various research objectives and current emerging technology in various fields, especially in health care service. The signal without noise, interference and irrelevant heartbeat respiration with proper distance and power level is more preferable in a system design to provide better health care monitoring system. The purpose of this paper is aimed to present a filtering technique using Matlab simulation tool to obtain a smooth and accurate heartbeat, and the correlation with distance of heartbeat detection based on Doppler Effect motion sensing principle. The measurement was taken at operating frequency 5.8GHz. The distance is varied from 1 feet to 4 feet. A comparative study is carried out based on experimental results. The measurements and Matlab simulation results provide a clear heartbeat detected signal and prove the relation in term of distance. The future work will focus on the different power level with fixed distance. The implication of this experimental work is to provide some information related to non-contact microwave heartbeat detection. The information shared is aimed to serve the similar scientific field and improve the system features.

**Keywords**

Hearbeat; Microwave; Doppler radar; Respiration
This paper presents brain lesion segmentation of diffusion-weighted magnetic resonance images (DW-MRI or DWI) based on thresholding technique. The lesions are solid tumour, acute infarction, haemorrhage, and abscess. Preprocessing is applied to the DWI for normalization, background removal and enhancement. Two different techniques which are Gamma-law transformation and contrast stretching are applied for the enhancement. For the image segmentation process, the DWI is divided by 88 regions. Then image histogram is calculated at each region to find the maximum number of pixels for each intensity level. The optimal threshold is determined by comparing normal and lesion regions. By using Gamma-law transformation, 0.48 is found as the optimal thresholding value whereas 0.28 for the contrast stretching. The proposed technique has been validated by using area overlap (AO), false positive rate (FPR), and false negative rate (FNR). Thresholding with gamma-law transformation algorithm provides better segmentation results with AO, FPR, FNR (0.68, 0.14, 0.18) compared to contrast stretching (0.62, 0.15, 0.23).
A case study on the efficacy of technical laboratory safety in polytechnic

Salleh Z., Mazlan E.M., Mazlan S.A., Hassan N.A., Patakor F.A.

Technical laboratories are typically considered as highly hazardous places in the polytechnic institution when addressing the problems of high incidences and fatality rates. In conjunction with several topics covered in the technical curricular, safety and health precaution should be highlighted in order to connect to few key ideas of being safe. Therefore the assessment of safety awareness in terms of safety and health about hazardous and risks at laboratories is needed and has to be incorporated with technical education and other training programmes. The purpose of this study was to determine the efficacy of technical laboratory safety in one of the polytechnics in northern region. The study examined three related issues that were; the availability of safety material and equipment, safety practice adopted by technical teachers and administrator’s safety attitudes in enforcing safety to the students. A model of efficacy technical laboratory was developed to test the linear relationship between existing safety material and equipment, teachers’ safety practice and administrators’ attitude in enforcing safety and to identify which of technical laboratory safety issues was the most pertinent factor to realize safety in technical laboratory. This was done by analyzing survey-based data sets particularly those obtained from samples of 210 students in the polytechnic. The Pearson Correlation was used to measure the association between the variables and to test the research hypotheses. The result of the study has found that there was a significant correlation between existing safety material and equipment, safety practice adopted by teacher and administrator’s attitude. There was also a significant relationship between technical laboratory safety and safety practice adopted by teacher and between technical laboratory safety and administrator attitude. Hence, safety practice adopted by teacher and administrator attitude is vital in realizing technical laboratory safety.

Keywords
Polytechnic; Safety attitudes; Safety practices; Technical laboratory
Evaluation of Web 2.0 Technologies For Developing Online Telehealth Systems

Jaspaljeet Singh Dhillon, Czarina Ramos, Burkhard C. Wünsche, Christof Lutteroth

Telehealth and telecare applications are a promising technology for improving the quality of care while using healthcare resources more effectively. Major obstacles to a more widespread use are the high initial costs and a vendor specific design, which makes it difficult and expensive to add new functionalities. The Internet offers an opportunity to make telehealth applications more accessible, while also adding social aspects and the opportunity for third-party developers to add content. A preliminary user study confirmed that elderly are interested in such an application, and provided guidelines for the user interface design and required functionalities. In this paper, we evaluate technologies for developing online telehealth platforms, and present a first prototype which is extendable and has social networking capabilities. Our results show that a combination of open web standards such as OpenSocial and a CMS such as Drupal represents a suitable design. We illustrate the capabilities of our design and prototype by developing a memory game, which can be submitted by third party developers, similar to a Facebook application, and which utilises the social context of our telehealth application.

