### **LIST OF PUBLICATIONS AND ABSTRACTS YEAR 2012**

No.	Publication	Page
1	Abdulsalam AM, Ithoi I, Al-Mekhalafi HM, Ahmed A, Surin J, Mak JW. Drinking water is a significant predictor of <i>Blastocystis</i> infection among rural Malaysian primary school children. <i>Parasitology</i> , 2012; 139(8): 1014-1020. (SCI IF: 2.961; HI: 70; Tier: Q1); (ISI IF: 2.961).	12
2	Ahlawa P. Survey on availability and usage of denture adhesives in Malaysia: A preliminary study. <i>Asian Journal of Pharmaceutical Health Sciences</i> , 2012; 2(1): 286-289. (IF: N/A)	13
3	Ahmad NA, Naimie Z, Lui JL, Aziz AA, Abdullah M, Kasim NAH, Kasim NLA, Toh CG, Thong YL, Razak AAA, Aziz ZAC, Sulaiman E, Gonzalez MAG, Bindal P. Clinical pairing revisited: A study at the University of Malaya, Malaysia. <i>Journal of Dental Education</i> , 2012; 76(10): 1377-1383. (SCI IF: 0.95, H-index: 34, Tier: Q2); (ISI IF: 0.963).	14
4	Al-Shookri A, Khor GL, Chan YM, Loke SC, Maskari M. Effectiveness of medical nutrition treatment delivered by dietitians on glycemic outcomes and lipid profiles of Arab, Oman type 2 diabetic patients. <i>Diabetic Medicine</i> , 2012; 29(2): 236–244. (SCI IF: 1.779; H-index: 86; Tier: Q1); (ISI IF: 2.902).	15
5	Ananda PK, Kumarappan CT, Christudas S, Kalaichelvana VK. Effect of <i>Biophytum sensitivum</i> on streptozotocin and nicotinamide-induced diabetic rats. <i>Asian Pacific Journal of Tropical Biomedicine</i> , 2012; 2(1): 31–35. (IF N/A).	16
6	Asif ICM, Manish G, Dinesh KC. Antimicrobial activity of <i>Tinospora crispa</i> root extracts. <i>International Journal of Research in Ayurveda and Pharmacy</i> , 2012; 3(3): 417-419. (IF: N/A).	17
7	Bayati OH, Yunus N, Ahmad SF. Tensile bond strengths of silicone soft liners to two chemically different denture base resins. <i>International Journal of Adhesives and Adhesion</i> , 2012; 34: 32–37. (SCI IF: 2.462; HI: 39; Tier: Q1); (ISI IF: 2.17).	18
8	Chan KK, Wong RSY, Shar Mariam Mohamed, Tengku Azmi Tengku Ibrahim, Maha Abdullah, Nadarajah VD. <i>Bacillus thuringiensis</i> parasporal proteins induce cell-cycle arrest and caspase-dependant apoptotic cell death in leukemic cells. <i>Journal of Environmental Pathology, Toxicology and Oncology</i> , 2012; 31(1): 75-86. (SCI IF: 0.651; HI: 28; Tier: Q1); (ISI IF: 1.107).	19
9	Cheong KC, Yusoff AF, Ghazali SM, Lim KH, Selvarajah S, Haniff J, Khor GL, Shahar S, Rahman JA, Zainuddin AA, Mustafa AN. Optimal BMI cut-off values for predicting diabetes, hypertension and hypercholesterolaemia in a multi-ethnic population. <i>Public Health Nutrition</i> , 2012; 1-7. doi: 10.1017/S1368980012002911. (SCI IF: 1.138; HI: 66; Tier: Q1); (ISI IF: 2.169).	20
10	Chew SC, Loh SP, Khor GL. Determination of folate content in commonly consumed Malaysian foods. <i>International Food Research</i>	22

Journal, 2012; 19(1): 189-197. (SCI IF: 0.475; HI: 5; Tier: Q3).

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Abdulsalam AM, Ithoi I, Al-Mekhalafi HM, Ahmed A, Surin J, Mak JW. Drinking water is a significant predictor of *Blastocystis* infection among rural Malaysian primary schoolchildren. *Parasitology*, 2012; 139(8): 1014-1020.

# Drinking water is a significant predictor of *Blastocystis* infection among rural Malaysian primary school children

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#### **Abstract**

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 school children, 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 (x2=4.246; P=0.039). Univariate and multivariate analyses showed that absence of a piped water supply (OR=3.13; 95% Cl=1.78, 5.46; P<0.001) and low levels of mothers' education (OR=3.41; 95% Cl=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.

**Key words:** *Blastocystis*, predictors, drinking water, school children, Malaysia.

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Ahlawa P. Survey on availability and usage of denture adhesives in Malaysia: A preliminary study. *Asian Journal of Pharmaceutical Health Sciences*, 2012; 2(1): 286-289.

# Survey on availability and usage of denture adhesives in Malaysia: A preliminary study.

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#### **Abstract**

Performance of dentures can be improved by making use of adjuncts like denture adhesives (DA), which act by enhancing the retentive and stabilizing properties of a denture. DA have been a subject of controversy despite the advantages associated with their use. If used appropriately, they could provide additional benefit to denture wearers especially in terms of comfort, better chewing ability as well as boost their confidence level and could also be a benefit to the clinicians prescribing them. The objective of this study was to look into the types and forms of DA commonly available in the markets and the response of people towards using them in two cities of Malaysia. This was a cross sectional study where two surveys were conducted using a standardized questionnaire. The first survey was to enquire from the pharmacies regarding the availability and sales of DA in the cities of Johore Bahru and Klang Valley. In the second survey the denture wearers were questioned regarding usage including the frequency of use, and their approach towards DA. From the first survey, 98% of the pharmacies were found to be selling denture adhesives which were available in cream, powder and cushion form. Polident Complete Comfort DA, Protefix, Fittydent and Steradent were the most commonly sold DA among these pharmacies, with sales of Polident being up to 98%. In the second survey, where all denture wearing patients were in the range of 40-85 years age, it was inferred that only 5.8% of all denture wearers were using DA. All DA users preferred to use cream form and frequency of placement was once (44.4%), or twice (22.2%) a day. Denture Adhesives are commonly available in Malaysian markets. However, usage and awareness regarding these products is relatively low among the population in Malaysia.

**Keywords**: Denture adhesives, Availability, Usage, Survey.

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Ahmad NA, Naimie Z, Lui JL, Aziz AA, Abdullah M, Kasim NAH, Kasim NLA, Toh CG, Thong YL, Razak AAA, Aziz ZAC, Sulaiman E, Gonzalez MAG, Bindal P. Clinical pairing revisited: A study at the University of Malaya, Malaysia. *Journal of Dental Education*, 2012; 76(10): 1377-1383.

### Clinical pairing revisited: A study at the University of Malaya, Malaysia.

Ahmad NA<sup>1</sup>, Naimie Z<sup>1</sup>, Lui JL<sup>1</sup>, Aziz AA<sup>1</sup>, Abdullah M<sup>1</sup>, Abu Kasim NH<sup>1</sup>, Abu Kassim NL<sup>2</sup>, Toh CG<sup>3</sup>, Thong YL<sup>1</sup>, Abdul Razak AA<sup>4</sup>, Abdullah H<sup>1</sup>, Che' Ab Aziz ZA<sup>1</sup>, Sulaiman E<sup>1</sup>, Gonzalez MA<sup>1</sup>, Bindal P<sup>1</sup>.

#### **Abstract**

This study is part of ongoing educational research conducted by the Department of Conservative Dentistry, University of Malaya, Malaysia, to evaluate the perception of clinical pairing. A thirteen-question survey was distributed to 148 dental students after they had experienced four-handed dentistry. The objectives were to identify the advantages, disadvantages, and the acceptance of the implementation of clinical pairing from the students' point of view. The responses from the open-ended questions were categorized into six main themes (areas of interest): quality-related (Q), patient-related (PT), partner-related (P), lecturer-related (T), infection control (IC), and learning environment (L). Data analysis was done using SPSS version 18. Results indicated that the students perceived they possessed enough knowledge regarding clinical pairing. However, it was found that they still preferred to work independently as compared to working in pairs. The benefits of clinical pairing may not be viewed in the same vein by both dental students and teachers. The quality-related theme was perceived by students as the main advantage of clinical pairing, whilst the partner-related theme was perceived otherwise. The study also revealed that students may have some preconceived notions about pairing that may have impaired their acceptance. As a consequence, some reluctance was seen in their responses.

**Keywords**: dental education, academic environment, dental school clinics, dental students, prosthodontics, Malaysia.

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Al-Shookri A, Khor GL, Chan YM, Loke SC, Maskari M. Effectiveness of medical nutrition treatment delivered by dietitians on glycemic outcomes and lipid profiles of Arab, Oman type 2 diabetic patients. *Diabetic Medicine*, 2012; 29(2): 236–244.

# Effectiveness of medical nutrition treatment delivered by dietitians on glycemic outcomes and lipid profiles of Arab, Oman type 2 diabetic patients.

Al-Shookri A<sup>1</sup>, Khor GL<sup>2</sup>, Chan YM<sup>3</sup>, Loke SC<sup>3</sup>, Al-Maskari M<sup>1</sup>

#### **Abstract**

#### Aims:

In this randomized controlled trial we evaluated the effectiveness of medical nutritional therapy on Arab patients with Type 2 diabetes in Oman delivered by a dietitian.

#### Methods:

Patients with Type 2 diabetes (n = 170) were randomly assigned to a group receiving usual nutritional care (n = 85) or a group receiving practice guidelines nutritional care (n = 85). Anthropometric (weight, height, BMI and waist circumference) and biochemical (fasting blood glucose, HbA1c) variables were measured at baseline and after each appointment. Patients were given 1–3 appointments with a dietitian over 6 months.

#### Results:

Those in the group receiving practice guidelines nutritional care (n = 85) had significant changes in HbA1c (-0.8%, P = 0.001), fasting plasma glucose (-1.3 mmol\l, P = 0.003) and weight (-5.1 kg, P = 0.05), whereas the patients in the usual nutritional care group (n = 85) had no significant improvements in either HbA1c (-0.4%, P = 0.248) or fasting plasma glucose (-0.2 mmol/l, P = 0.638) during the same period. We also found a significant difference between the group receiving practice guidelines nutritional care and the usual nutritional care group, respectively, in waist circumference ( $96.9 \pm 7.9$  vs.  $100.0 \pm 8.7$  cm, P = 0.019), triglycerides levels ( $1.42 \pm 0.58$  vs.  $1.98 \pm 0.96$  mmol\l, P = 0.001), cholesterol levels ( $5.1 \pm 1.0$  vs.  $5.5 \pm 0.9$  mmol/l, P = 0.009) and LDL cholesterol levels ( $3.58 \pm 0.98$  vs.  $3.89 \pm 0.98$  mmol/l, P = 0.046).

#### Conclusions:

Medical nutrition therapy provided by dietitians to Arab patients with Type 2 diabetes in Oman resulted in significant improvements in anthropometric and biochemical outcomes in both the usual nutritional care group and the group receiving practice guidelines nutritional care. Subjects with Type 2 diabetes tended to do better with practice guidelines nutritional care than with usual nutritional care. Ongoing medical counselling in nutrition by a trained dietitian is important for better long-term metabolic control.

**Keywords**: glycaemic outcomes, lipid profile, medical nutritional treatment, Oman patients with Type 2 diabetes.

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Ananda PK, Kumarappan CT, Christudas S, Kalaichelvana VK. Effect of *Biophytum* sensitivum on streptozotocin and nicotinamide-induced diabetic rats. *Asian Pacific Journal of Tropical Biomedicine*, 2012; 2(1): 31–35.

# Effect of *Biophytum sensitivum* on streptozotocin and nicotinamide-induced diabetic rats.

Ananda Prabu K<sup>1</sup>, Kumarappan CT<sup>2</sup>, Sunil Christudas<sup>3</sup>, Kalaichelvan VK<sup>1</sup>

#### **Abstract**

#### Objective:

To investigate the effect of aqueous solution of *Biophytum sensitivum* leaf extract (BSEt) on normal and streptozotocin (STZ)-nicotinamide-induced diabetic rats.

#### Methods:

Diabetes was induced in adult male Wistar rats by the administration of STZ-nicotinamide (40, 110 mg/kg b.w., respectively) intraperitoneally. BSEt (200 mg/kg) was administered to diabetic rats for 28 days. The effect of extract on blood glucose, plasma insulin, total haemoglobin, glycosylated haemoglobin, liver glycogen and carbohydrate metabolism regulating enzymes of liver was studied in diabetic rats.

#### Results:

BSEt significantly reduced the blood glucose and glycosylated haemoglobin levels and significantly increased the total haemoglobin, plasma insulin and liver glycogen levels in diabetic rats. It also increased the hexokinase activity and decreased glucose-6-phosphatase, fructose-1, 6-bisphosphatase activities in diabetic rats.

#### Conclusions:

The results of our study suggest that BSEt possesses a promising effect on STZ-nicotinamide-induced diabetes.

**Keywords**: *Biophytum sensitivum*, Carbohydrate metabolism, Diabetes mellitus, Streptozotocin-nicotinamide

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Asif ICM, Manish G, Dinesh KC. Antimicrobial activity of *Tinospora crispa* root extracts. *International Journal of Research in Ayurveda and Pharmacy*, 2012; 3(3): 417-419.

### Antimicrobial activity of *Tinospora crispa* root extracts.

Asif Iqbal Chittur Mohammed<sup>1</sup>, Gunjan Manish<sup>1</sup>, Chellappan Kumar Dinesh<sup>2</sup>.

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#### **Abstract**

The aim of this study was to determine the in vitro antimicrobial activity of ethanol, distilled water, methanol and chloroform crude extracts of the roots of *Tinospora crispa*. Antimicrobial activity was examined by disc diffusion method against gram positive bacterial strains of *Streptococcus pneumonia*, gram negative bacterial strains of *Escherichia coli* and fungal strains of *Candida albicans*. The maximum zone of inhibition was obtained with ethanol extract against *Escherichia coli* and *Streptococcus pneumonia* followed by chloroform extract against the same organisms. Whilst distilled water extract showed a minimal zone of inhibition, methanol extract showed a moderate zone of inhibition against the bacterial strains used. The values were compared with a standard antibiotic. The ethanol extract also showed the maximum zone of inhibition against the growth of *Candida albicans*, whereas the lowest activity was shown with distilled water crude extract. Methanol and chloroform crude extracts showed considerably moderate activities against the fungal strain, as compared to the standard antibiotic used.

**Keywords**: *Tinospora crispa* root, crude extracts, antimicrobial activity, disc diffusion method.

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Bayati OH, Yunus N, Ahmad SF. Tensile bond strengths of silicone soft liners to two chemically different denture base resins. *International Journal of Adhesives and Adhesion*, 2012; 34: 32–37.

### Tensile bond strengths of silicone soft liners to two chemically different denture base resins.

Omar Hilal Bayati<sup>1</sup>, Norsiah Yunus<sup>2</sup>, Siti Fauzza Ahmad<sup>2</sup>

#### **Abstract**

Silicone-based soft liners can be useful for patients who have difficulty to tolerate the hardbased dentures. However lack of adhesion to the denture base resin can be a problem that limits their clinical use. This study evaluated the tensile bond strengths (TBS) of four silicone soft liners (GC Soft, GC XSoft, Silagum, Mollosil) to two chemically different denture base resins, polymethyl methacrylate (PMMA) and urethane dimethacrylate (UDMA). Specimen consisted of soft liner material self-cured between two square plates of cured denture base resin measuring 20 x 20 x 4 mm. The circular bonding area of soft liner to each plate was 10 mm in diameter. Proprietary primer was applied to the surface of the denture base specimens before bonding following the manufacturers' recommendations. Ten specimens for each denture base-soft liner combination were prepared and tested under tension on a Shimadzu Universal Testing Machine at a cross head speed of 5 mm/min. The mode of failure was determined using a stereo-microscope at magnification of 10x. Two- and oneway ANOVA and post-hoc Dunnett-T3 and t-test were used for statistical analysis. There were significant differences in TBS values for the effect of denture base resins, soft liner and their interaction (p < 0.05). The TBS of soft liners to PMMA was significantly higher than to UDMA denture base resins except for Silagum where no significant difference was observed. A mixed mode of failure was more common for all soft liners bonded to PMMA except for Silagum while adhesive failure was more predominant in the UDMA group.

Keywords: Composite, Soft liner, Tensile bond, Surface treatment, Denture, lining materials.

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Chan KK, Wong RSY, Shar Mariam Mohamed, Tengku Azmi Tengku Ibrahim, Maha Abdullah, Nadarajah VD. *Bacillus thuringiensis* parasporal proteins induce cell-cycle arrest and caspase-dependant apoptotic cell death in leukemic cells. *Journal of Environmental Pathology, Toxicology and Oncology*, 2012; 31(1): 75-86.

# Bacillus thuringiensis parasporal proteins induce cell-cycle arrest and caspase-dependant apoptotic cell death in leukemic cells.

Kok-Keong Chan<sup>1</sup>, Rebecca Shin-Yee Wong<sup>1</sup>, Shar Mariam Mohamed<sup>1</sup>, Tengku Azmi Tengku Ibrahim<sup>2</sup>, Maha Abdullah<sup>3</sup>, Vishna Devi Nadarajah<sup>1</sup>.

#### **Abstract**

Bacillus thuringiensis (Bt) parasporal proteins with selective anticancer activity have recently garnered interest. This study determines the efficacy and mode of cell death of Bt 18 parasporal proteins against 3 leukemic cell lines (CEM-SS, CCRF-SB and CCRF-HSB-2). Cell-based biochemical analysis aimed to determine cell viability and the percentage of apoptotic cell death in treated cell lines; ultrastructural analysis to study apoptotic changes and Western blot to identify the parasporal proteins' binding site were performed. Bt 18 parasporal proteins moderately decreased viability of leukemic cells but not that of normal human T lymphocytes. Further purification of the proteins showed changes in inhibition selectivity. Phosphatidylserine externalization, active caspase-3, cell cycle, and ultrastructural analysis confirmed apoptotic activity and S-phase cell-cycle arrest. Western blot analysis demonstrated glyceraldehyde 3-phosphate dehydrogenase as a binding protein. We suggest that Bt 18 parasporal proteins inhibit leukemic cell viability by cell-cycle arrest and apoptosis and that glyceraldehyde 3-phosphate dehydrogenase binding initiates apoptosis.

**Keywords**: *Bacillus thuringiensis*, parasporal proteins, antileukemic activity, apoptotic cell death, cell cycle arrest.

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Cheong KC, Yusoff AF, Ghazali SM, Lim KH, Selvarajah S, Haniff J, Khor GL, Shahar S, Rahman JA, Zainuddin AA, Mustafa AN. Optimal BMI cut-off values for predicting diabetes, hypertension and hypercholesterolaemia in a multi-ethnic population. *Public Health Nutrition*, 2012; 1-7. doi: 10.1017/S1368980012002911.

# Optimal BMI cut-off values for predicting diabetes, hypertension and hypercholesterolaemia in a multi-ethnic population.

Kee Chee Cheong<sup>1</sup>, Ahmad F Yusoffa<sup>1</sup>, Sumarni M Ghazalia<sup>1</sup>, Kuang H Lima<sup>2</sup>, Sharmini Selvarajaha<sup>3</sup>, Jamaiyah Haniffa<sup>3</sup>, Geok L Khora<sup>4</sup>, Suzana Shahara<sup>5</sup>, Jamalludin Abd Rahmana<sup>6</sup>, Ahmad A Zainuddina<sup>2</sup>, Amal N Mustafaa<sup>1</sup>.

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#### Abstract

#### Objective:

To determine the optimal cut-offs of BMI for Malaysian adults.

#### Design

Population-based, cross-sectional study. Receiver operating characteristic curves were used to determine the cut-off values of BMI with optimum sensitivity and specificity for the detection of three cardiovascular risk factors: diabetes mellitus, hypertension and hypercholesterolaemia. Gender-specific logistic regression analyses were used to examine the association between BMI and these cardiovascular risk factors.

#### Setting:

All fourteen states in Malaysia.

### Subjects:

Malaysian adults aged ≥18 years (n 32 703) who participated in the Third National Health and Morbidity Survey in 2006.

#### Results:

The optimal BMI cut-off value for predicting the presence of diabetes mellitus, hypertension, hypercholesterolaemia or at least one of these cardiovascular risk factors varied from 23.3 to 24.1 kg/m2 for men and from 24.0 to 25.4 kg/m2 for women. In men and women, the odds ratio for having diabetes mellitus, hypertension, hypercholesterolaemia or at least one cardiovascular risk factor increased significantly as BMI cut-off point increased.

#### Conclusions:

Our findings indicate that BMI cut-offs of 23.0 kg/m2 in men and 24.0 kg/m2 in women are appropriate for classification of overweight. We suggest that these cut-offs can be used by

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health professionals to identify individuals for cardiovascular risk screening and weight management programmes.

Keywords: BMI, Optimal cut-off, Diabetes, Hypertension, Hypercholesterolaemia.

Chew SC, Loh SP, Khor GL. Determination of folate content in commonly consumed Malaysian foods. *International Food Research Journal*, 2012; 19(1): 189-197.

### Determination of folate content in commonly consumed Malaysian foods.

Chew SC<sup>1</sup>, Loh SP<sup>1</sup>, Khor GL<sup>2</sup>

#### **Abstract**

Currently, data concerning the content of naturally occurring dietary folate in Malaysian foods is scarce. The aim of this study was to determine the folate content of vegetables, fruits, legumes and cereals that were commonly consumed among Malaysians. The total folate content of 156 samples (51 vegetables, 33 fruits, 22 legumes and legume products, and 50 cereals and cereal products) available in Malaysia was determined by microbiological assay using *Lactobacillus casei* (*L. casei*) after trienzyme treatment with protease,  $\alpha$ -amylase and folate conjugase (from rat serum). An internal quality control system was used throughout the study by analyzing CRM 121 (wholemeal flour) and CRM 485 (lyophilized mixed vegetables); percent recovery (as mean  $\pm$  SD) of 97  $\pm$  2.0 and 101  $\pm$  4.0 was obtained. The range of folate content in vegetables, fruits, legumes and cereals were 1-11  $\mu$ g/100 g and 1-31on the basis of fresh weight and 1-31  $\mu$ g/100 g and 2-156  $\mu$ g/100 g on the basis of dry weight, respectively. This study has shown that some of these underutilized vegetables and fruits are good sources of folate and could fulfill the recommended dietary intake of total folate.

**Keywords**: Folate, Malaysia, vegetable, fruit, legume, cereal.

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Chew WK, Mak JW, Ambu S, Segarra I. Significant reduction of *Toxoplasma gondii* brain cysts after treatment with spiramycin co-administered with metronidazole in a mouse model of chronic toxoplasmosis. *Antimicrobial Agents and Chemotherapy*, 2012; 56(4): 1762-1768.

# Significant reduction of *Toxoplasma gondii* brain cysts after treatment with spiramycin co-administered with metronidazole in a mouse model of chronic toxoplasmosis.

Wai Kit Chew<sup>1</sup>, Ignacio Segarra<sup>2</sup>, Stephen Ambu<sup>3</sup>, Joon Wah Mak<sup>3</sup>

#### **Abstract**

Toxoplasma gondii is a parasite that generates latent cysts in the brain; reactivation of these cysts may lead to fatal toxoplasmic encephalitis, for which treatment remains unsuccessful. We assessed spiramycin pharmacokinetics coadministered with metronidazole, the eradication of brain cysts and the in vitro reactivation. Male BALB/c mice were fed 1,000 tachyzoites orally to develop chronic toxoplasmosis. Four weeks later, infected mice underwent different treatments: (i) infected untreated mice (n=9), which received vehicle only; (ii) a spiramycin-only group (n=9), 400 mg/kg daily for 7 days; (iii) a metronidazole-only group

(n9), 500 mg/kg daily for 7 days; and (iv) a combination group (n=9), which received both spiramycin (400 mg/kg) and metronidazole (500 mg/kg) daily for 7 days. An uninfected control group (n10) was administered vehicle only. After treatment, the brain cysts were counted, brain homogenates were cultured in confluent Vero cells, and cysts and tachyzoites were counted after 1 week. Separately, pharmacokinetic profiles (plasma and brain) were assessed after a single dose of spiramycin (400 mg/kg), metronidazole (500 mg/kg), or both. Metronidazole treatment increased the brain spiramycin area under the concentration time curve from 0 h to ∞ (AUC <sub>0-∞</sub>) by 67% without affecting its plasma disposition. Metronidazole plasma and brain AUC <sub>0-∞</sub> values were reduced 9 and 62%, respectively, after spiramycin coadministration. Enhanced spiramycin brain exposure after coadministration reduced brain cysts 15-fold (79±23 for the combination treatment versus 1,198±153 for the untreated control group [P<0.05]) and 10-fold versus the spiramycin-only group (768±125). Metronidazole alone showed no effect (1,028±149). Tachyzoites were absent in the brain. Spiramycin reduced in vitro reactivation. Metronidazole increased spiramycin brain penetration, causing a significant reduction of T. gondii brain cysts, with potential clinical translatability for chronic toxoplasmosis treatment.

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Chew WK, Mak JW, Ambu S, Segarra I. *Toxoplasma gondii*: Determination of the onset of chronic infection in mice and the in vitro reactivation of brain cyst. *Experimental Parasitology*, 2012; 130(1): 22–25.

# Toxoplasma gondii: Determination of the onset of chronic infection in mice and the in vitro reactivation of brain cyst.

Wai Kit Chew<sup>1</sup>, Mak Joon Wah<sup>2</sup>, Stephen Ambu<sup>3</sup>, Ignacio Segarra<sup>4</sup>.

#### **Abstract**

Toxoplasma gondii is an intra-cellular parasite that infects humans through vertical and horizontal transmission. The cysts remain dormant in the brain of infected humans and can reactivate in immunocompromised hosts resulting in acute toxoplasmic encephalitis which may be fatal. We determined the onset and progression of brain cysts generation in a mouse model following acute toxoplasmosis as well as the ability of brain cysts to reactivate in vitro. Male Balb/c mice, (uninfected control group, n = 10) were infected orally (study group, n = 50) with 1000 tachyzoites of *T. gondii* (ME49 strain) and euthanized at 1, 2, 4, 8 and 16 weeks post infection. Brain tissue was harvested, homogenized, stained and the number of brain cysts counted. Aliquots of brain homogenate with cysts were cultured in vitro with confluent Vero cells and the number of cysts and tachyzoites counted after 1 week. Brain cysts but not tachyzoites were detected at week 2 post infection and reached a plateau by week 4. In vitro Vero cells culture showed similar pattern for cysts and tachyzoites and reactivation of cyst in vitro was not influenced by the age of the brain cysts.

**Keywords**: *Toxoplasma gondii*, Brain chronic toxoplasmosis onset, In vitro reactivation.

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Chin LF, Kong SM, Seng HL, Tiong YL, Neo KE, Maah MJ, Khoo AS, Ahmad M, Hor TS, Lee HB, San SL, Chye SM, Ng CH. [Zn(phen)(O,N,O)(H(2)O)] and [Zn(phen)(O,N)(H(2)O)] with O,N,O is 2,6-dipicolinate and N,O is L-threoninate: Synthesis, characterization, and biomedical properties. *Journal of Biological and Inorganic Chemistry*, 2012; 17(7): 1093-1105.

# [Zn(phen)(O,N,O)(H(2)O)] and [Zn(phen)(O,N)(H(2)O)] with O,N,O is 2,6-dipicolinate and N,O is L-threoninate: Synthesis, characterization, and biomedical properties.

Lee-Fang Chin<sup>1</sup>, Siew-Ming Kong<sup>1</sup>, Hoi-Ling Seng<sup>2</sup>, Yee-Lian Tiong<sup>1</sup>, Kian-Eang Neo<sup>1</sup>, Mohd Jamil Maah<sup>3</sup>, Alan Soo-Beng Khoo<sup>4</sup>, Munirah Ahmad<sup>4</sup>, Tzi-Sum Andy Hor<sup>5</sup>, Hong-Boon Lee<sup>6</sup>, Swee-Lan San<sup>6</sup>, Soi-Moi Chye<sup>7</sup>, Chew-Hee Ng<sup>1</sup>.

### **Abstract**

Two ternary Zn(II) complexes, with 1,10-phenanthroline (phen) as the main ligand and a carboxylate-containing ligand [dipicolinate (dipico) or l-threoninate (I-Thr)] as the subsidiary ligand, were prepared and characterized by elemental analysis, Fourier transform IR, UV, and fluorescence spectroscopy, X-ray diffraction, molar conductivity, and electrospray spectrometry. ionization mass X-ray structure analysis shows  $[Zn(phen)(dipico)(H_2O)]\cdot H_2O$  (1) and  $[Zn(phen)(I-Thr)(H_2O)CI]\cdot 2H_2O$  (2) have octahedral geometry about the Zn(II) atom. Both complexes can inhibit topoisomerase I, and have better anticancer activity than cisplatin against nasopharyngeal cancer cell lines, HK1 and HONE-1, with concentrations causing 50 % inhibition of cell proliferation (IC<sub>50</sub>) in the low micromolar range. Complex 2 has the highest therapeutic index for HK1. Both Zn(II) complexes can induce cell death by apoptosis. Changing the subsidiary ligand in the Zn(II) complexes affects the UV-fluorescence spectral properties of the coordinated phen ligand. the binding affinity for some DNA sequences, nucleobase sequence-selective binding, the phase at which cell cycle progression was arrested for treated cancer cells, and their therapeutic index.

**Keywords**: Ternary zinc(II)–1,10-phenanthroline complex, Nasopharyngeal carcinoma, Dipicolinic acid, I-Threonine, Topoisomerase I.

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Cho Naing, Kassim AIBM. Scaling-up attention to non-malaria acute undifferentiated fever. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2012; doi:10.1016/j.trstmh.2012.03.003.

### Scaling-up attention to non-malaria acute undifferentiated fever.

Cho Naing, Ani Izzuani Binti Mohd Kassim.

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#### Abstract

Studies have reported that only a small fraction of fever cases in malaria—endemic areas are actually caused by malaria. Much greater emphasis is now needed to step up attention to the appropriate management of nonmalarial acute undifferentiated febrile illness. There is an overlap at the start of clinical manifestations of different febrile illnesses which makes it difficult to adhere to the clinical guidelines. The development of rigorous guidelines based on high quality research and a consensus from the core group of content experts are needed. An innovative financing mechanism for universal access to such appropriate management should also be considered.

**Keywords**: Nonmalaria fever, Undifferentiated acute fever, Clinical guidelines.

Cho Naing, Kyan Aung, Mak JW. Reporting 'number needed to treat' in meta-analyses: A cross-sectional study. *Journal of Evidence-based Medicine*, 2012; doi: 10.1111/jebm.12002.

### Reporting 'number needed to treat' in meta-analyses: A cross-sectional study.

Cho Naing<sup>1</sup>, Kyan Aung<sup>2</sup>, Joon Wah Mak<sup>1</sup>

#### Abstract

#### Aim:

In translating clinical research into practice, the summarization of data from randomized trials in terms of measures of effect to be readily appreciated by the point-of-care clinicians is important. In this context, the body of literature highlighted the 'number needed to treat' as a useful measure. The objectives of our study were to assess how meta-analyses described number needed to treat and corresponding 95% CI, and to explore issues related to reporting number needed to treat in the selected meta-analyses.

#### Method:

For an illustration, we searched for the Cochrane systematic reviews and non-Cochrane systematic reviews. Two-stage selection was done to identify eligible studies. First, we fixed a date and then, we searched meta-analyses in PUBMED available on the date fixed. Secondly, we purposively selected five Cochrane systematic reviews and three non-Cochrane systematic reviews, according to our inclusion criteria. The critical appraisal of meta-analyses identified for the current study was done with the 5-item quality checklist introduced to the current analysis.

### Results:

A total of 8 systematic reviews, 5 Cochrane systematic reviews and 3 non-Cochrane systematic reviews/meta-analyses, were identified for the present study. Of these 8 meta-analyses, some (50%; 4/8) described number needed to treat in the method session of the study. However, the majority (87.5%; 7/8) reported number needed to treat in the results. For the details, 80% in Cochrane reviews and 66.5% in non-Cochrane reviews reported number needed to treat in the results. Only two studies (25%; 2/8) reported susceptibility to publication bias, provided simplified interpretation or discussed number needed to treat.

#### Conclusion:

Although the Cochrane handbook for systematic reviews of interventions suggests the reviewers to include number needed to treat in reporting effect estimations, there still is a need to improve.

**Keywords**: number needed-to-treat; randomised controlled trials; meta-analysis; methodology.

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Cho Naing, Kyan Aung, Syed Imran Ahmed, Mak JW. Signal detection to identify serious adverse events (neuropsychiatric events) in travellers taking mefloquine for chemoprophylaxis of malaria. *Drug, Healthcare and Patient Safety,* 2012; 4: 87-92.

# Signal detection to identify serious adverse events (neuropsychiatric events) in travellers taking mefloquine for chemoprophylaxis of malaria.

Cho Naing<sup>1,3</sup>, Kyan Aung<sup>1</sup>, Syed Imran Ahmed<sup>2</sup>, Joon Wah Mak<sup>3</sup>

#### Abstract

### Background:

For all medications, there is a trade-off between benefits and potential for harm. It is important for patient safety to detect drug-event combinations and analyze by appropriate statistical methods. Mefloquine is used as chemoprophylaxis for travelers going to regions with known chloroquine-resistant *Plasmodium falciparum* malaria. As such, there is a concern about serious adverse events associated with mefloquine chemoprophylaxis. The objective of the present study was to assess whether any signal would be detected for the serious adverse events of mefloquine, based on data in clinicoepidemiological studies.

#### Materials and methods:

We extracted data on adverse events related to mefloquine chemoprophylaxis from the two published datasets. Disproportionality reporting of adverse events such as neuropsychiatric events and other adverse events was presented in the 2 × 2 contingency table. Reporting odds ratio and corresponding 95% confidence interval [CI] data-mining algorithm was applied for the signal detection. The safety signals are considered significant when the ROR estimates and the lower limits of the corresponding 95% CI are ≥2.

#### Results:

Two datasets addressing adverse events of mefloquine chemoprophylaxis (one from a published article and one from a Cochrane systematic review) were included for analyses. Reporting odds ratio 1.58, 95% CI: 1.49–1.68 based on published data in the selected article, and 1.195, 95% CI: 0.94–1.44 based on data in the selected Cochrane review. Overall, in both datasets, the reporting odds ratio values of lower 95% CI were less than 2.

#### Conclusion:

Based on available data, findings suggested that signals for serious adverse events pertinent to neuropsychiatric event were not detected for mefloquine. Further studies are needed to substantiate this.

**Keywords:** mefloquine, signal detection, reporting odds ratio, neuropsychiatric events

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Cho Naing, Kyan Aung, Yeoh PN. Buprenorphine for treating cancer pain. *Cochrane Database of Systematic Reviews*, 2012; DOI: 10.1002/14651858.CD009596.

### **Buprenorphine for treating cancer pain**

Cho-Min Naing<sup>1</sup>, Kyan Aung<sup>2</sup>, Peng Nam Yeoh<sup>3</sup>

#### **Abstract**

This is the protocol for a review and there is no abstract. The objectives are as follows: To determine the analgesic efficacy of buprenorphine analgesia in relieving cancer pain and to assess the adverse effects of buprenorphine in patients with cancer pain.

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Cho Naing, Mak JW, Ahmed SI, Mala Maung. Relationship between hepatitis C virus infection and type 2 diabetes mellitus: Meta-analysis. *World Journal of Gastroenterology*, 2012; 18(14): 1642-1651.

# Relationship between hepatitis C virus infection and type 2 diabetes mellitus: Meta-analysis.

Cho Naing, Joon Wah Mak, Syed Imran Ahmed, Mala Maung.

Faculty of Medicine and Health, International Medical University, Kuala Lumpur 57000, Malaysia

#### Abstract

Aim:

To investigate the association between hepatitis C infection and type 2 diabetes mellitus.

#### Methods:

Observational studies assessing the relationship between hepatitis C infection and type 2 diabetes mellitus were identified via electronic and hand searches. Studies published between 1988 to March 2011 were screened, according to the inclusion criteria set for the present analysis. Authors performed separate analyses for the comparisons between hepatitis C virus (HCV) infected and not infected, and HCV infected and hepatitis B virus infected. The included studies were further subgrouped according to the study design. Heterogenity was assessed using I 2 statistics. The summary odds ratios with their corresponding 95% CIs were calculated based on a random-effects model. The included studies were subgrouped according to the study design. To assess any factor that could potentially affect the outcome, results were further stratified by age group (proportion of  $\geq$  40 years), gender (proportion of male gender), body mass index (BMI) (proportion of BMI  $\geq$  27), and family history of diabetes (i.e., self reported). For stability of results, a sensitivity analysis was conducted including only prospective studies.

#### Results:

Combining the electronic database and hand searches, a total of 35 observational studies (in 31 articles) were identified for the final analysis. Based on random-effects model, 17 studies (n = 286 084) compared hepatitis C-infected patients with those who were uninfected [summary odds ratio (OR): 1.68, 95% CI: 1.15-2.45]. Of these 17 studies, 7 were both a cross-sectional design (41.2%) and cohort design (41.2%), while 3 were case-control studies (17.6%). Nineteen studies (n = 51 156) compared hepatitis C-infected participants with hepatitis B-infected (summary OR: 1.92, 95% CI: 1.41-2.62). Of these 19 studies, 4 (21.1%), 6 (31.6%) and 9 (47.4%) were cross-sectional, cohort and case-control studies, respectively. A sensitivity analysis with 3 prospective studies indicated that hepatitis C-infected patients had a higher risk of developing type 2 diabetes compared with uninfected controls (summary odds ratio: 1.41, 95% CI: 1.17-1.7; f = 0%). Among hepatitis C-infected patients, male patients (OR: 1.26, 95% CI: 1.03-1.54) with age over 40 years (summary OR: 7.39, 95% CI: 3.82-9.38) had an increased frequency of type 2 diabetes. Some caution must be taken in the interpretation of these results because there may be unmeasured confounding factors which may introduce bias.

#### Conclusion:

The findings support the association between hepatitis C infection and type 2 diabetes mellitus. The direction of association remains to be determined, however. Prospective studies with adequate sample sizes are recommended.

Keywords: Hepatitis C; Type 2 diabetes mellitus; Observational studies; Meta-analysis

Cho Naing, Mak JW, Kyan Aung, Wong JYR. Efficacy and safety of dihydroartemisinin-piperaquin for treatment of uncomplicated *Plasmodium falciparum* malaria in endemic countries: Meta-analysis of randomized controlled studies. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2012; doi: 10.1093/trstmh/trs019.

Efficacy and safety of dihydroartemisinin-piperaquin for treatment of uncomplicated *Plasmodium falciparum* malaria in endemic countries: Meta-analysis of randomized controlled studies.

Cho Naing<sup>1,2</sup>, Joon Wah Mak<sup>1</sup>, Kyan Aung<sup>2</sup>, Jadon YR Wong<sup>1</sup>

#### **Abstract**

The present review aimed to synthesise available evidence on the efficacy of dihydroartemisinin-piperaquine (DP) in treating uncomplicated Plasmodium falciparum malaria in people living in malaria-endemic countries by performing a meta-analysis of relevant studies. We searched relevant studies in electronic data bases up to December 2011. Published results from randomised controlled trials (RCTs) comparing efficacy of DP with other artemisinin-based combination therapies (ACTs), or non-ACTs, or placebo were selected. The primary endpoint was 28-day and 42-day treatment failure. We identified 26 RCTs. Many of the studies included in the present review were of high quality. Overall, DP, artesunate-mefloquine (MAS3) and artemether-lumefentrine (AL) were equally effective for reducing the risk of recurrent parasitaemia. The PCR confirmed efficacy of DP (99.5%) and MAS3 (97.7%) at day 28 exceeded 90%; both are efficacious. Comparable efficacy was also found for DP (95.6%) and AL (94.3%). The present review has documented that DP is comparable to other currently used ACTs such as MAS3 and AL in treating uncomplicated falciparum malaria. The better safety profile of DP and once-daily dosage improves adherence and its fixed co-formulation ensures that both drugs are taken together. Our conclusion is that DP has the potential to become a first-line antimalarial drug.

**Keywords**: Malaria, *Plasmodium falciparum*, Dihydroartemisinin-piperaquine, Treatment

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Cho Naing, Mak JW, Mala Maung, Wong SF, Ani Izzuani MK. Meta-analysis: The association between HIV infection and extrapulmonary tuberculosis. *Lung* 2012; doi 10.1007/s00408-012-9440-6.

### Meta-analysis: The association between HIV infection and extrapulmonary tuberculosis.

Naing Cho<sup>1,2</sup>, Mak Joon Wah<sup>1</sup>, Maung Mala<sup>2</sup>, Wong Shew Fung<sup>1</sup>, Kassim Ani<sup>1</sup>.

#### **Abstract**

#### Background:

Extrapulmonary tuberculosis has been an AIDS-defining condition. Individual studies that highlight the association between HIV and extrapulmonary TB are available. Our objectives were to synthesis evidence on the association between extrapulmonary tuberculosis and HIV and to explore the effective preventive measures of these two diseases.

#### Methods:

This is a meta-analysis of observational studies reporting effect estimates on how HIV is associated with extrapulmonary tuberculosis. We searched for the eligible studies in the electronic databases using search terms related to HIV and extrapulmonary tuberculosis. Where possible, we estimated the summary odds ratios using random effects meta-analysis. We stratified analysis by the type of study design. We assessed heterogeneity of effect estimates within each group of studies was assessed using I test.

#### Results:

Nineteen studies (7 case control studies and 12 cohort studies) were identified for the present study. The pooled analysis shows a significant association between HIV and extrapulmonary tuberculosis (summary odds ratio: 1.3; 95 % confidence interval (CI) 1.05-1.6; I: 0 %). In a subgroup analysis with two studies, a significant association was found between CD4+ count less than 100 and the incidence of extrapulmonary tuberculosis (summary OR: 1.31; 95 % CI 1.02-1.68; I: 0 %).

#### Conclusions:

Findings show evidence on the association between extrapulmonary tuberculosis and HIV, based on case control studies. Further studies to understand the mechanisms of interaction of the two pathogens are recommended.

**Keywords:** Extrapulmonary tuberculosis, HIV, Risk factor, Meta-analysis.

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Cho Naing, Mak JW, Nyunt Wai, Mala Maung. Diabetes and infectious hepatitis C (Is there type 2 diabetes excess in hepatitis C-infection?). *Current Diabetes Reports*, 2012; (in press).