Keywords

Web 2.0 technologies; Social networks; Health informatics; Telehealthcare
The world has started to appreciate more and more the value of information and its impact on the community. This paper shares the findings of a study done on information security implementation at Mosul’s health sector. The study was conducted via a self-administrated questionnaire and interview. The respondents are the IT managers and personnel with functions related to IT in selected hospitals in the city of Mosul. The findings reveal an ISG status that is in dire need for improvement to maintain suitable level of security of information which can be achieved through having good governance practices in place. However there are various degrees of implementation by the hospitals. It is recommended that these findings be used as basis for developing a secure information-based system for the respective hospitals.

Keywords
Data security; IT governance; Security governance; Information audit; ISG framework; Health
The Mental Health Diagnostic Expert System (MeHDES) is proposed to assist the Malaysian psychology industry in diagnosing and treating their mental patients, and also to allow each mental patient to have several options on selecting a treatment plan that fits their budget without jeopardizing their overall health conditions. MeHDES will be using three artificial intelligence (AI) reasoning techniques: rule-based reasoning, fuzzy logic, and fuzzy-genetic algorithm (fuzzy-GA). The human experts’ knowledge in the area of mental health and disorders will be transformed and encoded into a knowledge base using the rule-based reasoning technique; fuzzy logic then allows the severity level of a particular disorder to be measured; and fuzzy-GA will be used to determine and propose the suitable treatment for each of the mental patients based on their budget and their overall health conditions.
Towards A Ubiquitous Patient-Centric Telehealth System

Jaspaljeet Singh A/L Ranjit Singh

The elderly population is growing fast in most developed countries. The aging population, high medical expenses, the shrinking number of health workers and elderly carers demand for more healthcare innovation that empower health consumers to manage their health independently from home. Telehealth is thought to be a solution for effective elderly healthcare. However, the usage of telehealth is limited by a design often centered around the requirements of the clinical user, healthcare provider, and the equipment vendor. Many existing systems suffer from high initial costs, cannot be extended by third parties, require extra costs to add new functionalities, and are designed to create a continuing revenue source for the vendor. Furthermore, the systems are usually designed to manage diseases rather than prevent them, and do not address the social and psychological needs of the patient. Based on these shortcomings, we propose a novel web-based telehealth framework called Healthcare4Life, which is ubiquitous, extendable by third parties, contains social aspects, and puts the user in control. In contrast to previous work, we propose an open structure with a middleware-like functionality. The framework emphasises the need for social support and psychological factors influencing usage and compliance. In this paper, we describe telehealth usability requirements and analysis of existing consumer health informatics applications which leads to the design of a novel ubiquitous telehealth system.

Keywords

Telehealth; Telecare; Patient-centric design; Ubiquitous system; Human-computer interfaces
Leveraging Consumer Sensing Devices For Telehealth

Jaspaljeet Singh A/L Ranjit Singh

Home telehealth applications are increasingly gaining in popularity among patients due their promise to use healthcare resources more effectively and hence to lower costs. Commercial telehealth systems usually employ patient stations and vital sign monitoring equipment in order to fulfill the need of medical professionals by enabling close monitoring of patients with severe chronic diseases. However, due their high cost, vendor lock-in, and doctor centric design, these systems are not suitable for general healthcare applications such as improving cardiac fitness, monitoring overall health, improving muscle strength and balance of elderly, or assisting with dieting programs. We argue that many of these goals can be supported in a cost effective manner by leveraging mainstream sensing devices such as game controllers and smartphones. Open-ended web-based telehealth systems can be integrated with such devices, in order to add a social component, collect health data unobtrusively, and provide feedback and health related information. In this paper, we systematically categorise and analyse consumer-level sensing devices in terms of their potential to extend the capability of telehealth systems. We show that the devices have immense potential as tools for therapy and rehabilitation activities, diagnosis, health monitoring and social support, and we reveal opportunities for professionals in computer vision, graphics and signal processing to participate in this trend.