# Diabetes and infectious hepatitis C (Is there type 2 diabetes excess in hepatitis C-infection?)

Cho Naing<sup>1</sup>, Mak Joon Wah<sup>1</sup>, Nyunt Wai<sup>2</sup>, Mala Maung<sup>2</sup>.

#### **Abstract**

Individual epidemiologic studies as well as the pooled analysis of observational studies have indicated the association between type 2 diabetes (T2D) and hepatitis C virus infection (HCV). Whether HCV infection is the cause of diabetes or diabetic patients are more prone to get HCV infection is still in question. The objective of the present review was to provide answers to this issue, based on available evidence from epidemiologic, molecular, experimental and therapeutic studies. Our current understanding of how chronic HCV infection could induce T2D is incomplete, but it seems twofold based on both direct and indirect roles of the virus. HCV may directly induce insulin resistance (IR) through its proteins. HCV core protein was shown to stimulate suppressor of cytokine signaling, resulting in ubiquitination and degradation of tyrosine kinase phosphorylated insulin receptor substrates (IRS1/2) in proteasomes. HCV-nonstructural protein could increase protein phosphatase 2A which has been shown to inactivate the key enzyme Akt by dephosphorylating it. Insulin signaling defects in hepatic IRS-1 tyrosine phosphorylation and PI3-kinase association/activation may contribute to IR, which leads to the development of T2D in patients with HCV infection. The peroxisome proliferator-activated receptors (PPARs) are also implicated. PPARα/y, together with their obligate partner RXR, are the main nuclear receptors expressed in the liver. PPARα upregulates glycerol-3-phosphate dehydrogenase, glycerol kinase, and glycerol transport proteins, which allows for glucose synthesis during fasting states. Decreased activity of PPARs could attribute to HCV-induced IR. Immunemediated mechanisms may be involved in the indirect role of HCV in inducing IR. It is speculated that TNF-alpha plays a major role in the pathogenesis of IR through lowering IRS1/2. Furthermore, HCV infection- triggered ER stress could lead to the activation of PP2A, which inhibits both Akt and the AMP-activated kinase, the regulators of gluconeogenesis. In summary, we illustrate that HCV infection is accompanied by multiple defects in the upstream insulin signaling pathway in the liver that may contribute to the observed prevalence of IR and diabetes. Future studies are needed to resolve this issue.

**Keywords**: Type 2 diabetes, Hepatitis C infection, Insulin resistance, IRS1/2, HCV protein, Peroxisome proliferator-activated receptors  $\alpha/\gamma$ , TNF-alpha, ER.

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Cho Naing, Tan RYP, Soon WC, Parakh J, Sanggi SS. Preventive behaviours towards influenza A(H1N1)pdm09 and factors associated with the intention to take influenza A(H1N1)pdm09 vaccination. *Journal of Infection and Public Health*, 2012; (in press).

# Preventive behaviours towards influenza A(H1N1)pdm09 and factors associated with the intention to take influenza A(H1N1)pdm09 vaccination

Cho Naing, Rachel Yi Ping Tan, Wai Cheong Soon, Jehangirshaw Parakh, Sandip Singh Sanggi.

International Medical University, Kuala Lumpur 57000, Malaysia

#### Abstract

#### Purpose:

(i) To determine knowledge of, and self-protecting preventive behaviours towards influenza A(H1N1)pdm09 and (ii) to identify the factors influencing intention to take influenza A(H1N1)pdm09 vaccination among the study population.

#### Materials and methods:

This is a cross-sectional survey carried out in Mantin Town, a semi-urban area of Malaysia. A structured questionnaire consisted of sociodemographic characteristics, knowledge of pandemic influenza symptoms, mode of transmission, self-protecting preventive behaviours, and intention to receive the influenza A(H1N1)pdm09 vaccine was used for face-to-face interviews with the household members.

#### Results:

Of 230 who heard about pandemic influenza A(H1N1), 86% had misconception about mode of transmission of influenza A(H1N1)pdm09, and 52% had sufficient self-protecting behaviours. A majority (58.3%; 134/230) had intended to receive the vaccine. In the multivariate analysis, the intention to get vaccinated was significantly higher among 'those who trusted in efficacy of vaccine for prevention of influenza A(H1N1)pdm09' (p < 0.001), 'those who were equipped with higher education level' (p = 0.015) and 'those who worry about themselves contracting illness' (p = 0.008).

#### Conclusions:

Our findings highlight the need to scale up the community's knowledge regarding influenza A(H1N1)pdm09. Recognizing the factors affecting the acceptance of vaccination documented in this study will allow decision makers to devise effective and efficient vaccination strategies.

**Keywords**: Influenza A(H1N1)pdm09, Knowledge, Self-protection, Behaviours, Vaccination.

Chong HZ, Asmah Rahmat, Yeap SK, Abdah Md Akim, Noorjahan Banu Alitheen, Fauziah Othman, Gwendoline-Ee CL. In vitro cytotoxicity of *Strobilanthes crispus* ethanol extract on hormone dependent human breast adenocarcinoma MCF-7 cell. *BMC Complementary and Alternative Medicine*, 2012; 12: 35.

### In vitro cytotoxicity of *Strobilanthes crispus* ethanol extract on hormone dependent human breast adenocarcinoma MCF-7 cell

Hueh Zan Chong<sup>1,2</sup>, Asmah Rahmat<sup>1</sup>, Swee Keong Yeap<sup>3</sup>, Abdah Md Akim<sup>4</sup>, Noorjahan Banu Alitheen<sup>3</sup>, Fauziah Othman<sup>4</sup>, Cheng Lian Gwendoline-Ee<sup>5</sup>.

#### **Abstract**

#### Background:

Strobilanthes crispus has been traditionally used as antidiabetic, anticancer, diuretic, antilytic and laxative agent. However, cytotoxicity and antiproliferative effect of *S. crispus* is still unclear.

#### Results:

Strobilanthes cripus was able to reduce cell viability and proliferation in MTT and BrdU assays. Both cell cycle progression and Tunel assay suggested that IC50 of *S. crispus* ethanol extract induced sub-G1 cell cycle phase, and DNA fragmentation. On the other hand, translocation of mitochondria cytochrome c release, induction of caspase 3/7 and p53 while suppress XIAP on treated MCF-7 cell were also observed in this study.

#### Conclusion:

Our findings suggest that *S. crispus* ethanol extract induced apoptosis and DNA fragmentation on hormone dependent breast cancer cell line MCF-7 via mitochondria dependent p53 apoptosis pathway.

**Keywords**: Strobilanthes crispus, MCF-7, Apoptosis, p53.

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Chong HZ, Asmah Rahmat, Yeap SK, Abdah Md Akim, Noorjahan Banu Alitheen, Fauziah Othman, Gwendoline-Ee CL. In vitro evaluation of *Pandanus amaryllifolius* ethanol extract for induction of cell death on non-hormone dependent human breast adenocarcinoma MDA-MB-231 cell via apoptosis. *BMC Complementary and Alternative Medicine*, 2012; 12: 134-135.

# In vitro evaluation of *Pandanus amaryllifolius* ethanol extract for induction of cell death on non-hormone dependent human breast adenocarcinoma MDA-MB-231 cell via apoptosis

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### **Abstract**

### Background:

Our previous study had shown that *P. amaryllifolius* was able to selectively inhibit cell proliferation of hormone independent breast cancer cell line MDA-MB-231. To understand the mode of killing and mechanism of action for *P. amaryllifolius*, the ethanol extract was evaluated for their alteration of cell cycle progression, PS externalization, DNA fragmentation and expression of anti/pro-apoptotic related protein.

### Results:

Cell cycle progression analysis, Annexin V and Tunel assays suggested that IC50 of *P. amaryllifolius* ethanol extract induced G0/G1 cell cycle arrest, PS externalization and DNA fragmentation. On the other hand, ELISA for cytochrome c, caspase-3/7, 8 and 9 indicated that apoptosis was contributed by mitochondrial cytochrome c release via induction of caspase 3/7, 9, and p53 was associated with the suppression of XIAP in *P. amaryllifolius* treated MDA-MB-231 cells.

### Conclusion:

Our findings suggest that *P. amaryllifolius* ethanol extract induced apoptosis on hormone independent breast cancer cell line MDA-MB-231.

Keywords: Pandanus amaryllifolius, MDA-MB-231, Apoptosis, Cytochrome c, Caspase.

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Chu WL. Biotechnological applications of microalgae. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S24-S37.

### Biotechnological applications of microalgae

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### **Abstract**

Microalgae are important biological resources that have a wide range of biotechnological applications. Due to their high nutritional value, microalgae such as Spirulina and Chlorella are being mass cultured for health food. A variety of high-value products including polyunsaturated fatty acids (PUFA), pigments such as carotenoids and phycobiliproteins, and bioactive compounds are useful as nutraceuticals and pharmaceuticals, as well as for industrial applications. In terms of environmental biotechnology, microalgae are useful for bioremediation of agro-industrial wastewater, and as a biological tool for assessment and monitoring of environmental toxicants such as heavy metals, pesticides and pharmaceuticals. In recent years, microalgae have attracted much interest due to their potential use as feedstock for biodiesel production. In Malaysia, there has been active research on microalgal biotechnology for the past 30 years, tapping into the potential of our rich microalgal resources for high-value products and applications in wastewater treatment and assessment of environmental toxicants. A culture collection of microalgae has been established, and this serves as an important resource for microalgal biotechnology research. Microalgal biotechnology should continue to be regarded as a priority area of research in this country.

**Keywords**: Bioactive compounds, bioremediation, biotechnology, Chlorella, Dunaliella, microalgae, Spriulina.

Chua YCJ, Wazir NN, Chiu CK, Kareem BA. Management of osteonecrosis of the hip complicated with fracture: A case report. *Malaysian Orthopaedic Journal*, 2012; 6(4): 43-44.

# Management of osteonecrosis of the hip complicated with fracture: A case report

Chua YCJ, MBBS, Wazir NN, MS Orth, Chiu CK, MS Orth, Kareem BA, MS Orth.

Department of Orthopaedic Surgery, International Medical University, Kuala Lumpur, Malaysia

#### Abstract

A 47-year-old gentleman, with underlying seborrhoeic dermatitis that was treated with steroid therapy, and hepatitis B, presented with pain in his right hip. He was diagnosed with stage 2 osteonecrosis of the right hip (Ficat and Arlet classification). Core decompression and bone grafting was performed but recovery was complicated by a surgical site infection. Wound debridement, removal of bone graft and clearance of the bone tunnel were carried out. The patient was allowed to bear weight after surgery. Twelve days later, he developed right hip pain and radiographs showed fractured femur neck; the patient then underwent a two-stage total hip replacement (THR).

**Keywords**: Osteonecrosis, avascular necrosis, hip, core decompression, total hip replacement.

Chye SM, Tiong YL, Yip WK, Koh RY, Len YW, Seow HF, Ng KY, Ranjit DA, Chen SC. Apoptosis induced by para-phenylenediamine involves formation of ROS and activation of p38 and JNK in chang liver cells. *Environmental Toxicology*, 2012; (in press).

# Apoptosis induced by *para*-phenylenediamine involves formation of ROS and activation of p38 and JNK in chang liver cells

Soi Moi Chye<sup>1</sup>, Yee Lian Tiong<sup>1</sup>, Wai Kien Yip<sup>2</sup>, Rhun Yian Koh<sup>1</sup>, Yi Won Len<sup>3</sup>, Heng Fong Seow<sup>2</sup>, Khuen Yen Ng<sup>4</sup>, De Alwis Ranjit<sup>5</sup>, Ssu Ching Chen<sup>6</sup>.

### **Abstract**

Para-phenylenediamine (p-PD) is a suspected carcinogen, but it has been widely used as a component in permanent hair dyes. In this study, the mechanism of p-PD-induced cell death in normal Chang liver cells was investigated. The results demonstrated that p-PD decreased cell viability in a dose-dependent manner. Cell death via apoptosis was confirmed by enhanced DNA damage and increased cell number in the sub-G1 phase of the cell cycle, using Hoechst 33258 dye staining and flow cytometry analysis. Apoptosis via reactive oxygen species generation was detected by the dichlorofluorescin diacetate staining method. Mitogen-activated protein kinase (MAPK) activation was assessed by western blot analysis and revealed that p-PD activated not only stress-activated protein kinase (SAPK)/c-Jun N-terminal kinases (JNK) and p38 MAPK but also extracellular signal-regulated kinase (ERK). Cytotoxicity and apoptosis induced by p-PD were markedly enhanced by ERK activation and selectively inhibited by ERK inhibitor PD98059, thus indicating a negative role of ERK. In contrast, inhibition of p38 MAPK activity with the p38-specific inhibitor SB203580 moderately inhibited cytotoxicity and apoptosis induction by p-PD. Similarly, SP600125, an inhibitor of SAPK/JNK, moderately inhibited cytotoxicity and apoptosis induced by p-PD, thus implying that p38 MAPK and SAPK/JNK had a partial role in p-PD-induced apoptosis. Western blot analysis revealed that p-PD significantly increased phosphorylation of p38 and SAPK/JNK and decreased phosphorylation of ERK. In conclusion, the results demonstrated that SAPK/JNK and p38 cooperatively participate in apoptosis induced by p-PD and that a decreased ERK signal contributes to growth inhibition or apoptosis.

**Keywords:** *par*a-phenylenediamine, apoptosis, Chang liver cells, reactive oxygen species, MAP-kinases.

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Dutta S, Singh G, Sreejith S, Mamidi MK, Husin JM, Datta I, Pal R, Das AK. Cell therapy: The final frontier for the treatment of neurological diseases. *CNS Neuroscience and Therapeutics*, 2012; (in press).

## Cell therapy: The final frontier for the treatment of neurological diseases

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#### **Abstract**

Neurodegenerative diseases are devastating because they cause increasing loss of cognitive and physical functions and affect an estimated 1 billion individuals worldwide. Unfortunately, no drugs are currently available to halt their progression, except a few that are largely inadequate. This mandates the search of new treatments for these progressively degenerative diseases. Neural stem cells (NSCs) have been successfully isolated. propagated, and characterized from the adult brains of mammals, including humans. The confirmation that neurogenesis occurs in the adult brain via NSCs opens up fresh avenues for treating neurological problems. The proof-of-concept studies demonstrating the neural differentiation capacity of stem cells both in vitro and in vivo have raised widespread enthusiasm toward cell-based interventions. It is anticipated that cell-based neurogenic drugs may reverse or compensate for deficits associated with neurological diseases. The increasing interest of the private sector in using human stem cells in therapeutics is evidenced by launching of several collaborative clinical research activities between Pharma giants and research institutions or small start-up companies. In this review, we discuss the major developments that have taken place in this field to position stem cells as a prospective candidate drug for the treatment of neurological disorders.

**Keywords**: Cell transplantation and clinical trials, Neural differentiation, Neurorepair, Stem cells.

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Gomez EL, Gun SC, Somanath SD, Chinna K, Radhakrishnan AK. Ethnic differences in the prognostic utility of rheumatoid factor isotypes and anticyclic citrullinated peptides in rheumatoid arthritis patients: A cross-sectional study. *Modern Rheumatology*, 2012; (in press).

# Ethnic differences in the prognostic utility of rheumatoid factor isotypes and anticyclic citrullinated peptides in rheumatoid arthritis patients: A cross-sectional study

Edmund Luke Gomez<sup>1</sup>, Suk Chyn Gun<sup>2</sup>, Sushela Devi Somanath<sup>3</sup>, Karuthan Chinna<sup>4</sup>, Ammu K. Radhakrishnan<sup>3</sup>.

### **Abstract**

### Objectives:

The prognostic significance of rheumatoid factor (RF) and anticyclic citrullinated peptide antibody (anti-CCP) in rheumatoid arthritis (RA) remains contentious due to the conflicting lines of evidence. This study aims to determine the association between RF isotypes and anti-CCP with disease severity in RA patients from three ethnic groups.

### Methods:

A total of 147 RA patients from three different ethnic groups (Malays, Chinese, and Indians) who fulfilled the 1987 American College of Rheumatology (ACR) revised criteria for RA were recruited into this study. The seroprevalence of RF isotypes immunoglobulin (Ig)A, IgG, and IgM, as well as anti-CCP was determined using commercial enzyme-linked immunosorbent assay (ELISA) kits. Multinomial regression analysis was performed to assess the independent effects of autoantibody status on the development of deforming and erosive RA and the presence of extra-articular manifestations (EAM).

### Results:

In Chinese patients, we found a significant association (p\0.05) between IgG RF and anti-CCP and the presence of erosive disease, as well as IgM RF and IgG RF with the presence of joint deformities. In Indian patients, IgM RF was associated with deforming disease, whereas none of the antibodies were associated with disease severity in Malay patients. Multinomial regression analysis revealed that IgG RF was the most important predictor variable for erosive disease in Chinese patients, and IgM RF the only predictor variable associated with deforming disease in both Chinese and Indian RA patients.

## Conclusions:

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There is variability in the phenotypic association of RF isotypes and anti-CCP in relation to disease severity of RA in the three ethnic groups. RF, in particular, IgG and IgM, may be better prognosticators of severe disease in Chinese and Indian patients.

**Keywords**: Anticyclic citrullinated peptides, Autoantibodies, Rheumatoid arthritis, Rheumatoid factor, Rheumatoid factor isotypes.

Gorajana A, Rajendran A, Dua A, Pabreja A, Hoon TP. Preparation, characterization, and in vitro evaluation of nitrendipine solid dispersions. *Journal of Dispersion Science and Technology*, 2012; 33: 1-9.

# Preparation, characterization, and in vitro evaluation of nitrendipine solid dispersions

Adinarayana Gorajana<sup>1</sup>, Adhiyaman Rajendran<sup>1</sup>, Kamal Dua<sup>1</sup>, Kavita Pabreja<sup>2</sup>, Tee Phaik Hoon<sup>1</sup>

### Abstract

In order to enhance the absorption of dissolution rate of nitrendipine (NIT), solid dispersions were prepared using two water soluble carriers, polyvinylpyrrolidone K30 (PVP K30) and polyethylene glycol 4000 (PEG-4000), by solvent and fusion method. The dissolution profile of solid dispersions were compared to the pure drug in both pH 1.2 hydrochloric acid and pH 6.8 phosphate buffer and the results have shown profound improvement in drug release. The solubility of solid dispersion was increased by several folds when compared to pure NIT. The physicochemical properties of the solid dispersions were examined using analytical techniques. The results of microscopic studies, x-ray powder diffraction (XRPD), and differential scanning calorimetric (DSC) analysis confirmed the amorphous state of solid dispersion in comparison to the crystalline nature of pure drug, proposing that NIT was molecularly dispersed in the polymer matrices, which were accounted for by dissolution rate enhancement. Fourier transform infrared (FTIR) spectroscopic analysis indicated the presence of hydrogen bonding between NIT and the polymers, which also explained the improvement in solubility and dissolution rate. In conclusion, solid dispersion of NIT with PVP K30 and PEG-4000 improved the solubility and rate of dissolution, which may improve the absorption of the drug and subsequently the bioavailability of NIT.

**Keywords**: Bioavailability, dissolution rate, nitrendipine, PEG\-4000, PVP K30, solid dispersion, solubility.

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Hussein S, Ling APK, Ng TH, Ibrahim R, Paek KY. Adventitious roots induction of recalcitrant tropical woody plant, *Eurycoma longifolia* in response to auxins and carbon sources. *Romanian Biotechnological Letters*, 2012; 17: 6953-6963.

# Adventitious roots induction of recalcitrant tropical woody plant, *Eurycoma longifolia* in response to auxins and carbon sources

Sobri Hussein<sup>1</sup>, Anna Pick Kiong Ling<sup>2</sup>, Tze Hann Ng<sup>3</sup>, Rusli Ibrahim<sup>1</sup>, Kee Yoeup Paek<sup>4</sup>.

#### **Abstract**

Eurycoma longifolia is well known for its aphrodisiac and energy enhancing properties especially among the communities in Southeast Asia regions attributed to the bioactive compounds concentrated mainly in its tap root. Over-exploitation of the plants from the natural habitat has led to the shortage of the plant in the jungle. In this study, the effects of naphthaleneacetic acid (NAA), indole acetic acid (IAA) and indole butyric acid (IBA) at the concentrations of 0, 1, 3, 5 and 7 mg/L on adventitious roots induction from the leaf explants were tested on full strength Murashige and Skoog (MS) medium. The best auxin and the optimal concentration determined was NAA at 3 mg/L as measured in terms of percentage of explants forming roots and the number of roots formed per explant. In the study on sucrose concentrations, 3 mg/L of NAA-containing MS medium was supplemented with sucrose at 10, 30, 50 and 70 g/L. The results revealed that 50g/L sucrose that produced 3.2 roots per explant was better than 30g/L in inducing adventitious roots. Further studies using different carbon sources revealed that glucose recorded the highest rooting percentage (42.2%) while sucrose gave the highest root number (3.0) per explant. This study reported the first successful adventitious roots induction of E. longifolia, which promise a high potential of large scale commercial production in bioreactor for the pharmaceutical industries.

**Keywords**: adventitious root, aphrodisiac, carbon source, *Eurycoma longifolia*, plant growth regulators, tissue culture.

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Khajotia R, Raman S. Bilateral spontaneous persistent open pneumothorax with chylothorax. *Canadian Family Physician*, 2012; 58: 757-760.

### Bilateral spontaneous persistent open pneumothorax with chylothorax

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### **Abstract**

Multiple pulmonary cystic lesions might occur owing to many causes, such as pulmonary Langerhans histiocytosis (*eosinophilic granuloma*), bullous emphysema, cystic fibrosis, idiopathic pulmonary fibrosis, and lymphangioleiomyomatosis (LAM).

Lymphangioleiomyomatosis is predominantly a disease that affects women of childbearing age. Rarely, however, sporadic LAM (S-LAM) has been reported in men, leading clinicians to now believe that the possibility of LAM should be seriously considered in men with diffuse cystic lung disease. We have reported one such case of possible S-LAM in an otherwise phenotypically normal 19-year-old man who initially presented to his family physician with bilateral, spontaneous, open pneumothoraces accompanied by a chylous effusion (chylothorax) on the left side.

Khajotia R. Mediastinal shift: A sign of significant clinical and radiological importance in diagnosis of malignant pleural effusion. *Malaysian Family Physician*, 2012; 31(1): 75-86.

# Mediastinal shift: A sign of significant clinical and radiological importance in diagnosis of malignant pleural effusion

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#### Abstract

Mediastinal shift (upper and lower) is a clinical and radiological marker of significant importance, which at times helps to determine the aetiological cause of the underlying pathology. Tracheal shift is an indicator of upper mediastinal shift, while a shift in the position of the heart indicates a lower mediastinal shift. Since the pleural cavity is confined by the rib cage, in case of a moderately large pleural effusion, the structures in the thoracic cavity normally get 'pushed' to the opposite side resulting in a shift of the upper and lower mediastinum. This is clinically and radiologically detected by a shift in the trachea and heart to the side opposite to the pleural effusion. This is commonly seen in pleural effusions resulting from tuberculosis or other infections. However, in some cases even a large pleural effusion fails to shift the mediastinum to the opposite side. In fact, in some cases, the trachea and heart are observed to be central or even shifted to the same side as the effusion. This finding is of immense importance as it is a clinical indicator of a more serious condition which needs prompt diagnosis and urgent management. We report here, one such case of a middle-aged man who presented to the emergency department with complaints of increasing breathlessness and whose clinical and radiological examination revealed a moderately large right-sided pleural effusion with the trachea and heart also shifted to the right side.

Khan SA, Moorthy J, Omar H, Hasan SS. People living with HIV /AIDS (PLWHA) and HIV/AIDS associated oral lesions: A study in Malaysia. *BMC Public Health*, 2012; 12: 850.

# People living with HIV /AIDS (PLWHA) and HIV/AIDS associated oral lesions: A study in Malaysia

Saad A Khan<sup>1</sup>, Jayanthy Moorthy<sup>1</sup>, Hanan Omar<sup>1</sup>, Syed Shahzad Hasan<sup>2</sup>.

### **Abstract**

### Background:

The continuous increase in number of people living with HIV/AIDS (PLWHA) represents a serious health and economic burden. HIV positive individuals with oral lesions have significantly lower oral health-related quality of life than HIV positive individuals without oral lesions. The objective of this study was to assess the knowledge, attitude and practices (KAP) within a cohort of HIV/AIDS positive patients towards HIV/AIDS associated oral lesions.

### Methods:

Two hundred seventy patients attending a national referral hospital of infectious disease in Malaysia were recruited for the study. The study involved the administration of a validated interview-based questionnaire designed to elicit knowledge, attitude and practices of these patients towards HIV associated oral lesions. The last part of the questionnaire assessed the training provided to the patients in relation to the oral lesions associated with the disease and the effectiveness of this training. Data analysis was carried out using SPSS version 18.

### Results:

Thirty seven percent of patients were reported as knowledgeable, while sixty four percent reported to have positive attitude towards the care of oral hygiene. Sixty six percent of the patients reported that they would seek professional care when experiencing oral lesion. Training was reported effective for 93% patients.

### Conclusions:

Patients were non-knowledgeable in relation to oral manifestations of the disease and one third of the participating patients showed negative attitudes towards oral health care and reported various measures to manage oral lesions rather than seeking professional care. Developing effective educational methodologies can empower patients with knowledge that may translate to positive attitudes and practices.

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Khan SA, Omar H, Babar MG, Toh CG. Utilization of debate as an educational tool for dental students to learn health economics. *Journal of Dental Education*, 2012; 76 (12): 1675–1683.

# Utilization of debate as an educational tool for dental students to learn health economics

Saad A Khan, Hanan Omar, Muneer Gohar Babar, Chooi G Toh.

School of Dentistry, International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

Health economics, a special branch of science applying economic principles to the health delivery system, is a relatively young subdiscipline. The literature is scanty about teaching health economics in the medical and dental fields. Delivery methods of this topic vary from one university to another, with lectures, seminars, and independent learning reported as teaching/learning tools used for the topic. Ideally, debates should foster the development of logical reasoning and communication skills. Health economics in dentistry is taught under the community oral health module that constitutes part of an outcome-based dental curriculum in a private dental school in Kuala Lumpur, Malaysia. For this study, the students were divided into two groups: active participants (active debaters) and supporting participants (nonactive debaters). The debate style chosen for this activity was parliamentary style. Active and nonactive debaters' perceptions were evaluated before and after the activity through a structured questionnaire using a five-point rating scale addressing the topic and perceptions about debate as an educational tool. Cronbach's alpha coefficient was used as a measure of internal consistency for the questionnaire items. Among a total of eighty-two third-year dental students of two successive cohorts (thirty-eight students and forty-four students), seventy-three completed the questionnaire, yielding a response rate of 89 percent. Students' responses to the questionnaire were analyzed with the Kruskal-Wallis analysis of variance test. Results revealed that the students felt that their interest in debate, knowledge of the topic, and reinforcement of the previous knowledge had improved following participation in the debate. Within the limitations of this study, it can be concluded that debate was a useful tool in teaching health economics to dental students.

**Keywords**: health economics, debate, dentistry, community oral health, Malaysia.

Khor GL, Misra S. Micronutrient interventions on cognitive performance of children aged 5-15 years in developing countries. *Asia Pacific Journal of Clinical Nutrition*, 2012; 21(4): 476-486.

# Micronutrient interventions on cognitive performance of children aged 5-15 years in developing countries

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#### **Abstract**

It is estimated that more than 200 million young children worldwide fail to reach their potential in cognitive development owing to undernutrition. Numerous studies have assessed the effects of micronutrient supplementation on growth and cognitive development in infants, toddlers and preschoolers. However, micronutrient interventions on the cognitive performance of older children are limited. This article seeks to provide an update on micronutrient interventions and cognitive outcomes among children aged 5-15 years in developing countries. A total of 13 randomized controlled trials published since 2000 were identified. Majority of these studies assessed the effects of micronutrient-fortified foods on various domains of cognitive function. Among key micronutrients assessed were iron, zinc, iodine and vitamin A. This review found a lack of consistency in the impact of micronutrient supplementation on intelligence, long term mental functions and school examination grades of the children. A beneficial effect of micronutrient supplementation on short term memory was more consistently reported. Overall, the evidence from this review for the impact of micronutrients on cognitive performance in older children remains equivocal. In light of the growing interest on the influence of nutrition on cognition, it is important that culturallyappropriate and sufficiently sensitive assessment tools be used for measuring the desired cognitive outcomes that are most likely to be affected by the nutrients under study.

**Keywords**: micronutrients, cognitive performance, children aged 5-15 years.

Kim KS, Sinniah D, Kee TK. Neonatal rash: A case study. *Australian Family Physician*, 2012; 41(9): 707-709.

## Neonatal rash: A case study

Kwa Siew Kim<sup>1</sup>, Davendralingam Sinniah<sup>2</sup>, Tan Kah Kee<sup>3</sup>.

### **Abstract**

Case study: An infant, aged 48 days, is brought in by her mother to her doctor because of a rash that started during the neonatal period.

**Keywords**: infant, bites and stings, toxicology, skin diseases, infections.

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Koh KC, Slavin MA, Thursky KA, Lau E, Hicks RJ, Drummond E, Wong PS, Worth LJ. Impact of fluorine-18 fluorodeoxyglucose positron emission tomography on diagnosis and antimicrobial utilization in high-risk patients with febrile neutropenia. *Leukemia and Lymphoma*, 2012; (in press).

# Impact of fluorine-18 fluorodeoxyglucose positron emission tomography on diagnosis and antimicrobial utilization in high-risk patients with febrile neutropenia

Kwee Choy Koh<sup>1</sup>, Monica A Slavin<sup>2</sup>, Karin A Thursky<sup>2</sup>, Eddie Lau<sup>3</sup>, Rodney J Hicks<sup>3</sup>, Elizabeth Drummond<sup>3</sup>, Peng Shyan Wong<sup>4</sup>, Leon J Worth<sup>2</sup>

### **Abstract**

Early and targeted antimicrobial therapy improves outcomes in patients with febrile neutropenia (FN). We evaluated the impact of fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) on antimicrobial utilization in the management of FN. A cohort of patients with FN and hematological malignancy was identified. Cases (in whom FDG-PET was performed, n = 37) were compared with controls (in whom conventional investigations excluding FDG-PET were performed, n = 76). An underlying cause for FN was determined in 94.6% of cases, compared to 69.7% of controls. FDG-PET had a significant impact on antimicrobial utilization compared to conventional imaging (35.1% vs. 11.8%; p = 0.003), and was associated with shorter duration of liposomal amphotericin-B therapy for systemic fungal infection (median 4.0 days cases vs. 10.0 days controls; p = 0.001). Cases had a longer length of hospitalization (p = 0.016). In the management of patients with high-risk FN, FDG-PET improves diagnostic yield and allows rationalization of antifungal therapy. The impact upon healthcare costs associated with antimicrobial therapy for FN requires further evaluation.

**Keywords:** FDG-PET, febrile neutropenia, hematological malignancy, infection.

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Krishnan K, Mitra NK, Yee LS, Yang HM. A comparison of neurotoxicity in cerebellum produced by dermal application of chlorpyrifos in young and adult mice. *Journal of Neural Transmission*, 2012; 119(3): 345-52.

# A comparison of neurotoxicity in cerebellum produced by dermal application of chlorpyrifos in young and adult mice

K Krishnan<sup>1</sup>, LS Yee<sup>1</sup>, HM Yang<sup>1</sup>, NK Mitra<sup>2</sup>.

#### **Abstract**

Chlorpyrifos (CPF), an organophosphate pesticide inhibits acetylcholinesterase (AChE) and causes neuromuscular incoordination among children and elderly. The objectives of the present study were to compare the neurotoxic effects of dermal application of CPF on the cerebellum in the parameters of glial fibrillary acidic protein (GFAP) expression in young and adult mice and to correlate with the changes in acetylcholinesterase levels. Male Balb/c mice, 150 days old (adult) and 18 days old (young) were dermally applied with ½ LD(50) of CPF over the tails for 14 days. Serum AChE concentration was estimated and GFAP immunostaining was performed on sagittal paraffin sections through the vermis of cerebellum. Although reduced in both age-groups exposed to CPF, percentage of reduction in serum AChE was more in adult compared to the young. Under GFAP immunostaining, brown colour fibres and glial cells were observed in cerebellar cortex and medulla in both the experimental groups. The mean GFAP-positive glial cell count in cerebellar medulla per mm(2) of section was significantly (p < 0.05) increased in adult mice exposed to CPF when compared with age-matched control. In conclusion, this study confirmed that dermal exposure of CPF was able to exert neurotoxic effect in both young and adult mice. However, the quantitative results revealed that adult mice showed more GFAP expression in cerebellum when compared with the young, when exposed to CPF.

Keywords: Chlorpyrifos, Dermal toxicity, Cerebellum, GFAP.

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Krishnappa P, Ramakrishnappa S, Kulkarni MH, Giriyan S. Follicular carcinoma of the thyroid presenting as distant metastases: A case report and review of the literature. *The Internet Journal of Laboratory Medicine*, 2012; 5(1): DOI: 10.5580/2b25.

# Follicular carcinoma of the thyroid presenting as distant metastases: A case report and review of the literature

Purushotham Krishnappa<sup>1</sup>, Sowmya Ramakrishnappa<sup>2</sup>, Mohan H Kulkarni<sup>3</sup>, Sujatha Giriyan<sup>3</sup>.

### **Abstract**

### Context:

Follicular carcinoma of the thyroid presenting as a distant metastases is rare.

### Case Report:

We present a rare case of a 42 year old patient with follicular carcinoma of the thyroid who presented with pathological fracture of the tibia at the time of diagnosis. The cytological samples from the fracture site showed follicular neoplasm. Histopathological study of the resected thyroid specimen showed a tumor with capsule and vascular invasion.

### Conclusions:

The present case emphasizes that it is unusual for this neoplasm to initially present as distant metastases, although metastases in the late stages of the disease is more common presentation. Thyroid follicular carcinoma should be included in the differential diagnosis in cases of extrinsic tumoral lesions.

**Keywords:** follicular carcinoma, fracture, metastases, thyroid, tibia.

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Kwa SK, Sivalingam N. Issues in emergency contraception for the adolescent. *Malaysian Family Physician*, 2012; 7(1): 37-40.

## Issues in emergency contraception for the adolescent

Kwa Siew Kim, Sivalingam Nalliah.

Department of Family Medicine, International Medical University Clinical School, Jalan Rasah, 70300 Seremban, Negeri Sembilan, Malaysia

### **Abstract**

Maria, a 17-year-old single nulliparous college student, presents at the general practitioner (GP) clinic with this request: "Doctor, I did 'something' with my boyfriend. Can you give me some medication? I don't want to become pregnant?"

Lai NM, Teng CL, Nalliah S. Assessing undergraduate competence in evidence-based medicine: A preliminary study on the correlation between two objective instruments. *Education for Health*, 2012; 25(1): 33-39.

# Assessing undergraduate competence in evidence-based medicine: A preliminary study on the correlation between two objective instruments

NM Lai<sup>1</sup>, CL Teng<sup>2</sup>, S Nalliah<sup>3</sup>

### **Abstract**

### Context:

The Fresno test and the Berlin Questionnaire are two validated instruments for objectively assessing competence in evidence-based medicine (EBM). Although both instruments purport to assess a comprehensive range of EBM knowledge, they differ in their formats. We undertook a preliminary study using the adapted version of the two instruments to assess their correlations when administered to medical students. The adaptations were made mainly to simplify the presentation for our undergraduate students while preserving the contents that were assessed.

### Methods:

We recruited final-year students from a Malaysian medical school from September 2006 to August 2007. The students received a structured EBM training program within their curriculum. They took the two instruments concurrently, midway through their final six months of training. We determined the correlations using either the Pearson's or Spearman's correlation depending on the data distribution.

### Results:

Of the 120 students invited, 72 (60.0%) participated in the study. The adapted Fresno test and the Berlin Questionnaire had a Cronbach's alfa of 0.66 and 0.70, respectively. Inter-rater correlation (r) of the adapted Fresno test was 0.9. The students scored 45.4% on average [standard deviation (SD) 10.1] on the Fresno test and 44.7% (SD 14.9) on the Berlin Questionnaire (P = 0.7). The overall correlation between the two instruments was poor (r = 0.2, 95% confidence interval: -0.07 to 0.42, P = 0.08), and correlations remained poor between items assessing the same EBM domains (r = 0.01-0.2, P = 0.07-0.9).

#### Discussion:

The adapted versions of the Fresno test and the Berlin Questionnaire correlated poorly when administered to medical students. The two instruments may not be used interchangeably to assess undergraduate competence in EBM.

**Keywords:** Assessment, evidence-based medicine, medical education

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Leong CO, Chen SC, Tiong YL, Loh VF, Ng CH, Chye SM. 4-Chloro-1,2-phenylenediamine induces apoptosis in Mardin–Darby canine kidney cells via activation of caspases. *Environmental Toxicology*, 2012; (in press).

# 4-Chloro-1,2-phenylenediamine induces apoptosis in Mardin-Darby canine kidney cells via activation of caspases

Leong Chee Onn, Chen Ssu Ching, Tiong Yee Lian, Loh Veng Foon, Ng Chew Hee, Chye Soi Moi.

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### Abstract

4-Chloro-1,2-phenylenediamine (4-Cl-o-PD) is a halogenated aromatic diamine that was used as a precursor for manufacturing permanent hair dyes. Despite its well-documented mutagenic and carcinogenic effects in a number of in vitro and in vivo models, its cytotoxicity and mode of action have not received similar attention. Here, we investigated the effect of 4-Cl-o-PD on Mardin-Darby canine kidney cells. It induced apoptosis and the evidence suggests its initiation by reactive oxygen species (ROS). The results of various assays used show a dose-dependent (i) decrease in cell viability, (ii) increase in cells at sub-G1 phase and the G0/G1 phase arrested in cell cycle, (iii) increase in intracellular ROS accompanied by depletion of glutathione, and (iv) that apoptotic cell death probably involves activation of both intrinsic and extrinsic pathways.

**Keywords:** 4-chloro-1,2-phenylenediamine, Mardin-Darby canine kidney cells, apoptosis, caspase, reactive oxygen species.

Li YT, Chua MJ, Kunnath AP, Chowdhury EH. Reversing multidrug resistance in breast cancer cells by silencing ABC transporter genes with nanoparticle facilitated delivery of target siRNAs. *International Journal of Nanomedicine*, 2012; 7: 2473-2481.

# Reversing multidrug resistance in breast cancer cells by silencing ABC transporter genes with nanoparticle facilitated delivery of target siRNAs

Yong Tsuey Li<sup>1</sup>, Ming Jang Chua<sup>1</sup>, Anil Philip Kunnath<sup>1</sup>, Ezharul Hoque Chowdhury<sup>1,2</sup>.

### **Abstract**

### Background:

Multidrug resistance, a major impediment to successful cancer chemotherapy, is the result of overexpression of ATP-binding cassette (ABC) transporters extruding internalized drugs. Silencing of ABC transporter gene expression with small interfering RNA (siRNA) could be an attractive approach to overcome multidrug resistance of cancer, although delivery of siRNA remains a major hurdle to fully exploit the potential of siRNA-based therapeutics. Recently, we have developed pH-sensitive carbonate apatite nanoparticles to efficiently carry and transport siRNA across the cell membrane, enabling knockdown of the cyclin B1 gene and consequential induction of apoptosis in synergy with anti-cancer drugs.

#### Methods and results:

We report that carbonate apatite-mediated delivery of the siRNAs targeting *ABCG2* and *ABCB1* gene transcripts in human breast cancer cells which constitutively express both of the transporter genes dose-dependently enhanced chemosensitivity to doxorubicin, paclitaxel and cisplatin, the traditionally used chemotherapeutic agents. Moreover, codelivery of two specific siRNAs targeting *ABCB1* and *ABCG2* transcripts resulted in a more robust increase of chemosensitivity in the cancer cells, indicating the reversal of ABC transporter-mediated multidrug resistance.

### Conclusion:

The delivery concept of multiple siRNAs against *ABC* transporter genes is highly promising for preclinical and clinical investigation in reversing the multidrug resistance phenotype of breast cancer.

**Keywords:** carbonate apatite, siRNA, gene expression, transfection, breast cancer, ABC transporter, multidrug resistance, chemosensitivity.

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<sup>&</sup>lt;sup>2</sup> Jeffrey Cheah School of Medicine and Health Sciences, Faculty of Medicine, Nursing and Health Sciences, Monash University, Kuala Lumpur, Malaysia

Liew SC, Das-Gupta E, Wong SF, Lee N, Safdar N, Jamil A. Association of methylentetraydrofolate reductase (MTHFR) 677 C > T gene polymorphism and homocysteine levels in psoriasis vulgaris patients from Malaysia: A case-control study. *Nutrition Journal*, 2012; 11:1.

# Association of methylentetraydrofolate reductase (MTHFR) 677 C > T gene polymorphism and homocysteine levels in psoriasis vulgaris patients from Malaysia: A case-control study

Siaw C Liew<sup>1</sup>, Esha Das-Gupta<sup>2</sup>, Shew F Wong<sup>1</sup>, Nagarajah Lee<sup>3</sup>, Najeeb Safdar<sup>4</sup>, Adawiyah Jamil<sup>5</sup>.

#### **Abstract**

### Background:

The methylenetetrahydrofolate reductase (MTHFR) enzyme catalyzes the reduction of 5, 10-methylenetetrahydrofolate to 5-methyltetrahydrofolate and methyl donors. The methyl donors are required for the conversion of homocysteine to methionine. Mutation of MTHFR 677 C > T disrupts its thermostability therefore leads to defective enzyme activities and dysregulation of homocysteine levels.

### Methods:

This case-control study (n = 367) was conducted to investigate the correlation of the MTHFR gene polymorphism [NM\_005957] and psoriasis vulgaris amongst the Malaysian population. Overnight fasting blood samples were collected from a subgroup of consented psoriasis vulgaris patients and matched controls (n = 84) for the quantification of homocysteine, vitamin  $B_{12}$  and folic acid levels.

#### Results:

There was no significant increase of the MTHFR 677 C > T mutation in patients with psoriasis vulgaris compared with controls ( $\chi^2 = 0.733$ , p = 0.392). No significant association between homocysteine levels and MTHFR gene polymorphism in cases and controls were observed (F = 0.91, df = 3, 80, p = 0.44). However, homocysteine levels in cases were negatively correlated with vitamin B<sub>12</sub> (r = -0.173) and folic acid (r = -0.345) levels. Vitamin B<sub>12</sub> and folic acid levels in cases were also negatively correlated (r = -0.164).