Keywords
Telehealth; Human computer interfaces; Elderly
Assimilation of Healthcare Information Systems (HIS): An Analysis And Critique

Hidayah Bte Sulaiman

The assimilation of information systems throughout the healthcare industry has increased dramatically since it is now perceived that Information Systems/Information Technology (IS/IT) will be able to bring about immense benefit to medical personnel in delivering better services. However, the enthusiasm of having new information systems implemented usually deteriorates dramatically once the system is acquired. This causes a major issue in the assimilation of the newly implemented technology which could provide a negative impact on the successful use of the information system. This study describes the design and preliminary analysis on the technology innovation assimilation issues in a healthcare setting with the aim of developing a technology innovation assimilation model for hospitals to successfully assimilate and sustain the use of the healthcare information systems. Findings indicate that there are various technology, organization and environment elements that should be considered and also barriers that relevant healthcare factions need to overcome in order to successfully assimilate the healthcare information systems.

Keywords

Assimilation: Technology innovation; Technology-organization-environment; Healthcare information system; Healthcare
A Feasibility Study Scheme of an Android-based Integrated Wearable ECG Monitoring System

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Ubiquitous healthcare system is becoming essential in the attempt to improve healthcare delivery. Not only it is able to facilitate two-way communication between physician and patient, but it is also useful for the caregivers to maximize efficiency in running daily activities. Managing ischemia heart disease, one of the deadly diseases, would definitely benefit from such ubiquitous healthcare system. The current treatment method for ischemia requires patients to be physically present at their respective treatment centres for regular monitoring. This increases the need for remote monitoring method, due to the urgent nature of treating ischemia heart attack. Therefore, this paper presents preliminary system architecture and feasibility study of HeartPals, a low-cost Android-based integrated wearable electrocardiography (ECG) monitoring system that enables ischemia patients to be remotely monitored by their physicians. We also propose TOFUSER, a Technology-Oriented Feasibility Study Scheme for End-users as an extended feasibility study scheme to allow users to verify the preliminary requirements of the technology and users’ requirements of HeartPals.

Keywords
Healthcare; Physiological signal device; Android devices; ECG monitoring system; Feasibility study
Maternal Weight Gain and Correlation with Birth Weight Infants

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Objective

Maternal weight gain affect the infant birth weight. Aim of this study was to describe maternal weight gain during all trimester of pregnancy and its correlation with the birth weight.

Methods

Pregnant women who got antenatal care in Adam Malik General Hospital and Sundari Hospital, underwent body weight measurement during routine examination at first, second and third trimester and also at delivery time at those hospital. Baby birth weight also measured after delivery.

Results

Maternal weight gain increased its peak point at the second and third trimester with overall total weight gain ranged at 5 – 20 kg during pregnancy. Baby birth on normal weight ranged at 2500 – 4000 grams (SD + 399.86). Maternal weight gain was more higher in the primi gravida group compared with multi and grandemulti gravida groups. There is correlation between maternal weight gain with baby birth weight with p = 0.03 (p<0.05, CI 95%), even the correlation was weak.

Conclusion

Maternal weight gain in the second and third trimester showed statistically significance difference with baby birth weight. Adequate total maternal weight gain based on IOM recommendation considered for resulting a better outcome and better birthweight of the babies.
Cost-Effectiveness of Clinical Pharmacy Education on Infection Management among Patients with Chronic Kidney Disease in an Indonesian Hospital

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Objectives

This study evaluated the clinical and economic impacts of clinical pharmacy education (CPE) on infection management among patients with chronic kidney disease (CKD) stages 4 and 5 in Haji Adam Malik Hospital, Indonesia.

Methods

A quasi-experimental economic evaluation comparing CPE impact on 6-month CKD mortality was conducted on the basis of payer perspective. The experimental group (n = 63) received care by health care providers who were given CPE on drug-related problems and dose adjustment. The control group (n = 80) was based on the historical cohort of patients who received care before the CPE. Measure of clinical outcome applied in this study was number of lives saved/100 patients treated. Cost-effectiveness ratios for CKD stages 4 and 5 patients without CPE and with CPE and incremental cost-effectiveness ratios (ICERs) for CKD stages 4 and 5 patients were analyzed.