### Conclusions:

Our results indicate that there was no significant association between the MTHFR gene polymorphism and psoriasis vulgaris in the Malaysian population. There was no significant increase of the plasma homocysteine level in the psoriasis patients compared to the controls.

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Liew SC, Das-Gupta E, Chakravarthi S, Wong SF, Lee N, Safdar N, Jamil A. Differential expression of the angiogenesis growth factors in psoriasis vulgaris. *BMC Research Notes*, 2012; 5: 201.

# Differential expression of the angiogenesis growth factors in psoriasis vulgaris

Siaw-Cheok Liew<sup>1</sup>, Esha Das-Gupta<sup>2</sup>, Srikumar Chakravarthi<sup>1</sup>, Shew-Fung Wong<sup>1</sup>, Nagarajah Lee<sup>3</sup>, Najeeb Safdar<sup>4</sup>, Adawiyah Jamil<sup>5</sup>.

### **Abstract**

### Background:

Angiogenesis has been reported to be one of the contributory factors to the pathogenesis of psoriasis vulgaris. This study aims to compare the expression of different angiogenesis growth factors namely (1) the vascular endothelial growth factor (VEGF) subfamily: A, B, C, D and placenta growth factor (PIGF); (2) nerve growth factor (NGF) and (3) von Willebrand factor (vWFr) in the skins of patients with psoriasis vulgaris and non-psoriatic volunteers.

### Results:

Comparative immunohistochemistry study was performed on the paraffin-sectioned psoriatic and healthy skins with the abovementioned markers. VEGF-C (p = 0.016) and NGF (p = 0.027) were expressed intensely in the cases when compared with the controls. The NGF was the only marker that was solely expressed in the cases and absent in all the controls.

### Conclusion:

The NGF (angiogenesis) and VEGF-C (lymphangiogenesis) might play a crucial role in the pathogenesis of psoriasis vulgaris and could be researched further as potential new targeted therapies for psoriasis vulgaris.

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Lim PH. Current trends, innovations and issues in nursing education to cater for the bottom billion nurses. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S69-S74.

# Current trends, innovations and issues in nursing education to cater for the bottom billion nurses

Pek-Hong Lim

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### **Abstract**

Nurse education is undergoing a process of transition. Nurses worldwide are working towards achievement of higher levels of education and training through an improved education system. Current trends and innovations in nursing education are emerging to prepare more nurses and to deliver education to students across geographical boundaries while taking into consideration their work and family responsibilities. The current trends and innovations in nursing education range from full time face-to-face interactions to distance education programmes. Teaching approaches such as blended learning, online or e-Learning have provided nurses with an avenue for continuing education for development and progression in their career pathways. Every nurse aspires to reach her highest potential. While the current trends and innovations in nursing education provides the flexibility for nurses to continue learning and upgrade their professional qualifications, there are issues to be considered in catering to the needs of the bottom billion nurses. An exploration of related issues will include views from different perspectives, such as that of the institution/provider, instructor/facilitator and student/learner involved in the development and implementation of the related education programmes.

Keywords: Trends, Innovations, Issues, Nursing Education, Nurses.

Lim VKE. The process of medical curriculum development in Malaysia. *International Journal of User-Driven Healthcare*, 2012; 2(1): 33-39.

### The process of medical curriculum development in Malaysia

VKE LIM

International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

The first medical school established in Malaysia was the Faculty of Medicine at the University of Malaya in 1963 (Danaraj, 1988). Today, there are 33 medical schools, both public and private. All medical schools require accreditation by the National Accreditation Board and the Malaysian Medical Council. These two regulatory bodies set the minimum standards for accreditation and they include standards that pertain to curricular issues. Apart from adhering to major broad principles, medical schools generally are given a free hand in designing and developing their own curricula. The faculty members of the school determine the nature of the curriculum with the dean playing a vital role in moderating competing demands from the various academic departments. The influence of the Medical Education Department or Unit varies. The Ministry of Health, as the predominant employer of doctors, gives regular feedback to the deans on the performance of their graduates. There has not been any major initiative to involve other important stakeholders, including the public, in the design and development of medical curricula in the country.

**Keywords**: Developing Countries, Malaysia, Medical Curriculum, Medical Education, Medical Schools.

Lim VKE. Antibiotic stewardship. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S75-S79.

## **Antibiotic stewardship**

Victor Lim

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### **Abstract**

The discovery of antibiotics had been one of the most significant events in the history of medicine. Antibiotics had saved countless number of lives and had contributed significantly to the health of mankind. The emergence of resistance is however a major threat to the continued usefulness of antibiotics. There are now strains of bacteria which are resistant to virtually all available antibiotics and these strains are increasingly being encountered in clinical practice. The development of new agents had not kept pace with resistance and it is unlikely that there will be major breakthroughs in the near future. The world needs to conserve and prolong the useful lives of the existing agents. This can only be achieved through good antibiotic stewardship programmes. As antibiotic resistance is a global threat all major stakeholders have to work together to meet this challenge.

**Keywords**: antibiotic, resistance, stewardship.

Loh YL, Das-Gupta E, Gun SC, Khajotia RR. Recurrent monoarthritis with tender erythematous nodules in a 28-year-old man: A diagnostic dilemma. *The Journal of Bioscience and Medicine*, 2012; 2: 1.

# Recurrent monoarthritis with tender erythematous nodules in a 28-year-old man: A diagnostic dilemma

Yet Lin Loh<sup>1</sup>, Esha Das Gupta<sup>1</sup>, Suk Chyn Gun<sup>1</sup>, Rumi R Khajotia<sup>1</sup>.

### **Abstract**

Cutaneous polyarteritis nodosa (CPAN) is a rare form of vasculitis that involves small and medium-sized arteries of the dermis and subcutaneous tissue. CPAN should be considered a separate disease entity and distinguished from systemic polyarteritis nodosa (PAN) as the clinical course and management of these conditions differ from each other. While PAN is a vasculitis of medium-sized muscular arteries involving the liver, kidneys, heart, lungs, gastrointestinal tract and musculoskeletal system, and is potentially life-threatening, cutaneous PAN is a localized cutaneous vascular disorder characterized by necrotizing arteritis of medium-sized vessels in the dermis and subcutaneous tissue which usually runs a chronic but benign course. Patients with CPAN usually present with fever, myalgias, arthralgias, neuralgias, and neuropathies, but are usually normotensive and lack life-threatening organ involvement. Moreover, arthritis and weight loss are seldom seen in CPAN, and have rarely been reported in the past in medical literature. We have reported here, a rare case of cutaneous polyarteritis nodosa (CPAN) which presented with vasculitic plaques and recurrent monoarthritis of the right knee joint, accompanied by significant weight loss.

**Keywords:** Recurrent monoarthritis, painful erythematous nodules, weight loss, polyarteritis nodosa, skin biopsy.

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Low SY, Tan BS, Choo HL, Tiong KH, Khoo AS, Leong CO. Suppression of BCL-2 synergizes cisplatin sensitivity in nasopharyngeal carcinoma cells. *Cancer Letter*, 2012; 314: 166-175.

# Suppression of BCL-2 synergizes cisplatin sensitivity in nasopharyngeal carcinoma cells

Soon Yang Low<sup>1</sup>, Boon Shing Tan<sup>1</sup>, Heng Lungh Choo<sup>2</sup>, Kai Hung Tiong<sup>2</sup>, Alan Soo-Beng Khoo<sup>3</sup>, Chee-Onn Leong<sup>1</sup>.

#### Abstract

The efficacy of cisplatin for treating nasopharyngeal carcinoma (NPC) is limited by the dose-related toxicities and the development of resistance to cisplatin. Recent studies have shown that B cell lymphoma-2 (BCL-2) is overexpressed and confers chemoresistance in NPC. Thus, targeted therapy against BCL-2 may enhance the antitumour effects of chemotherapy by sensitizing the tumor cells to undergo apoptosis. This study evaluated the combined effects of BCL-2 inhibition and cisplatin in NPC cells. Our results demonstrate that inhibition of BCL-2 by small-hairpin RNA (shRNA) or the BCL-2 inhibitor YC137, synergizes cisplatin sensitivity in NPC cells that overexpress BCL-2. We also show that YC137 enhance cisplatin-induced apoptosis in HK1 and CNE1 cells through suppression of BCL-2 protein expression, induction of mitochondrial depolarization and activation of caspase 9 and caspase 3/7. These findings suggest that the combination of BCL-2 inhibition and cisplatin represents a promising strategy for treating NPC.

**Keywords**: Nasopharyngeal carcinoma, BCL-2, Cisplatin, YC137, Combination therapy, Synergism.

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Low TH, Loke YH, Chiu CK. Minimally invasive retrieval of incarcerated flexible intramedullary reamer. *European Journal of Orthopedic Surgery and Traumatology*, 2012; (in press).

# Minimally invasive retrieval of incarcerated flexible intramedullary reamer

Tze Hau Low<sup>1</sup>, Yean Hwe Loke<sup>1</sup>, Chee Kidd Chiu<sup>1,2</sup>.

#### **Abstract**

Reaming is an integral step of long bone nailing and is associated with low complication rate. We report a case of a flexible reamer that was broken and incarcerated in the femoral canal during a femoral canal reaming. The reamer was used without a ball-tipped guide wire, and thus, the routine extraction using the guide wire was not possible. The incarcerated reamer was successfully extracted after medullary decompression with small drilling corticotomies adjacent to the reamer head. This case report serves as a reminder of the importance of using the ball-tipped guide wire with a flexible reamer. It also describes a simple and minimally invasive technique of removing an incarcerated flexible reamer.

**Keywords**: Corticotomy, Extraction, Femoral nail, Reamer, Incarcerated reamer.

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Lum SK, Goo ZQ, Jasiah Z, Low SW. Lessons learnt from 454 negative appendicectomies. *ANZ Journal of Surgery*, 2012; 82(Suppl. 1): 72.

### Lessons learnt from 454 negative appendicectomies

Siew Kheong Lum, Zhen Qiang Goo, Jasiah Zakaria, See Wei Low.

International Medical University, Seremban, Malaysia

#### Abstract

### Purpose:

To determine the characteristics of patients with negative appendicectomy in a medium resource hospital in Asia.

### Methodology:

This is a five-year, single center, retrospective study on 2,864 patients who underwent appendicectomy in Hospital Tuanku Jaafar, Seremban, Malaysia. Statistical analysis was done by SPSS ver.19.

#### Results:

Appendicitis is a disease of the young. 75% occurs between the age of 10–39 years. The negative appendicectomy rate was 15.8%. Although 62.8 % (285/454) of the negative appendicectomies occured in the age group 10–29 years, subgroup analysis showed there was little difference between all age groups. A diagnostic error was made in 6.8% (104/1525) of males and 26.1% (350/1339) of females. Of the misdiagnosis, the reason was gynaecological in origin in 33.9% (154/454), due to other surgical conditions in 3.1% (14/454), and not apparent in 63% (286/454).

#### Conclusion:

Negative appendicectomies occur mainly in females of all age groups and is not necessarily confined to those in the reproductive age group. The cause of abdominal pain in 2/3 of negative appendicectomies remains obscure.

Mahadeva S, Yasav H, Everett SM, Goh KL. Economic impact of dyspepsia in rural and urban Malaysia. *Journal of Neurogastroenterology and Motility*, 2012; 18(1): 43-57.

## **Economic impact of dyspepsia in rural and urban Malaysia**

Sanjiv Mahadeva<sup>1</sup>, Hematram Yadav<sup>2</sup>, Simon M Everett<sup>3</sup>, Khean-Lee Goh<sup>1</sup>

#### **Abstract**

### Background/Aims:

The economic impact of dyspepsia in regions with a diverse healthcare system remains uncertain. This study aimed to estimate the costs of dyspepsia in a rural and urban population in Malaysia.

#### Methods:

Economic evaluation was performed based on the cost-of-illness method. Resource utilization and quality of life data over a specific time frame, were collected to determine direct, indirect and intangible costs related to dyspepsia.

### Results:

The prevalences of dyspepsia in the rural (n = 2,000) and urban (n = 2,039) populations were 14.6% and 24.3% respectively. Differences in socioeconomic status and healthcare utilisation between both populations were considerable. The cost of dyspepsia per 1,000 population per year was estimated at USD14,816.10 and USD59,282.20 in the rural and urban populations respectively. The cost per quality adjusted life year for dyspepsia in rural and urban adults was USD16.30 and USD69.75, respectively.

### Conclusions:

The economic impact of dyspepsia is greater in an urban compared to a rural setting. Differences in socioeconomic status and healthcare utilisation between populations are thought to contribute to this difference.

**Keywords**: Asia, Dyspepsia, Health, Population, Quality-adjusted life years.

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Mak JW. Mentorship in the research setting. *International eJournal of Science, Medicine and Education (IeJSME)*, 2012; 6(1): 11-14.

### Mentorship in the research setting

Joon-Wah Mak

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### **Abstract**

The research mentorship programme is unique in that it is a planned journey undertaken by the mentor and mentee, preferably with well-defined milestones along the journey. During the journey, familiar landmarks will be pointed out by the mentor. In path-finding situations the experience and wisdom of the mentor and the critical appraisal of both mentor and mentee will contribute to learning from the encounter. In most mentor-mentee partnerships, a formal acceptance to the relationship, well-defined landmarks measuring progress in the journey, regular appraisal of the skills developed and acquired, and phased, judicious modification in the individual roles of that relationship will be required. Although there is no consensus on the elements of mentorship, there are some strategies which can contribute to the success of the relationship. Critical success factors include convergence of the research area within the broad expertise of the research mentor. The research mentor should have a proven research track record and is committed to serve in that official capacity. The research mentoring process is dynamic and characteristics of both mentor and mentee contribute to the robustness of that relationship. The mentee would have identified some attributes of the mentor that are desirable and is willing to work hard to achieve, build on, and improve upon. In the research setting endpoint measurements of success will be based on recognition of the research standing of the mentee, measurable outcomes such as number of papers in top tier journals, citation indices, etc. consultancies attracted as well as invitations to deliver plenaries in scientific conferences, patents filed and research findings translated and applied, and other measures of research productivity. In the pursuit of research excellence the mentee would have imbibed values of professionalism and ethics in research and would have constantly kept in mind that to be successful, the mentee would be able to excel beyond his mentor and that the next generation of researchers will seek mentorship from him.

**Keywords**: Research mentors, endpoint measurements, successful mentorship.

Mak JW. Pathology of lymphatic filariasis. *International eJournal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S80-S86.

### Pathology of lymphatic filariasis

Joon-Wah Mak

Vice-President (Research) and Dean, School of Postgraduate Studies & Research, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Developing and adult worms of the human lymphatic filarial parasites (Wuchereria bancrofti, Brugia malayi, and Brugia timori) are located mainly in the lymphatic system and occasionally in aberrant sites like subcutaneous and conjunctival cysts. Lymphatic pathology ranging from dilatation of lymphatic channels and lymphangiectasia are detected on ultrasonography in apparently healthy, amicrofilaraemic, but filarial antigen positive individuals in endemic areas. Microfilariae are distributed in various organs and may be associated with immune mediated pathology at these sites; tropical pulmonary eosinophilia is characterized by intense immune mediated destruction of microfilariae in the lung parenchyma. In the spleen and other sites, nodular granulomatous lesions can occur where microfilariae are trapped and destroyed. The finding of Wolbachia endosymbionts in all stages of lymphatic filarial parasites has provided new insight on the adverse reactions associated anti-filarial chemotherapy. Inflammatory lipopolysaccharide (LPS)-like molecules released from endosymbionts on death of the parasites are largely responsible for the adverse reactions encountered during anti-filarial chemotherapy. Prenatal tolerance or sensitization to parasite derived molecules can immune-modulate and contribute to both pathology and susceptibility/resistance to infection. Pathological responses thus depend not only on exposure to filarial antigens/infection, but also on host-parasiteendosymbiont factors and to intervention with antifilarial treatment. Treatment induced or host mediated death of parasites are associated with various grades of inflammatory response, in which eosinophils and LPS from endosymbionts play prominent roles, leading to death of the parasite, granulomatous formation, organization and fibrosis.

The non-human primate (*Presbytis* spp.) model of *Brugia malayi* developed for the tertiary screening of anti-filarial compounds has provided unique opportunities for the longitudinal study of the pathology associated with lymphatic filariasis. The pathology in this non-human primate model closely follows that seen in human lymphatic filarial infections and correlates with clinical evidence of lymphatic pathology as detected with ultrasonography. These studies also show that successful treatment as detected by loss of motility and calcification of worms on ultrasonography is associated with reversal of early dilatations of lymphatic channels.

**Keywords**: lymphatic filariasis, pathology, immunopathology, *Brugia*, *Wuchereria*.

Meka SV, Nali SR, Songa AS, Kolapalli VRM. Characterization and in vitro drug release studies of a natural polysaccharide *Terminalia catappa* Gum (Badam Gum). *AAPS PharmSciTech*, 2012: doi: 10.1208/s12249-012-9873-5.

# Characterization and in vitro drug release studies of a natural polysaccharide *Terminalia catappa* Gum (Badam Gum)

Venkata Srikanth Meka<sup>1,3</sup>, Sreenivasa Rao Nali<sup>2</sup>, Ambedkar Sunil Songa<sup>2</sup>, Venkata Ramana Murthy Kolapalli<sup>2</sup>.

### Abstract

The main objective of the present study is the physicochemical characterization of naturally available *Terminalia catappa* gum (Badam gum [BG]) as a novel pharmaceutical excipient and its suitability in the development of gastroretentive floating drug delivery systems (GRFDDS) to retard the drug for 12 h when the dosage form is exposed to gastrointestinal fluids in the gastric environment. As BG was being explored for the first time for its pharmaceutical application, physicochemical, microbiological, rheological, and stability studies were carried out on this gum. In the present investigation, the physicochemical properties, such as micromeritic, rheological, melting point, moisture content, pH, swelling index, water absorption, and volatile acidity, were evaluated. The gum was characterized by scanning electron microscopy, differential scanning calorimetry (DSC), powder X-ray diffraction studies

(PXRD), and Fourier transform infrared spectroscopy (FTIR). Gastroretentive floating tablets of BG were prepared with the model drug propranolol HCl by direct compression methods. The prepared tablets were evaluated for all their physicochemical properties, in vitro buoyancy, in vitro drug release, and rate order kinetics. PBG 04 was selected as an optimized formulation based on its 12-h drug release and good buoyancy characteristics. The optimized formulation was characterized with FTIR, DSC, and PXRD studies, and no interaction between the drug and BG was found. Thus, the study confirmed that BG might be used in the gastroretentive drug delivery system as a release-retarding polymer.

**Keywords**: badam gum, floating, gastroretentive, propranolol HCl, *Terminalia catappa*.

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Meka SV, Rao NS, Sunil SA, Ram BJ, Murthy KVR. Statistical optimization of a novel excipient (CMEC) based gastroretentive floating tablets of propranolol HCl and its in vivo buoyancy characterization in healthy human volunteers. *DARU Journal of Pharmaceutical Sciences*, 2012; 20: 21.

# Statistical optimization of a novel excipient (CMEC) based gastroretentive floating tablets of propranolol HCI and its in vivo buoyancy characterization in healthy human volunteers

Venkata Srikanth Meka<sup>1</sup>, Sreenivasa Rao Nali<sup>2</sup>, Ambedkar Sunil Songa<sup>2</sup>, Janaki Ram Battu<sup>2</sup>, Venkata Ramana Murthy Kolapalli<sup>2</sup>.

### **Abstract**

The objective of the present investigation is to formulate gastro retentive floating drug delivery systems (GRFDDS) of propranolol HCl by central composite design and to study the effect of formulation variables on floating lag time, D1hr (% drug release at 1 hr) and t90 (time required to release 90% of the drug). 3 factor central composite design was employed for the development of GRFDDS containing novel semi synthetic polymer carboxymethyl ethyl cellulose (CMEC) as a release retarding polymer. CMEC, sodium bicarbonate and Povidone concentrations were included as independent variables. The tablets were prepared by direct compression method and were evaluated for in vitro buoyancy and dissolution studies. From the polynomial model fitting statistical analysis, it was confirmed that the response floating lag time and D1hr is suggested to quadratic model and t90 is suggested to linear model. All the statistical formulations followed first order rate kinetics with non-Fickian diffusion mechanism.

The desirability function was used to optimize the response variables, each having a different target, and the observed responses were highly agreed with experimental values. Statistically optimized formulation was characterized by FTIR and DSC studies and found no interactions between drug and polymer. The results demonstrate the feasibility of the model in the development of GRFDDS containing a propranolol HCI. Statistically optimized formulation was evaluated for in vivo buoyancy studies in healthy humans for both fed and fasted states. From the results, it was concluded that gastric residence time of the floating tablets were enhanced at fed stage but not in fasted state.

**Keywords**: Propranolol HCl, Gastro retentive, Floating, Central composite, Carboxymethyl ethyl cellulose.

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Meka SV, Sunil SA, Rao NS, Ram BJ, Latha K, Murthy KVR. Thermal sintering: A novel technique in the design of gastroretentive floating tablets of propranolol HCl and its evaluation. *Investigación Clínica*, 2012; 53(3): 7–20.

# Thermal sintering: A novel technique in the design of gastroretentive floating tablets of propranolol HCl and its evaluation

Venkata Srikanth Meka<sup>1</sup>, Ambedkar Sunil Songa<sup>2</sup>, Sreenivasa Rao Nali<sup>2</sup>, Janaki Ram Battu<sup>2</sup>, Latha Kukati<sup>3</sup>, Venkata Ramana Murthy Kolapalli<sup>2</sup>.

### **Abstract**

The aim of the present investigation was to formulate thermally sintered floating tablets of propranolol HCl, and to study the effect of sintering conditions on drug release, as well as their in vitro buoyancy properties. A hydrophilic polymer, polyethylene oxide, was selected as a sintered polymer to retard the drug release. The formulations were prepared by a direct compression method and were evaluated by in vitro dissolution studies. The results showed that sintering temperature and time of exposure greatly influenced the buoyancy, as well as the dissolution properties. As the sintering temperature and time of exposure increased, floating lag time was found to be decreased, total floating time was increased and drug release was retarded. An optimized sintered formulation (sintering temperature 50°C and time of exposure 4 h) was selected, based on their drug retarding properties. The optimized formulation was characterized with FTIR and DSC studies and no interaction was found between the drug and the polymer used.

**Keywords**: gastroretentive, thermal sintering, propranolol HCl, polyethylene oxide.

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Nayanatara AK, Tripathi Y, Nagaraja HS, Jeganathan PS, Ramaswamy C, Ganaraja B, Sheila RP, Kamath A. Effect of chronic immobilization stress on some selected physiological, biochemical and lipid parameters in Wistar Albino rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 2012; 3(1): 34-42.

# Effect of chronic immobilization stress on some selected physiological, biochemical and lipid parameters in Wistar Albino rats

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- <sup>2</sup> Department of Human Biology, International Medical University, Malaysia 3 Department of Physiology, KS Hegde Medical College, Mangalore

### Abstract

### Objective:

Exposure to stressful situations is among the most common human experiences. Chronic stress exposure has detrimental effect on several cell functions. In this study, we investigated the changes in selected biochemical and lipid parameters following exposure to chronic unpredictable stressors for 10 days.

### Methods:

Wistar strain adult albino rats were divided into two group as non stressed group (n = 8) and stressed group (n = 8). The stressed groups were exposed to 10 days of chronic unpredictable stress (CUS). At the end of the 10th day the animals were anaesthetized and blood samples were collected through cardiac puncture. The blood samples of both the groups were analyzed for selected biochemical and lipid parameters. The results were analyzed statistically by using student's t test. P<0.05 was considered as significant.

### Results:

All the biochemical (serum glutamic oxaloacetic transaminase (SGOT) serum glutamic pyruvic transaminase (SGPT), blood sugar, tissue malondialdehyde (MDA) and serum lipid profile (cholesterol, serum triglyceride (TG), low-density lipoproteins (LDL) were significantly increased in the stressed group when compared to the non stressed group. The serum high-density lipoproteins (HDL) level did not show any statistically significant changes. The weight of the adrenal gland also showed a significant increase in the stressed group.

### Conclusion:

The present data indicate that cumulative effect of repeated chronic unpredictable stressors on a daily basis for a period of 10 days increases the biochemical and lipid parameters.

**Keywords**: chronic unpredictable stressors, serum glutamic oxalo acetic transaminase, serum glutamic pyruvic transaminase, blood sugar, tissue malondialdehyde, serum lipid profile.

# INTERNATIONAL MEDICAL UNIVERSITY (IMU)

Ng TKW, Low CX, Kong JP, Cho YL. Use of red palm oil in local snacks can increase intake of provitamin A carotenoids in young aborigine children: A Malaysian experience. *Malaysian Journal of Nutrition*, 2012; 18(3): 1-5.

# Use of red palm oil in local snacks can increase intake of provitamin A carotenoids in young aborigine children: A Malaysian experience

Ng TKW, Low CX, Kong JP, Cho YL.

Department of Nutrition and Dietetics, International Medical University, 57000 Kuala Lumpur, Malaysia

#### **Abstract**

### Introduction:

Carotenoid-rich red palm oil (RPO)-based snacks have been provided to children in impoverished communities to improve their vitamin A status. The non-availability of information on the acceptability of RPO-based snacks by Malaysian aborigines (Orang Asli) children forms the basis of this study.

#### Methods:

Twenty-one Orang Asli children, majority of whom had normal body mass index for age (BMI-for-age) and aged  $4.73 \pm 0.92$  years in Sungai Tekir, Negeri Sembilan were provided with three freshly-prepared snacks (springroll, curry puff or doughnut) each containing one teaspoon or 5 ml of RPO per serving, on separate mornings. On the fourth morning, one serving each of all 3 different snacks was provided together on a plate to every child for consumption and preference for the snacks recorded. The children's habitual vitamin A intakes were assessed by a semi-quantitative food frequency questionnaire (FFQ) and carotenoid retention tests for the prepared snacks were performed by column chromatography.

### Results:

Fifty-four percent of the children did not meet their RNI for vitamin A. Based on acceptance criterion of consuming at least one-half serving of the snacks provided, springroll and curry puff recorded 100% acceptability while doughnut had 82% acceptability. Preference of snack was in the order, springroll (47%)> doughtnut (35%)> curry puff (18%), but a Ztest test for proportions showed no statistical significance. Carotenoid retention tests showed great variation between snacks namely, doughnut (100%) >springroll (84%)>curry puff (45%).

Conclusion: The overall findings indicate that the RPO-based snacks are highly acceptable and can be used to improve the dietary intake of provitamin A carotenoids of Malaysian Orang Asli children.

**Keywords**: Red palm oil snacks, carotenoids, acceptability, Orang Asli children.

Ng TKW, Nalliah S, Azlinda Hamid, Wong SR, Chee SL, Augustine CA. Omega-6 and omega-3 fatty acid nutrition amongst Malaysians are far from desirable. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(2): 4-9.

### Omega-6 and omega-3 fatty acid nutrition amongst Malaysians are far from desirable

Tony Kock Wai Ng<sup>1</sup>, Sivalingam Nalliah<sup>2</sup>, Azlinda Hamid<sup>3</sup>, Siew Rong Wong<sup>1</sup>, Sim Ling Chee<sup>1</sup>, Cheryl Andrea Augustine<sup>1</sup>.

### **Abstract**

This paper reviews available reports on the omega-6 (linoleic acid, LA) and omega-3 fatty acid [alpha-linolenic acid (ALA) + eicosapentaenoic acid (EPA) + docosahexaenoic acid) intakes amongst Malaysians against Malaysian Recommended Nutrient Intakes (RNI), focussing particularly on pregnant and lactating women because of the availability of data for these latter vulnerable groups. Overall, the omega-6 and omega-3 fatty acid nutrition amongst Malaysians are poor and far from desirable. The nutritional situation regarding these long-chain polyunsaturated fatty acids (LCPUFA) amongst Malaysian pregnant and lactating women is alarming and warrants urgent attention in nutrition promotion activities/counselling. Daily consumption of LA by these women and other Malaysians studied ranged from 3.69 - 5.61 % kcal with 38-60% of individuals not meeting their RNIs. Daily intakes of omega-3 fatty acids faired worse, averaging 0.21- 0.33 % kcal with as high as 92% of subjects in one study not meeting their RNIs. The omega-6 to omega-3 fatty acid ratios obtained in the studies reviewed are about 20:1, which is way above the World Health Organisation-recommended ratio of 5-10:1. Dietary sources of these omega- fatty acids in the subjects studied are chicken, fish and milk. Since local foods are not particularly rich in LCPUFA such as EPA and DHA, the options to improve EPA/DHA nutrition amongst Malaysians are the greater consumption of omega-3 enriched foods and in the case of pregnant and lactating women, LCPUFA supplementation may warrant serious consideration.

**Keywords**: Omega-6 and omega-3 fatty acids, Malaysians intake.

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Nyunt Wai, Thing SW, Liing TN. Self-measured bed-time, arising and day blood pressures of normotensive young male and female adults. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2011; 5(1): 31-33. (published in 2012)

# Self-measured bed-time, arising and day blood pressures of normotensive young male and female adults

Nyunt Wai, Sze Wei Thing, Ting Ngiik Liing

Human Biology Division, School of Medical Sciences, International Medical University (IMU), Kuala Lumpur, Malaysia

### **Abstract**

Morning surge in blood pressure is an independent cardiovascular risk factor in the middle aged and the elderly. Whether such a surge occurs in young subjects is not known. Eighty normotensive subjects (age:  $21.8 \pm 1.3$  yr) measured their own blood pressure (BP) using an automatic device (Omron HEM-7080,) on going to bed and on waking up, for 2 consecutive days. In contrast to large morning BP surges reported for older age groups, there was much smaller but significant (P<0.002) rise only in the DBP ( $1.9 \pm 5$  mm Hg) on waking up on day 2 in young subjects. The duration of sleep and the time the subjects slept influence the sleep-wake BP change.

**Keywords**: bed-time vs. arising blood pressure, self-measured, normotensive, young adults.

Ong ST, Yip SP, Keng PS, Lee SL, Hung YT. Papaya (*Carica papaya*) seed as a low-cost sorbent for zinc removal. *African Journal of Agricultural Research*, 2012; 7(5): 810-819.

### Papaya (Carica papaya) seed as a low-cost sorbent for zinc removal

Siew-Teng Ong<sup>1</sup>, Shiau-Ping Yip<sup>1</sup>, Pei-Sin Keng<sup>2</sup>, Siew-Ling Lee<sup>3</sup>, Yung-Tse Hung<sup>4</sup>.

### **Abstract**

The potential of using papaya seed as a sorbent for the removal of Zn from aqueous solution was investigated. The sorption characteristics of the sorbent was studied under various experimental conditions, such as pH, contact time, concentration of Zn(II), agitation rate and sorbent's particle size. The equilibrium data have been studied using Langmuir, Freundlich and Brunauer-Emmett-Teller equations. The best correlation was obtained using Langmuir isotherm with the regression coefficient value of 0.9799 and maximum sorption capacity of 19.88 mg/g. The effective pH for the maximum uptake of Zn(II) was at pH 5.0. An increase in percentage uptake of Zn(II) can be observed with increasing contact time and agitation rate. Decrease in sorbent particle size led to an increase in the sorption of Zn(II) and this could be explained by an increase in surface area and hence binding site. Equilibrium was attained around 60 min indicating this sorbent could be a potential material for continuous flow system.

**Keywords**: Papaya seed, sorption, zinc, heavy metal removal, kinetics, modelling.

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Pan Y, Mak JW, Ong CE. Development and validation of HPLC methods for the determination of CYP2D6 and CYP3A4 Activities. *Current Pharmaceutical Analysis*, 2012; (in press).

### Development and validation of HPLC methods for the determination of CYP2D6 and CYP3A4 Activities

Yan Pan<sup>1</sup>, Joon Wah Mak<sup>1</sup>, Chin Eng Ong<sup>2</sup>.

### **Abstract**

Employment of in vitro experimentation to measure the effect of new chemical entities on human cytochrome P450 (CYP) marker activities represents a convenient approach in studying drug metabolism and pharmacokinetics. In this study, simple and accurate high performance liquid chromatograhic (HPLC) methods were developed and validated for quantitative analysis of CYP2D6-mediated dextromethorphan O-demethylation and CYP3A4-mediated testosterone 6β-hydroxylation. Both the assays showed a good linearity in the substrate concentration range of 0.05 – 20.0 μM and 0.01 – 100.0 μM with limit of detection (LOD) of 0.01 μM and 0.001 μM for CYP2D6 and CYP3A4, respectively. The intra-and inter-day precisions were from 7.21% to 12.22% and 3.09% to 14.60% for CYP2D6; and from 4.77% to 9.19% and 3.65% to 11.84% for CYP3A4. Assay accuracy for CYP2D6 ranged from 85.3% to 104.9% over dextrorphan concentrations of 0.05-5.0 μM; and that of CYP3A4 was 105.1% to 109.6% at hydroxytestosterone concentrations of 0.01-50 μM. Enzyme kinetic parameters obtained (Km and Vmax) using the two assays were within reported ranges. Thus, the assays were able to serve as activity markers in the assessment of pharmacokinetic drug interaction and metabolism mediated by CYP2D6 and CYP3A4.

**Keywords**: Cytochrome P450, CYP2D6, CYP3A4, HPLC, Validation.

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Pan Y, Tiong KH, Abd-Rashid BA, Ismail Z, Ismail R, Mak JW, Ong CE. Inhibitory effects of cytochrome P450 enzymes CYP2C8, CYP2C9, CYP2C19 and CYP3A4 by *Labisia pumila* extracts. *Journal of Ethnopharmacology*, 2012; 143(2): 586-591.

# Inhibitory effects of cytochrome P450 enzymes CYP2C8, CYP2C9, CYP2C19 and CYP3A4 by *Labisia pumila* extracts

Yan Pan<sup>1</sup>, Kai Hung Tiong<sup>1</sup>, Badrul Amini Abd-Rashid<sup>2</sup>, Zakiah Ismail<sup>2</sup>, Rusli Ismail<sup>3</sup>, Joon Wah Mak<sup>1</sup>, Chin Eng Ong<sup>4</sup>.

#### **Abstract**

Ethnopharmacological relevance:

Labisa pumila (LP), popularly known with its local name, *Kacip Fatimah*, is a well known herb grown in Indochina and Southeast Asia and is traditionally used to regain energy after giving birth in women. The propensity of LP to cause drug-herb interaction via cytochrome P450 (CYP) enzyme system has not been investigated.

### Aim of the study:

To evaluate the in vitro inhibitory effects of various LP extracts (aqueous, ethanol, dichloromethane (DCM) and hexane) on cytochrome P450 2C8 (CYP2C8), CYP2C9, CYP2C19 and CYP3A4 activities.

### Materials and methods:

Probe substrate-based high performance liquid chromatography (HPLC) methods were established for CYP2C9, CYP2C19 and CYP3A4 whereas a fluorescence-based enzyme assay was established for CYP2C8. The metabolite formations were examined after incubation of probe substrate with respective CYP isoform in the present or absent of LP extracts. The inhibitory effect of LP was characterized with kinetic parameters IC50 and Ki values.

### Results:

LP extracts showed differential effect of CYP activities with the order of inhibitory potency as follows: dichloromethane4hexane4ethanol4aqueous. This differential effect was only observed in CYP2C isoforms but not CYP3A4. Both the hexane and DCM extracts exhibited moderate to potent inhibition towards CYP2C activities in different modes including non-competitive, competive and mixed-type. The DCM effect was notably strong for CYP2C8 and CYP2C9 showing Ki values of below 1 mg/ml. The selectivity of LP for CYP2C isoforms rather than CYP3A4 may be attributed to the presence of relatively small, lipophilic yet slightly polar compounds within the LP extracts.

### Conclusions:

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The results of our study revealed that phytoconstituents contained in LP, particularly in hexane and dichloromethane extracts, were able to selectively inhibit CYP2C isoforms. The inactivation was characterized by low Ki values, in particular, in CYP2C8 and CYP2C9. These in vitro data indicate that LB preparations contain constituents that can potently inhibit CYP2C activities and suggest that this herb should be examined for potential pharmacokinetic drug interactions in vivo.

**Keywords**: *Lamisia pumila*, Herbal extracts, Cytochromes P450, CYP2C subfamily, Drugherb interactions.

Pang CY, Mak JW, Ismail R, Ong CE. In vitro modulatory effects of flavonoids on human cytochrome P450 2C8 (CYP2C8). *Naunyn Schmiedebergs Archives of Pharmacol*ogy, 2012; 385(5): 495-502.

# In vitro modulatory effects of flavonoids on human cytochrome P450 2C8 (CYP2C8)

Chia Yong Pang<sup>2</sup>, Joon Wah Mak<sup>2</sup>, Rusli Ismail<sup>3</sup>, Chin Eng Ong<sup>1</sup>.

### **Abstract**

The inhibitory effects of five flavonoids with distinct chemical classes (flavones [luteolin], flavonols [quercetin and quercitrin], and flavanones [hesperetin and hespiridin]) on cDNA-expressed CYP2C8 were investigated. CYP2C8 was co-expressed with NADPH-cytochrome P450 reductase in *Escherichia coli* and used to characterise potency and mechanism of these flavonoids on the isoform. Tolbutamide 4-methylhydroxylase, a high-performance liquid chromatography-based assay, was selected as marker activity for CYP2C8. Our results indicated that the flavonoids inhibited CYP2C8 with different potency. The order of inhibitory activities was quercetin > luteolin > hesperetin > hesperidin > quercitrin. All of these compounds however exhibited mechanism-based inhibition. A number of structural factors were found to be important for inhibition; these include the molecular shape (volume to surface ratio), the number of hydroxyl groups as well as glycosylation of the hydroxyl group. Quercetin was the most potent inhibitor among the flavonoids examined in this study, and our data suggest that it should be examined for potential pharmacokinetic drug interactions pertaining to CYP2C8 substrates in vivo.

**Keywords**: Cytochrome P450, CYP2C8, Flavonoids, In vitro inhibition

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Parolia A, Mohan M, Kundabala M, Shenoy R. Indian dental students' preferences regarding lecture courses. *Journal of Dental Education*, 2012; 76(3): 366-71.

### Indian dental students' preferences regarding lecture courses

Abhishek Parolia<sup>1</sup>, Mandakini Mohan<sup>1</sup>, M Kundabala<sup>2</sup>, Ramya Shenoy<sup>3</sup>.

### **Abstract**

Teaching and learning activities in the dental clinic or hospital are a challenging area for students as well as teachers. With various teaching methodologies being used in dental schools around the world, gaining greater understanding of students' attitudes toward these methodologies would be useful for dental educators. The objective of this study was to explore the preferences of dental students in India about various aspects of lecture courses. A structured survey consisting of ten closed-ended questions was developed, and 2,680 undergraduate students from forty-three dental schools in India were approached via e-mail with a follow-up postal mailing. Of these, 1,980 students responded, for a response rate of 73.8 percent. Most of the students reported preferring lectures with the aid of PowerPoint and chalkboard. They preferred morning lectures from 8 am to 10 am for a maximum of thirty to forty minutes for each lecture, and they preferred to receive information about the lecture topic in advance. The students said that delivery of clinical demonstrations was beneficial after the lectures, and they preferred learning-based rather than exam-oriented education. The respondents also said that attendance should be made compulsory and that numerical marking of examinations should not be replaced by a grading system.

**Keywords**: dental education, dental students, teaching methodologies, India.

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Pau A, Sabri BA. Relationship between emotional intelligence and job satisfaction in newly qualified Malaysian dentists. *Asia Pacific Journal of Public Health*, 2012; (in press).

### Relationship between emotional intelligence and job satisfaction in newly qualified Malaysian dentists

Allan Pau<sup>1</sup>, Budi Aslinie Sabri<sup>2</sup>

#### **Abstract**

Job satisfaction (JS) is considered to be a key factor in workforce retention. This article reports on the association between emotional intelligence (EI) and JS in newly qualified dentists employed in the Malaysian 3-year compulsory service. A postal questionnaire survey collected data on sociodemographic and occupational characteristics, EI, and JS. In a sample of 342 (58.9%) respondents, sociodemographic characteristics were not statistically significantly associated with both EI and JS total scores, whereas overseas graduates scored more highly on the EI scale compared with local graduates. Linear regression analysis indicated that EI was the only statistically significant predictor of JS. EI was statistically significantly associated with JS with patient relationships (r = 0.28; P = .001), peer support (r = 0.30; P = .001), professional development (r = 0.21; P = .001), quality of care (r = 0.57; P = .001), supporting staff (r = 0.24; P = .001), overall JS (r = 0.28; P = .001), and total JS score (r = 0.40; P = .001). However, EI was not statistically significantly associated with JS with income (r = 0.06; P = .302). These findings have implications for the development of interventions to enhance EI and JS in order to promote retention of dentists in the public sector.

**Keywords**: emotional intelligence, job satisfaction, professional competence, dentists, workforce, staff retention.

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Phua CS, Vejayan J, Ambu S, Ponnudurai G, Gorajana A. Anti-bacterial activities of L-amino acid oxidase purified from King Cobra (*Ophiophagus hannah*) venom. *Journal of Venomous Animals and Toxins including Tropical Diseases*, 2012; 18(2): 198-207.

# Anti-bacterial activities of L-amino acid oxidase purified from King Cobra (Ophiophagus hannah) venom

Phua CS<sup>1</sup>, Vejayan J<sup>2</sup>, Ambu S<sup>1</sup>, Ponnudurai G<sup>1</sup>, Gorajana A<sup>1</sup>.

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#### **Abstract**

Some constituents of snake venom have been found to display a variety of biological activities. The antibacterial property of snake venom, in particular, has gathered increasing scientific interest due to antibiotic resistance. In the present study, king cobra venom was strains of Staphylococcus aureus [including screened against three resistant Staphylococcus aureus (MRSA)], three other species of gram-positive bacteria and six gram-negative bacteria. King cobra venom was active against all the 12 bacteria tested. and was most effective against Staphylococcus spp. (S. aureus and S. epidermidis). Subsequently, an antibacterial protein from king cobra venom was purified by gel filtration, anion exchange and heparin chromatography. Mass spectrometry analysis confirmed that the protein was king cobra L-amino acid oxidase (Oh-LAAO). SDS-PAGE showed that the protein has an estimated molecular weight of 68 kDa and 70 kDa under reducing and nonreducing conditions, respectively. The minimum inhibitory concentrations (MIC) of Oh-LAAO for all the 12 bacteria were obtained using radial diffusion assay method. Oh-LAAO had the lowest MIC value of 7.5 µg/mL against S. aureus ATCC 25923 and ATCC 29213, MRSA ATCC 43300, and S. epidermidis ATCC 12228. Therefore, the LAAO enzyme from king cobra venom may be useful as an antimicrobial agent.