Results

Lives saved (%) in the treatment of CKD without CPE: CKD stage 4, 78.57; CKD stage 5, 57.58. Lives saved (%) in the treatment of CKD with CPE: CKD stage 4, 88.89; CKD stage 5, 65.45. Cost-effectiveness ratios for stage 4 with and without CPEs were Rp3,348,733.27 and Rp3,519,931.009, respectively. Cost-effectiveness ratios for stage 5 with and without CPEs were Rp7,137,874.93 and Rp7,871,822.27, respectively. ICERs were Rp2,045,341.22 for CKD stage 4 and Rp1,767,585.60 for CKD stage 5.

Conclusions

Treatment of CKD stages 4 and 5 with CPE was more effective and cost-effective compared with treatment of CKD stages 4 and 5 without CPE. The ICERs indicated that extra costs were required to increase life saved in both stages.

Keywords

Chronic kidney disease; Clinical pharmacy education; Cost-effectiveness; DRPs; Infection
The sensing mechanism and detection of low concentration acetone using chitosan-based sensors

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This paper aims to discuss the usage of chitosan film sensors to detect acetone concentrations in human breath, in order to precisely diagnose diabetes mellitus in patients. Acetone concentration in the breath varies from 0.3 to 0.9 ppm in healthy people to more than 1.8 ppm for diabetics. This makes acetone a suitable chemical marker for diabetes diagnosis. Therefore, the preliminary study on the electrical laboratory testing of the chitosan film sensor properties to acetone vapor-contaminated air in range of 0.1–100 ppm was carried out at room temperature (∼25–30 °C) in normal air. Our results suggested that the proposed acetone-based gas sensor can operate at room temperature with a high performance demonstrated by good response, recovery, stability and repeatability. This trouble free, painless and steadfast technique will improve the current gold standard in diagnosing diabetes, enabling quick and early detection.

Keywords

Chitosan-based acetone sensor; Diabetes mellitus; Acetone vapor; Electrical properties; Electrochemical deposition
Ant plant (*Myrmecodia tuberosa*) hypocotyl extract modulates TCD4+ and TCD8+ cell profile of doxorubicin-induced immune-suppressed Sprague Dawley rats *In Vivo*

Sumardi, Hertiani, T., Sasmito, E.

*Myrmecodia tuberosa* Jack (Rubiaceae) has been used as part of traditional Indonesian remedies for a wide range of therapeutic usages in West Papua. Our preliminary study revealed the significant potency of these plant extracts and fractions as an immunomodulator by an *in vitro* technique on Balb/c mice. This study explored the effect of *M. tuberosa* hypocotyl ethanol extract on the TCD4+ and TCD8+ cell profiles of doxorubicin (Dox)-induced immune-suppressed Sprague Dawley (SD) rats by an *in vivo* method. Dried powder of *M. tuberosa* hypocotyl was macerated in 95% ethanol. Following solvent evaporation in a vacuum, the ethanol extract (EE) was partitioned to yield an n-hexane fraction (FH) and residue (FNH). FNH was further partitioned to yield ethyl acetate (FEtOAc) and water fractions (FW). The extract and fractions in the concentrations 10, 20, 50, and 100 µg/mL were tested on macrophage cells by the latex bead method, while the proliferation of lymphocyte cells was evaluated by the MTT assay. The total phenolic and flavonoid contents of those fractions were evaluated. The active fraction was administrated orally on Dox-induced SD rats for 28 days by an *in vivo* method to observe the TCD4+ and TCD8+ cell profiles. The *in vivo* assay showed that the FNH could maintain the number of TCD4+ cells, but not the number of TCD8+ cells. The ED$_{50}$ observed was 24.24 mg/kg BW. Steroid/terpenoid compounds were detected in this fraction along with the phenolics and flavonoids. The FNH contained 3.548 ± 0.058% GAE of total phenolics and 0.656 ± 0.026% QE of total flavonoids *M. tuberosa* hypocotyl extract is a potent immunomodulatory agent and may act as co-chemotherapy in Dox use.