**Keywords:** L-amino acid oxidase, king cobra, antibacterial activity, *Ophiophagus hannah*.

Poh YW, Gan SY, Tan EL. Effects of II-6, II-10 and Tgf-B on the expression of survivin and apoptosis in nasopharyngeal carcinoma TwO1 cells. *Experimental Oncology (Online)*, 2012; 34(2): 85-89.

# Effects of II-6, II-10 and Tgf-B on the expression of survivin and apoptosis in nasopharyngeal carcinoma TwO1 cells

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#### **Abstract**

The aim of this study is to investigate whether IL-6, IL-10 and TGF-β are able to confer resistance to apoptosis in nasopharyngeal carcinoma cells by upregulating the expression of survivin.

### Methods:

The human nasopharyngeal carcinoma cell line TW01 (WHO NPC Type I) was cultured in DMEM-F12 Ham medium containing 10% FBS in a humidified atmosphere of 5% CO2 and 37°C and treated with different concentrations of IL-6, IL-10 and TGF-β. Survivin mRNA expression was measured by real-time quantitative PCR and Western blot. Apoptosis was determined based on the assay for caspase-3 activity.

### Results:

Of all the cytokines tested, only TGF- $\beta$  (10 pg/mL) induced the over-expression of survivin at a significant level and this correlated with resistance to apoptosis (p  $\leq$  0.05). To confirm if survivin is responsible for resistance to apoptosis, YM155 which is a survivin inhibitor was used and the results showed that YM155 abrogated the protective effect of TGF- $\beta$ . Interestingly, IL-10 did not significantly alter the expression of survivin.

### Conclusions:

We conclude that TGF- $\beta$  up-regulates the expression of survivin leading to the resistance to apoptosis in NPC TW01 cells.

**Keywords:** apoptosis, interleukin 6, interleukin 10, nasopharyngeal carcinoma, survivin, transforming growth factor  $\beta$  (TGF- $\beta$ ).

Ponnampalam SN, Tan WYJ, Wazir NN, George J. Unusual cause of neuropathy: Extensive dural spread of primary cervical osteosarcoma. *Acta Radiologica Short Reports*, 2012; (in press).

### Unusual cause of neuropathy: Extensive dural spread of primary cervical osteosarcoma

Stephen N Ponnampalam<sup>1,2</sup>, Wilkinson YJ Tan<sup>3</sup>, Nayyer Naveed Wazir<sup>3</sup>, John George<sup>4</sup>

### **Abstract**

We report a very rare case of a high grade osteosarcoma of the cervical spine in a 62-yearold woman. She presented with a relatively short history of a swelling in the posterior neck and cervical lymphadenopathy. This was associated with hoarseness of the voice, significant weight loss, and right upper arm radicular symptoms initially, progressing to paraplegia. Based on MR and CT imaging of the neck and an excision biopsy of an enlarged right supraclavicular lymph node, the histology revealed a high grade primary osteosarcoma of the cervical spine.

Keywords: Osteosarcoma, metastasis, paraplegia.

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<sup>&</sup>lt;sup>4</sup> Department of Biomedical Imaging, University of Malaya Medical Center, Kuala Lumpur, Malaysia

Poovaneswaran P, Yeo SY, Gwee ZL, Wong ZH, Tan HH. AOS15 Assessment of cognitive function in patients with breast and colon cancers undergoing chemotherapy: Results from an exploratory pilot study. *European Journal of Cancer*, 2012; 48(Suppl. 4): S9.

# AOS15 Assessment of cognitive function in patients with breast and colon cancers undergoing chemotherapy: Results from an exploratory pilot study

S Poovaneswaran, SY Yeo, ZL Gwee, ZH Wong, HH Tan.

International Medical University, Negeri Sembilan, Malaysia

### Abstract

### Background:

Memory loss after chemotherapy is one of the most commonly reported post-treatment symptoms by patients with cancer. This deterioration in cognitive function, commonly referred to as chemobrain or chemofog, was largely unacknowledged by the medical community until in recent years. An exploratory pilot study was undertaken in Tuanku Jaafar Hospital, Negeri Sembilan, Malaysia. The aim in the study was to assess the effect of chemotherapy on cognitive function of patients with breast and colon cancers.

### Methods:

Ten patients with cancer (6 patients with breast cancer patients and 4 with colorectal cancer) who were receiving adjuvant chemotherapy (anthracycline and/or 5-fluorouracil) were assessed using the Montreal Cognitive Assessment (MoCA) and the Mini Mental State Examination (MMSE) before the first cycle of chemotherapy and again after the third cycle.

### Findings:

There were mean reductions of 6.1% in MoCA and 5.3% in MMSE; no difference was noted between patients with breast and those with colorectal cancer.

### Interpretation:

The reductions in both the tests suggest that chemotherapy does have an impact on cognitive function, although it must be noted that the sample size was small. Based on the results of this exploratory pilot study, we aim to do a further larger scale, longer study to assess cognitive function after chemotherapy.

Poovaneswaran S, Paleri V, Charlton F, Dobrowsky W, Kelly C. Cutaneous metastases from head and neck squamous cell carcinoma: Case report and literature review. *Medical Journal of Malaysia*, 2012; 67(4): 430-432.

# Cutaneous metastases from head and neck squamous cell carcinoma: Case report and literature review

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### **Abstract**

The presence of cutaneous metastases in squamous cell carcinomas of the head and neck (SCCHN) is rare and associated with a dismal prognosis. It is vital to distinguish these lesions from direct invasion of the skin by SCCHN or primary cutaneous malignancies as the prognosis is vastly different and so is the management. In this case report, we present four cases of cutaneous metastases and also briefly review the literature pertaining to this phenomenon.

Keywords: Cutaneous Metastases, Squamous Cell Carcinoma of Head and Neck.

Prabu SL, Suriyaprakash TNK, Dinesh KC, Suresh KC, Ragavendran T. Nutraceuticals: A review. *Elixir Pharmacy*, 2012; 46: 8372-8377.

### **Nutraceuticals: A review**

S. Lakshmana Prabu<sup>1</sup>, T.N.K. Suriya Prakash<sup>2</sup>, C. Dinesh Kumar<sup>3</sup>, S. SureshKumar<sup>1</sup>, T. Ragavendran<sup>1</sup>.

### **Abstract**

Consumers are deeply concerned about how their health care is managed, administered and priced. They are frustrated with the expensive, high-tech disease treatment approach predominantly in modern medicine. Positioned at the interface between food and drugs, a growing body of products is assuming importance; the consumer is now looking for complementary or alternative beneficial products and that's why nowadays they are using nutraceuticals. Increasingly, they are using natural dietary supplements and other forms of nutraceuticals as part of a tremendous surge to have physiological benefits or to provide protection against diseases. Functional foods and nutraceutical products represent a value added growth opportunity both domestically and internationally. Development of better characterized and research proven products will help enhance consumer confidence in nutraceutical and functional food products in the world. This article briefly discusses about the basic information about the nutraceuticals and its importance.

**Keywords**: Nutraceuticals, Functional foods, Herbals, Nutrient, Dietary supplements.

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Prabu SL, Suriyaprakash TNK, Dinesh KC, Suresh KS. Nutraceuticals and their medicinal importance. *International Journal of Health and Allied Sciences*, 2012: 1(2): 47-53.

### Nutraceuticals and their medicinal importance

Sakthivel Lakshmana Prabu<sup>1</sup>, Timmakondu Narasimman Kuppusami Suriyaprakash<sup>2</sup>, Chellappan Dinesh Kumar<sup>3</sup>, Subramaniam Suresh Kumar<sup>1</sup>

#### **Abstract**

Lifestyles of human beings have changed drastically due to the industrial age, increasing work, living speed, longer work schedules, and various psychological pressures, which have led to an increased incidence of diabetes, obesity, various cancers and vascular diseases. With recent advances in medical and nutrition sciences, natural products and health-promoting foods have received extensive attention in the public. To achieve better quality of life, people started eating more vegetables, fruits, dietary supplements, nutraceuticals, phytotherapeutical substances and other plant foods. The demand for nutraceuticals and phytonutrients has increased over the past few years and they are being used by people for various therapeutic outcomes. This article brings out the importance of nutraceuticals and their usage in various diseases and ailments.

**Keywords:** Health benefits, nutraceuticals, nutrient, therapeutic activity.

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<sup>&</sup>lt;sup>3</sup> Department of Life Sciences, School of Pharmacy and Health Sciences, International Medical University, 57000 Kuala Lumpur, Malaysia

Prabu SL, Suriyaprakash TNK, Dinesh KC. Intellectual Property rights and its development in India. *Pharma Times*, 2012; 44(7): 19-22.

### Intellectual Property rights and its development in India

S. Lakshmana Prabu<sup>1</sup>, T.N.K. Suriyaprakash<sup>2</sup>, C. Dinesh Kumar<sup>3</sup>.

### **Abstract**

Intellectual Property Rights are patents, copyrights, trademarks, geographical indicators, protection of undisclosed information, layout designs of integrated circuits, industrial designs and traditional knowledge that are recognized by the Trade Related Intellectual Property Rights agreement (TRIPS) and governed by the WTO (World Trading Organization). In the present article, development of Intellectual Property Law in India, Evaluation of an International Intellectual Property Regime, New Dimensions and issues for resolution, Importance of IPR in developing countries and its impact are discussed in brief.

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Pridmore S, Kuipers P, Majeed Z, Restifo S, Lee A, Appleton J. A pilot investigation of the operationalized predicaments of suicide (OPS) framework. *Malaysian Journal of Medical Science*, 2012; 19(3): 50-59.

# A pilot investigation of the operationalized predicaments of suicide (OPS) framework

Saxby Pridmore<sup>1</sup>, Pim Kuipers<sup>2</sup>, Abdul Majeed Zainab<sup>3</sup>, Sam Restifo<sup>4</sup>, Adrian Lee<sup>1</sup>, Julie Appleton<sup>2</sup>

### **Abstract**

### Background:

Suicide may be conceptualized as an escape from intolerable predicaments, in particular, mental illness and environmental stressors. The operationalized predicaments of suicide (OPS) is a 4 category framework designed to assist in the classification of suicide. The objective was to examine whether this framework is potentially useful.

### Method:

18 psychiatrists from 6 different countries examined 12 written coroners' reports of suicide and rated each report according to the OPS. 16 of these raters then also completed a qualitative questionnaire regarding the framework.

### Results:

In 89.8% of cases the raters where able to make a decision regarding the drivers which led to the suicides. The respondent displayed modest inter-rater correlation (Kappa = 0.42; P<0.0001). In the qualitative section, respondents supported the face validity of OPS and considered it potentially useful. Feedback allowed improved wording of the OPS instructions.

### Conclusion:

The OPS has potential as a useful framework. The OPS instructions have been improved and further studies are justified.

**Keywords**: mental health, suicide, public health, social medicine.

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Primack BA, Carroll MV, McNamara M, Klem ML, King B, Rich M, Chan CW, Nayak S. Role of video games in improving health-related outcomes: A systematic review. *American Journal of Preventive Medicine*, 2012; 42(6): 630–638.

### Role of video games in improving health-related outcomes: A systematic review

Brian A. Primack<sup>1,2,3</sup>, Mary V. Carroll<sup>1</sup>, Megan McNamara<sup>5</sup>, Mary Lou Klem<sup>4</sup>, Brandy King<sup>6</sup>, Michael O. Rich<sup>6</sup>, Chun W. Chan<sup>7</sup>, Smita Nayak<sup>1,2</sup>.

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- <sup>2</sup> Center for Research on Health Care, University of Pittsburgh, Pittsburgh, Pennsylvania
- <sup>3</sup> Division of Adolescent Medicine, Department of Pediatrics, University of Pittsburgh, Pennsylvania
- <sup>4</sup> Health Sciences Library System, University of Pittsburgh, Pittsburgh, Pennsylvania
- <sup>5</sup> Department of Internal Medicine, Case Western Reserve University, Cleveland, Ohio
- <sup>6</sup> Center on Media and Child Health, Children's Hospital Boston, Boston, Massachusetts
- <sup>7</sup> Department of Family Medicine, International Medical University, Kuala Lumpur, Malaysia

#### Abstract

### Context:

Video games represent a multibillion-dollar industry in the U.S. Although video gaming has been associated with many negative health consequences, it also may be useful for therapeutic purposes. The goal of this study was to determine whether video games may be useful in improving health outcomes.

### Evidence Acquisition:

Literature searches were performed in February 2010 in six databases: the Center on Media and Child Health Database of Research, MEDLINE, CINAHL, PsycINFO, EMBASE, and the Cochrane Central Register of Controlled Trials. Reference lists were hand-searched to identify additional studies. Only RCTs that tested the effect of video games on a positive, clinically relevant health consequence were included. Study selection criteria were strictly defined and applied by two researchers working independently. Study background information (e.g., location, funding source); sample data (e.g., number of study participants, demographics); intervention and control details; outcomes data; and quality measures were abstracted independently by two researchers.

### Evidence Synthesis:

Of 1452 articles retrieved using the current search strategy, 38 met all criteria for inclusion. Eligible studies used video games to provide physical therapy, psychological therapy, improved disease self-management, health education, distraction from discomfort, increased physical activity, and skills training for clinicians. Among the 38 studies, a total of 195 health outcomes were examined. Video games improved 69% of psychological therapy outcomes, 59% of physical therapy outcomes, 50% of physical activity outcomes, 46% of clinician skills outcomes, 42% of health education outcomes, 42% of pain distraction outcomes, and 37% of disease self-management outcomes. Study quality was generally poor; for example, two thirds (66%) of studies had follow-up periods of <12 weeks, and only 11% of studies blinded researchers.

### Conclusions:

There is potential promise for video games to improve health outcomes, particularly in the areas of psychological therapy and physical therapy. RCTs with appropriate rigor will help build evidence in this emerging area.

Radhakrishnan AK. Advances in immunotherapy using dendritic cells. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S113-S117.

### Advances in immunotherapy using dendritic cells

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### **Abstract**

The immune system is the host natural defence against cancer. Cancers are caused by progressive growth of the progeny of a single transformed host cell. The immune system is generally not able to mount immune responses to "self-antigens", due to various mechanisms of immunological tolerance that are in place. This means that despite possessing a natural defence against tumours, many of the cancer patients may not be able to mount an effective immune response to fight the tumours. Dendritic cells (DC) are highly specialised in antigen presenting that can initiate and stimulate immune responses. These cells have the ability to stimulate naïve T cell proliferation and perform specific stimulatory and tolerogenic functions respectively. When the DC are activated by antigens, these cells undergoes further maturation and migrate to secondary lymphoid tissues, present antigen to T cells and finally induce an immune response. The ability of the DC to activate naïve and primed T-lymphocytes makes these cells a good candidate to be explored as a potential immunotherapeutic agent that can modulate antitumour immune responses in the affected host.

**Keywords**: dendritic cells, immunotherapy, anti-tumour.

Rajabalaya R, Ding SC, David SRN. Design and in vitro evaluations of transdermal delivery of ondansetron hydrochloride for the treatment of chemotherapy-induced nausea and vomiting. *Tropical Journal of Pharmaceutical Research*, 2012; (in press).

# Design and in vitro evaluations of transdermal delivery of ondansetron hydrochloride for the treatment of chemotherapy-induced nausea and vomiting

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#### Abstract

### Purpose:

To develop and evaluate matrix-type ondansetron hydrochloride (OS) transdermal patch for the treatment of chemotherapy-induced nausea and vomiting.

### Methods:

Transdermal patches were prepared by solvent casting method using ethyl cellulose and polyvinyl pyrrolidone as matrix materials, and dibutyl phthalate and dibutyl sebacate as plasticizers. The formulations were evaluated for patch thickness, tensile strength, moisture content, water absorption capacity and drug content. In vitro drug release and permeation of the patches were determined using a Franz diffusion cell.

### Results:

The tensile strength of all the formulations was in the range from 6.09 to 9.85 Mpa indicating that the patches were strong. Maximum drug release in 8 h for dibutyl phthalate DBP and dibutyl sebacate DBS patches was 38.9 (DB6) and 53.4 % (DS3), respectively, which are significantly (p < 0.01) higher than the lowest values of 17.8 (for DB1) and 35.0 % for (DS5), respectively. Drug release rate was 1.89 and 3.93  $\mu$ g/h/cm², respectively with DS2 and DB2 showing the highest permeation rate of 5.39  $\mu$ g/h/cm². Patches containing DBP followed Higuchi release model while patches formulated with DBS followed first order release kinetics.

### Conclusion:

Ondansetron matrix-type transdermal patches formulated with suitable amounts of chemical enhancers for better patient compliance are feasible.

**Keywords**: Ondansetron hydrochloride, Chemical enhancers, Plasticizers, Dibutyl phthalate, Dibutyl sebacate, Permeation, Patch.

Rajabalaya R, Tan WX, David SRN. Preparation and evaluation of transdermal drug delivery of ondansetron hydrochloride: Effect of vegetable oils as permeation enhancer. *Latin American Journal of Pharmacy*, 2012; 31(7): 1005-1012.

# Preparation and evaluation of transdermal drug delivery of ondansetron hydrochloride: Effect of vegetable oils as permeation enhancer

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#### **Abstract**

The objectives of this study were to develop and characterize the matrix type transdermal drug delivery system (TDDS) of ondansetron hydrochloride (ODH). The matrix patch contains different ratios of Eudragit RS 100 and polyvinyl pyrrolidone (PVP) with different concentrations of plasticizer like triethyl citrate (TEC) and dibutyl sebacate (DBS) as well as vegetable oils such as linseed oil, castor oil and eugenol were added and prepared by solvent casting method. Thickness, tensile strength, drug content, moisture content and water absorption studies of the matrix patches were measured. The in vitro drug release and permeation studies were carried out in Franz diffusion cell. The percentage of drug release increased with increasing amounts of PVP and plasticizer, whereas DBS containing patches exhibited higher than TEC containing patches. It may conclude that transdermal patches which use Eudragit RS 100 as the base polymer with higher amount of PVP and plasticizer DBS and additions of linseed oil were suitable for the development of ODH transdermal patches.

**Keywords:** Ondansetron hydrochloride, Plasticizers, Transdermal, Vegetable oils.

Rajiah K, Kumar A, Chandrasekhar S. Antibiotics surveillance: A survey on the susceptibility of microorganisms to antibiotics in respiratory tract infections. *European Journal of Hospital Pharmacy*, 2012; 19: 94-95.

# Antibiotics surveillance: A survey on the susceptibility of microorganisms to antibiotics in respiratory tract infections

Ashok Kumar<sup>1</sup>, Kingston Rajiah<sup>2</sup>, Chandrasekhar S<sup>3</sup>.

### **Abstract**

### Background:

Resistance to antibiotics is clearly increasing in many Asian countries and is of particular concern in *Streptococcus pneumoniae*. The genetic relationship between penicillin-resistant *S. pneumoniae* strains from across Asia suggests that resistant clones have spread within and between countries. This study is done to evaluate the resistance patterns of microorganisms to antibiotics in respiratory tract infections by undertaking a surveillance study by using antibiogram reports.

### Methods:

The study was designed to determine the susceptibility of respiratory isolates of microorganisms to antibiotics. The bacterial strains were isolated from patients suffering from respiratory tract infections. This study had two phases. Phase-I: Retrospective study and Phase-II: Prospective Study. 147 subjects were included whose antibiogram reports available in the study.

### Results:

The analysis of microbial culture reports obtained from the patients' files showed that in the retrospective study among the various specimens sent for obtaining culture report, sputum specimens were most commonly employed in 49.09% of the cases whereas in the remaining cases bronchial wash (41.81%), pleural fluids (5.45%) and throat swab (3.63%) specimens were used. In the prospective study, bronchial wash was more commonly used in about 48.64% of cases while sputum specimen was used in 45.94% of the patients. Pleural fluids and throat swab were used in 2.7% of patients

#### Conclusions:

The sensitivity of Pencillins against all the isolates of organisms fell far above the acceptable levels indicating wide spread and inappropriate use of Penicillin in the community. Cephalosporins were found to be highly sensitive to gram negative species understandably. Monobactams showed absolute sensitivity towards *Pseudomonas* but were found to be resistant against *Klebsiella*. So it is the time to think, plan and formulate a strong antibiotic policy to address this present scenario.

Keywords: Susceptibility, Microorganisms, Antibiotics, Respiratory tract infections.

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<sup>&</sup>lt;sup>3</sup> Clinical Pharmacist, Kovai medical center and hospital, Coimabatore, India

Rajinikanth PS, Balasubramaniam J, Kumar JMT, Rajesh YV. Spray drying as an approach for enhancement of dissolution and bioavailability of raloxifene hydrochloride. *International Journal of Drug Delivery*, 2012; (in press).

# Spray drying as an approach for enhancement of dissolution and bioavailability of raloxifene hydrochloride

PS Rajinikanth<sup>1</sup>, J Balasubramaniam<sup>2</sup>, M Thilek kumar<sup>1</sup>, YV Rajesh<sup>1</sup>.