**Keywords**

Ant plant; Doxorubicin; *Myrmecodia tuberosa* hypocotyl; TCD4+; TCD8+
A randomized comparison of dihydroartemisinin-piperaquine and artesunate-amodiaquine combined with primaquine for radical treatment of vivax malaria in sumatera, Indonesia

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Background: A high prevalence of chloroquine-resistant Plasmodium vivax in Indonesia has shifted first-line treatment to artemisinin-based combination therapies, combined with primaquine (PQ) for radical cure. Which combination is most effective and safe remains to be established.

Methods: We conducted a prospective open-label randomized comparison of 14 days of PQ (0.25 mg base/kg) plus either artesunate-amodiaquine (AAQ + PQ) or dihydroartemisinin-piperaquine (DHP + PQ) for the treatment of uncomplicated monoinfection P. vivax malaria in North Sumatera, Indonesia. Patients were randomized and treatments were given without prior testing for G6PD status. The primary outcome was parasitological failure at day 42. Patients were followed up to 1 year.

Results: Between December 2010 and April 2012, 331 patients were included. After treatment with AAQ + PQ, recurrent infection occurred in 0 of 167 patients within 42 days and in 15 of 130 (11.5%; 95% confidence interval [CI], 6.6%-18.3%) within a year. With DHP + PQ, this was 1 of 164 (0.6%; 95% CI, 0.01%-3.4%) and 13 of 143 (9.1%; 95% CI, 4.9%-15.0%), respectively (P > .2). Intravascular hemolysis occurred in 5 patients, of which 3 males were hemizygous for the G6PD-Mahidol mutation. Minor adverse events were more frequent with AAQ + PQ.

Conclusions: In North Sumatera, Indonesia, AAQ and DHP, both combined with PQ, were effective for blood-stage parasite clearance of uncomplicated P. vivax malaria. Both treatments were safe, but DHP + PQ was better tolerated.

Keywords: Indonesia; Plasmodium vivax; Primaquine; Radical cure
Retinal thickness changes after phacoemulsification

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**Purpose:** To determine the effect of phacoemulsification on macular volume and thickness using spectral domain optical coherence tomography examinations.

**Methods:** Twenty-seven eyes of 27 subjects who underwent phacoemulsification were studied. All nine areas of the macula were examined by spectral domain optical coherence tomography preoperatively and 2 months postoperatively. Effective phacoemulsification time and absolute phacoemulsification time were also recorded.

**Results:** There were statistically significant differences in macular thickness between preoperative and postoperative spectral domain optical coherence tomography examinations in nine areas including macular volume. In the paracentral macular area, the thickness of three quadrants significantly increased (superior $P=0.015$; temporal $P=0.001$; and nasal $P=0.023$). Peripheral macular thickness also increased significantly in the superior ($P=0.05$) and temporal macular areas ($P<0.001$). The macular volume increased significantly after phacoemulsification ($P<0.001$). There were no correlations between absolute/effective phacoemulsification time and macular cellular structures ($P>0.05$), but a significant correlation ($P=0.011$) was found between absolute phacoemulsification time and change in macular volume.

**Conclusion:** Macular thickness changes in the nasal, superior, and temporal quadrants of the paracentral area and the superior and temporal quadrants of the peripheral area, as well as macular volume, may be used as detailed biomarkers to measure the effects of intraocular pressure fluctuations and maneuvers in phacoemulsification intraocular surgeries.
Study of the effects of Tween 80 and palm kernel oil on in vitro ascorbic acid penetration through rabbit skin

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Background: It is well known that drugs can be applied to the skin to get advantages like easy of access and the avoidance of first pass metabolism. However, the slow transport of many drugs across the skin makes a limitation. To overcome this problem, enhancers can be used.

Objective: To investigate the penetration enhancing effect of Tween 80 and palm kernel oil on the in vitro skin penetration of ascorbic acid.

Methods: In this study, varies ointment formula were made: F1 (without Tween 80, 35% palm kernel oil), F2 (2.5% Tween 80, 35% palm kernel oil), F3 (5% Tween 80, 35% palm kernel oil), F4 (10% Tween 80, 35% palm kernel oil), F5 (without palm kernel oil, 5% Tween 80), F6 (25% palm kernel oil, 5% Tween 80), and F7 (ascorbic acid solution, 50% glycerin as solvent), and each formula contained 10% ascorbic acid. The ascorbic acid ointment was applied to the skin and then the skin was attached to diffusion cell. At a certain interval of time, ascorbic acid content in the receptor chamber was assayed using UV spectrophotometer at wavelength 266.8 nm.

Results: This study showed that Tween 80 and palm kernel oil could enhance ascorbic acid skin penetration, but Tween 80 must be used in low concentration (2.5% and 5%). Tween 80 in high concentration (10%) decreased the penetration. For palm kernel oil, the concentration of ascorbic acid penetrated increased with the increased of the concentration of palm kernel oil used.

Conclusion: This study suggests that Tween 80 and palm kernel oil can be used to enhance ascorbic acid penetration through rabbit skin.

Keywords
Ascorbic acid; Penetration; Tween 80; Palm kernel oil
Immunophenotypic patterns of childhood acute leukemias in Indonesia


Background: Immunophenotyping, as suggested by WHO, may improve diagnosis of childhood leukemia since it offers a better classification of the hematopoietic lineage of malignant cells as compared to morphology. Therefore, we aimed to determine the proportion of the immunophenotypic subtypes of acute leukemia in Indonesian children.

Methods: Samples were obtained from patients (0-14 years of age) in 4 hospitals in Indonesia. We analyzed 541 suspected leukemia samples presented over a 4-year period (March 2006 - July 2010) by flow cytometry. Immunophenotyping allowed classification into acute myeloid leukemia (AML) and ALL (B-lineage and T-lineage ALL).

Results: Of 541 samples, 136 were tested using a single color method and 405 with a three-color method. Concordance with morphology was very good (κ=0.82) using the three-color method with a panel of 15 monoclonal antibodies (n=387). A relatively high percentage of acute leukemia was classified as AML (23%). Of the ALL samples 83% were B-lineage ALL and 17% T-lineage ALL. Nine out of 239 morphological ALL were labeled AML, and 12/79 morphological AML were in fact ALL.

Conclusion: Immunophenotyping in a multi-center study proved feasible and appears particularly important for prognostic assessment of childhood leukemia in low income countries such as Indonesia.
The association with age, human tissue kallikreins 6 and 10 and hemostatic markers for survival outcome from epithelial ovarian cancer

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Purpose: To assess known cancer biomarkers CA-125, human tissue kallikreins KLK6 and KLK10, hemostatic markers and age with 5-year survival outcome from epithelial ovarian cancer.

Methods: Forty-one benign cyst cohorts and 83 patients diagnosed with ovarian cancer were recruited. The following assays were performed: fibrinogen, vWF antigen, d-dimer, ATIII activity, tPA, PAI-1, uPAR, KLK6, KLK10 and CA-125. Follow-up visits of cancer patients of more than 60 months were noted. Data between those who survived past 60 months and mortality from cancer were analyzed.

Results: Only 24 patients lived past 60 months, and 31 died (advanced stage n = 27). Those living past 60 months were significantly older and associated with similar pre-operative levels seen in benign cyst cohorts especially for KLK6, fibrinogen, vWF, AT levels despite upregulation of d-dimer, CA-125 and KLK10. Ovarian cancer cohorts living past 60 months were younger than those who died within 12 months (n = 12). Mortality within 12 months was associated with older age, upregulation of KLK6, fibrinogen, d-dimer, vWF, tPA antigen and reduced ATIII levels. Similarly, mortality within 36 months of disease showed older age with upregulation of CA-125, KLK6 d-dimer vWF antigen and tPA antigen levels. Late stage cancer (III/IV) showed upregulated CA-125, KLK6, KLK10, d-dimer and reduced AT compared to early stage cancer (I/II). The 5-year survival rate for early cancer was 80%, advanced 22.9% and overall 5-year survival rate was 43.6%.

Conclusion: Older age together with the novel biomarkers studied and their association with adverse outcome from epithelial ovarian cancer was seen especially within 12 and 36 months of disease. Those who lived past 60 months of disease showed similar pre-operative levels seen in benign cyst cohorts despite elevated d-dimer, CA125 and KLK 10. An enlarged study is needed to confirm these findings.