### **Abstract**

The present study investigated the effect of spray drying raloxifene HCI (RHCL) with different classes of hydrophilic carriers (different grades of polyvinyl pyrrolidones) and cellulosic polymers) in order to determine the potential effect on dissolution rate and bioavailability of RHCL. Preformulation studies were conducted to select the appropriate carriers and drug: carrier ratio for preparing the spray dried compositions. The solid state interactions of the spray dried mixtures were evaluated by DSC & XRD. Preformulation studies revealed that amorphous compositions of RHCL could be obtained only with Plasdones (K12, K29/32 and S630). DSC studies showed that the crystalline nature of RHCL was significantly reduced on spray drying. Significant enhancement in dissolution rate was observed with the prepared spray dried compositions and out of the three grades of Plasdone, Plasdone K12 demonstrated the maximum enhancement in rate of release of RHCL. The pharmacokinetics of spray dried composition (1:1 RHCL: K12) and pure RHCL was evaluated following oral administration (25 mg/kg) in healthy female Sprague Dawley rats. The extent of the mean plasma exposures of RHCL was 7-fold higher in animals treated with spray dried mixture of RHCL, K12 (1:1) compared to animals treated with RHCL. Spray drying of RHCL with Plasdones, especially Plasdone K12, reduced drug crystallinity, increased the rate and extent of dissolution, and improved bioavailability.

**Keywords:** Dissolution enhancement, Bioavailability, Spray drying, roloxifene, poorly soluble drug.

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Rajinikanth PS, Neo WK, Garg S. Self-nanoemulsifying drug delivery systems of valsartan: Preparation and in-vitro characterization. *International Journal of Drug Delivery*, 2012; (in press).

### Self-nanoemulsifying drug delivery systems of valsartan: Preparation and invitro characterization

PS Rajinikanth<sup>1</sup>, Neo Woei Keat<sup>1</sup>, Sanjay Garg<sup>2</sup>.

### **Abstract**

The main objective this study is to prepare and evaluate the selfnanoemulsifying drug delivery

(SNEDDS) system in order to achieve a better dissolution rate of a poorly water soluble drug valsartan. The present research work describes a SNEDDS of valsartan using labrasol, Tween 20 and Polyethylene glycol (PEG) 400. The pseudo-ternary phase diagrams with presence and absence of drug were plotted to check for the emulsification range and also to evaluate the effect of valsartan on the emulsification behavior of the phases. The mixtures consisting of oil (labrasol) with surfactant (tween20), co-surfactant (PEG 400) were found to be optimum formulations. Prepared formulations were evaluated for its particle size distribution, nanoemulsifying properties, robustness to dilution, self emulsication time, turbidity measurement, drug content and in-vitro dissolution. The optimized formulations are further evaluated for heating cooling cycle, centrifugation studies, freeze thaw cycling, particle size distribution and zeta potential were carried out to confirm the stability of the formed SNEDDS formulations. The prepared formulation has a significant improvement in terms of the drug solubility as compared with marketed tablet and pure drug, thus, this greater dissolution of valsartan from formulations could lead to higher absorption and higher oral bioavailability.

**Keywords:** Self Emulsifying Drug Delivery System, Nanoemulsion, Valsartan, Enhancement of dissolution, poorly soluble drug,

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Rathbone, MJ. Delivering drugs to farmed animals using controlled release science and technology. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S118-S128.

# Delivering drugs to farmed animals using controlled release science and technology

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### **Abstract**

This article presents an overview of long acting products used in animal health, production and reproduction. The topic represents a niche field of controlled release that few formulation scientists become specialists and experts in, but it is a field which has made significant contribution to the area of controlled release technology, and one which is of major importance to human kind due to their dependence on farmed animals as a source of hide, protein, milk and eggs.

**Keywords:** Intravaginal drug delivery, veterinary drug delivery, animal health, controlled release, oestrous control.

Renton T, Al-Haboubi M, Pau A, Shepherd J, Gallagher JE. What has been the United Kingdom's experience with retention of third molars? *Journal of Oral and Maxillofacial Surgery*, 2012; 70(9) (Suppl. 1): S48-57.

### What has been the United Kingdom's experience with retention of third molars?

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#### Abstract

### Background:

In 2000, the first National Institute of Clinical Excellence (NICE) guidelines related to third molar (M3) surgery, a commonly performed operation in the United Kingdom, were published. This followed research publications and professional guidelines in the 1990s that advised against prophylactic surgery and provided specific therapeutic indications for M3 surgery. The aim of the present report was to summarize the available evidence on the effects of guidelines on M3 surgery within the United Kingdom.

### Materials and Methods:

Data from primary care dental services and hospital admissions in England and Wales during a 20-year period (Hospital Episode Statistics 1989/1990 to 2009/2010), and from private medical insurance companies were analyzed. The volume and, where possible, the nature of the M3 surgery activity over time were assessed together, as were the collateral effects of the guidelines, including patient age at surgery and the indications for surgery.

#### Results:

The volume of M3 removal decreased in all sectors during the 1990s before the introduction of the NICE guidelines. During the 20-year period, the proportion of impacted M3 surgery decreased from 80% to 50% of admitted hospital cases. Furthermore, an increase occurred in the mean age for surgical admissions from 25.5 to 31.8 years. The change in age correlated with a change in the indications for M3 surgery during that period, with a reduction in "impaction," but an increase in "caries" and "pericoronitis" as etiologic factors, in accordance with the NICE guidelines.

### Conclusion:

The significant decrease in M3 surgery activity occurred before the NICE guidelines. Thus, M3 surgery has been performed at a later age, with indications for surgery increasingly in accordance with the NICE guidelines. The importance of clinical monitoring of the retained M3s is discussed.

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# INTERNATIONAL MEDICAL UNIVERSITY (IMU)

Sandeep S, Dinesh KC, Indra PS, Anandarajagopal K. Pharmacognostical profile of *Paereria foetida* Linn. leaves. *International Journal of Pharmaceutical Sciences and Research*, 2012; 3(7): 2075-2081.

### Pharmacognostical profile of Paereria foetida Linn. leaves

Sandeep Shetti<sup>1</sup>, Dinesh Kumar Chellappan<sup>2</sup>, Indra Prakash Sharma<sup>1</sup>, Anandarajagopal Kalusalingam<sup>3</sup>.

#### Abstract

The leaves of *Paederia foetida* Linn. (*P. foetida*) are commonly known as skunk vine or Chinese fever vine, are used for various ailments medicinally throughout Asia and other tropical parts of the world by traditional healers. The plant is mainly used for arthritis and rheumatic disorders. The whole plant shows tonic, astringent and antiphlogistic actions and has been used in tenesmus. This present work presents a detailed pharmacognostical study of the leaf of the crude drug *P. foetida*. The samples were studied using procedures of light, confocal microscopy, WHO recommended physico-chemical determinations and authentic phytochemical procedures. The physico-chemical, morphological and histological parameters presented in this study may be proposed as parameters to establish the authenticity of *P. foetida* and may possibly help to differentiate the drug from its adulterants.

**Keywords:** Paederia foetida, Leaves, Pharmacognostical, Physicochemical.

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Saravanan C, Rangaswamy K. Effectiveness of counselling on the attitudes of mothers towards their children with intellectual disability. *Asia Pacific Journal of Counselling and Psychotherapy*, 2012; 1: 1-13.

# Effectiveness of counselling on the attitudes of mothers towards their children with intellectual disability

Coumaravelou Saravanan<sup>1</sup> & Karuppannan Rangaswamy<sup>2</sup>

### **Abstract**

Mothers of children with intellectual disability have more negative attitudes towards them compared with mothers' of normally developing children. If attitudes of mothers are negative, psychological intervention for their children may be less effective. The primary aim of this study was to compare the attitudes of mothers before and after psychological counselling to change their negative attitudes. Thirty-two mothers of children with mild intellectual disability participated in eight individual counselling sessions. The Binet-Kamat Test of General Mental ability was used to measure the children's intellectual quotient and The Parental Attitude Scale was used to measure the attitudes of mothers towards their children with mild intellectual disability. Results showed that mothers who exhibited higher negative attitudes, such as over-protection, domination, rejection, hostility, acceptance, permissiveness, education and future, and home-management in the pre-assessment showed significant reduction in their negative attitudes in the post-assessment after they had participated in psychological counselling. Overall, the psychological counselling was effective in modifying mothers' negative attitudes towards their children with intellectual disability.

**Keywords:** parental attitudes, intellectually disabled children, psychological counselling.

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Selvaduray KR, Radhakrishnan AK, Kutty MK, Nesaretnam K. Palm tocotrienols decrease levels of pro-angiogenic markers in human umbilical vein endothelial cells (HUVEC) and murine mammary cancer cells. *Genes and Nutrition*, 2012; 7(1): 53-61.

# Palm tocotrienols decrease levels of pro-angiogenic markers in human umbilical vein endothelial cells (HUVEC) and murine mammary cancer cells

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### **Abstract**

Anti-angiogenic therapy is widely being used to halt tumour angiogenesis. In this study, the anti-angiogenic activity of palm tocotrienol-rich fraction (TRF) and its individual components (γ- and δ-tocotrienol) were first investigated in vitro in human umbilical vein endothelial cells (HUVEC) and 4T1 mouse mammary cancer cells. Results showed reduced levels of Interkeukin (IL)-8 and IL-6, two pro-angiogenic cytokines in HUVEC treated with palm tocotrienols compared with  $\alpha$ -tocopherol ( $\alpha$ -T) and control cells (P < 0.05). The production of IL-8 and IL-6 was lowest in  $\delta$ -tocotrienol ( $\delta$ -T3)-treated cells followed by  $\gamma$ -tocotrienol ( $\gamma$ -T3) and TRF. There was significant (P < 0.05) reduction in IL-8 and vascular endothelial growth factor (VEGF) production in 4T1 cells treated with TRF or δ-T3. There was decreased expression of VEGF and its receptors; VEGF-R1 (fms-like tyrosine kinase, Flt-1) and VEGF-R2 (Kinase-insert-domain-containing receptor, KDR/Flk-2) in tumour tissues excised from mice supplemented with TRF were observed. There was also decreased expression of VEGF-R2 in lung tissues of mice supplemented with TRF. These observations correlate with the smaller tumour size recorded in the tocotrienol-treated mice. This study confirms previous observations that palm tocotrienols exhibit anti-angiogenic properties that may inhibit tumour progression.

**Keywords:** Angiogenesis Palm tocotrienol, IL-6 IL-8, VEGF, VEGF receptors.

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Senel S, Rathbone MJ, Cansız M, Pather I. Recent developments in buccal and sublingual delivery systems. *Expert Opinion on Drug Delivery*, 2012; 9(6): 1-14.

### Recent developments in buccal and sublingual delivery systems

Şenel S<sup>1</sup>, Rathbone MJ<sup>2</sup>, Cansız M<sup>3</sup>, Pather I<sup>4</sup>.

#### **Abstract**

#### Introduction:

There have been several advances in the delivery of drugs through the buccal mucosa over the last 5 years, which have resulted in a number of new buccal delivery products appearing on the market.

#### Areas covered:

This review discusses the most recent developments in the area of buccal and sublingual drug delivery, with a focus on marketed drugs. Likely future directions are also considered and reported.

#### Expert opinion:

The future potential of buccal and sublingual delivery systems looks favorable. It is envisaged that in the future, buccal and sublingual delivery technologies will provide a platform for the successful delivery of vaccines and antigens. It is also foreseen that physical means of enhancing drug uptake (e.g., sonophoresis, iontophoresis and electroporation) will be commercialized for buccal delivery, thereby expanding the current drug candidate list for this area. The formulation of delivery systems for photosensitizers in photodynamic therapy is a potential emerging area, while buccal and sublingual delivery, in general, is attractive for the development of intellectual property.

**Keywords**: allergen, buccal, buccal iontophoresis, orally dispersing tablets, oral films, sublingual, vaccine.

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Shoji Y, Choo HL, Leong CO. Detection of human herpesvirus 6 (HHV-6) in saliva of healthy adults in Malaysia. *Malaysian Journal of Medicine and Health Sciences*, 2012; 8(2): 31-40.

# Detection of human herpesvirus 6 (HHV-6) in saliva of healthy adults in Malaysia

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#### **Abstract**

The aim of this study was to evaluate the prevalence of HHV-6 infection in healthy adults in Malaysia.

#### Methods:

The level of HHV-6 in saliva was investigated in 36 healthy adults, age 19 to 23 years, at Kuala Lumpur, Malaysia using variant-specific TaqmanTM quantitative real-time PCR (qPCR).

#### Results:

The amount of HHV-6 DNA in the saliva of healthy adults ranged from negative to 10,000 HHV-6 genomes/ml of saliva (median, 360 genomes/ml of saliva). Of the 36 samples tested, 30 (83%) contained HHV-6 DNA. HHV-6B was the only variant detected in the saliva of all the positive cases.

#### Conclusions:

The detection of HHV-6 DNA in saliva by real-time PCR assay provides a sensitive and specific quantitation of HHV-6. Our pilot study suggests the wide prevalence of HHV-6 in saliva from healthy adults.

**Keywords:** Herpesvirus 6, HHV-6, prevalence, real-time PCR, saliva.

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Shyam S, Ng TKW, Arshad F. Adding glycaemic index and glycaemic load functionality to DietPLUS, a Malaysian food composition database and diet intake calculator. *Asia Pacific Journal of Clinical Nutrition*, 2012; 21(2): 201-208.

# Adding glycaemic index and glycaemic load functionality to DietPLUS, a Malaysian food composition database and diet intake calculator

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#### **Abstract**

This paper outlines the methodology to add glycaemic index (GI) and glycaemic load (GL) functionality to food DietPLUS, a Microsoft Excel-based Malaysian food composition database and diet intake calculator. Locally determined GI values and published international GI databases were used as the source of GI values. Previously published methodology for GI value assignment was modified to add GI and GL calculators to the database. Two popular local low GI foods were added to the DietPLUS database, bringing up the total number of foods in the database to 838 foods. Overall, in relation to the 539 major carbohydrate foods in the Malaysian Food Composition Database, 243 (45%) food items had local Malaysian values or were directly matched to International GI database and another 180 (33%) of the foods were linked to closely-related foods in the GI databases used. The mean  $\pm$  SD dietary GI and GL of the dietary intake of 63 women with previous gestational diabetes mellitus, calculated using DietPLUS version3 were, 62  $\pm$  6 and 142  $\pm$  45, respectively. These values were comparable to those reported from other local studies. DietPLUS version3, a simple Microsoft Excel-based programme aids calculation of diet GI and GL for Malaysian diets based on food records.

**Keywords:** glycaemic index, glycaemic load, diet, dietary carbohydrate, Malaysia.

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Siar CH, Pua CK, Toh CG, Romanos G, Ng KH. Cementum status in natural teeth opposing implant-borne bridgework in *Macaca fascicularis*. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology,* 2012; (in press).

## Cementum status in natural teeth opposing implant-borne bridgework in *Macaca fascicularis*

Chong Huat Siar<sup>1</sup>, Chee Keong Pua<sup>2</sup>, Chooi Gait Toh<sup>3</sup>, George Romanos<sup>4</sup>, Kok Han Ng<sup>5</sup>.

#### Abstract

### Objective:

The objective of this study was to investigate the cementum status in natural teeth opposing implant-supported bridgework.

#### Methods:

Maxillary premolars and molars opposing immediate-loading (IL) and delayed-loading (DL) mandibular implant supported bridgework in 4 *Macaca fascicularis* were harvested after 3 months of functional loading. Another 2 monkeys without mandibular fixed prostheses served as control. The cervical (CCW) and apical cementum width (ACW), and resorption craters (RCs) were measured.

#### Results:

No significant differences were observed between test and control groups for mean CCW (control =  $26.79 \pm 3.28$ , IL =  $21.29 \pm 9.12$ , and DL =  $20.32 \pm 5.65 \mu m$ ) and for ACW (control =  $937.97 \pm 353.74$ , IL =  $955.26 \pm 720.05$ , and DL =  $750.56 \pm 517.26 \mu m$ ) (P > .05). In test and control monkeys, RCs were uncommon and showed no significant differences in width (control =  $0.71 \pm 0.38$ , IL =  $1.02 \pm 0.49$ , DL =  $0.85 \pm 1.02 \mu m$ ) and depth (control =  $0.15 \pm 0.07$ , IL =  $0.25 \pm 0.40$ , DL =  $0.22 \pm 0.15 \mu m$ ) (P > .05).

### Conclusions:

Present findings suggest that implant-supported bridgework does not produce any adverse effects on the cementum of opposing natural teeth after 3 months of functional loading. (Oral Surg Oral Med Oral Pathol Oral Radiol 2012; 114(suppl 5) (suppl 5):S46-S53)

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Siar CH, Toh CG, Ali TBT, Seiz D, Ong ST. Dimensional profile of oral mucosa around combined tooth-implant supported bridgework in macaque mandible. *Clinical Oral Implants Research*, 2012; 23: 438–446.

# Dimensional profile of oral mucosa around combined tooth-implant supported bridgework in macaque mandible

Chong Huat Siar<sup>1</sup>, Chooi Gait Toh<sup>2</sup>, Tara Bai Taiyeb Ali<sup>1</sup>, Doris Seiz<sup>3</sup>, Siew Tin Ong<sup>4</sup>.

#### Abstract

#### Purpose:

A stable oral mucosa is crucial for long-term survival and biofunctionality of implants. Most of this evidence is derived from clinical and animal studies based solely on implant-supported prosthesis. Much less is known about the dimensions and relationships of this soft tissue complex investing tooth-implant-supported bridgework (TISB). The aim here was to obtain experimental evidence on the dimensional characteristics of oral mucosa around TISB with two different abutment designs.

#### Methods:

Sixteen 3-unit TISB were constructed bilaterally in the mandible of eight adult *Macaca fascicularis*. An implant system with a standard progressive thread design was the bone-anchoring implant in the second mandibular molar region while the second mandibular premolar served as the natural tooth abutment. Eight implants were connected with the tapered abutment, the remaining with butt-joint abutment, in a split-mouth design. These were allowed to functional load for 6 months before sacrification for histomorphometry. Six soft tissue indices were scored: coronal gingival mucosa-to-implant top distance (DIM); sulcus depth (SD); junctional epithelium (JE); connective tissue contact (CTC); implant top to first bone-to-implant contact distance (DIB); and biologic width (BW=SD+JE+CTC); corresponding parameters in the natural tooth abutment were also measured.

#### Results:

Mucosal dimensions in tapered implants ( $^*BW=3.33\pm0.43$ ; SD=1.03±0.24; JE=1.08±0.13; CTC=1.22±0.23 mm) were comparable with those of natural tooth abutments (BW=3.04±0.18; SD=0.93±0.1; JE=0.78±0.1; Attachment=1.33±0.09 mm), but differed from butt-joint implants ( $^*BW=4.88\pm1.24$ ; SD=1.47±0.38; JE=1.49±0.4; CTC=1.92±0.93 mm) ( $^*P<0.05$ ).

### Conclusions:

Results suggested that soft tissue dimensions around TISB are influenced by the implant–abutment interface and abutment material used. Mucosa investing tapered abutment tends to recapitulate soft tissue physiologic dimensions of natural tooth.

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**Keywords**: abutments, dental implants, histomorphometry, oral mucosa, soft tissues.

Singh S, Ganesh S. Phenotype variations in Lafora progressive myoclonus epilepsy: possible involvement of genetic modifiers? *Journal of Human Genetics*, 2012: doi:10.1038/jhg.2012.29.

# Phenotype variations in Lafora progressive myoclonus epilepsy: Possible involvement of genetic modifiers?

Shweta Singh<sup>1</sup>, Subramaniam Ganesh<sup>2</sup>.

#### **Abstract**

Lafora progressive myoclonus epilepsy, also known as Lafora disease (LD), is the most severe and fatal form of progressive myoclonus epilepsy with its typical onset during the late childhood or early adolescence. LD is characterized by recurrent epileptic seizures and progressive decline in intellectual function. LD can be caused by defects in any of the two known genes and the clinical features of these two genetic groups are almost identical. The past one decade has witnessed considerable success in identifying the LD genes, their mutations, the cellular functions of gene products and on molecular basis of LD. Here, we briefly review the current literature on the phenotype variations, on possible presence of genetic modifiers, and candidate modifiers as targets for therapeutic interventions in LD.

**Keywords:** epilepsy, genetic modifiers, glycogen metabolism, Mendelian disorders, neurodegeneration, protein-protein interaction.

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Sinniah D. Shock in children. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl.1): S129-S136.

#### Shock in children

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#### **Abstract**

Shock, a major cause of morbidity and mortality in children, is the most anxiety-provoking emergency that needs to be addressed urgently and effectively by the attending paediatrician. It is a state where the metabolic demands of the tissue are not met due to circulatory dysfunction. Unlike adults, hypotension is a very late feature of shock in children. As the child's condition worsens, the clinical presentation of the different causes of shock become similar, and nullify any aetiological differences. Regardless of the type of shock, the final common pathway is inadequate tissue perfusion and oxygen supply to meet cellular demands. Delayed recognition and treatment result in progression from compensated reversible shock to uncompensated irreversible shock with widespread multiple system organ failure to death. This paper reviews the physiological basis, and pathophysiological classification of the various types of shock and their respective aetiologies. The clinical features of the different types of shock are described, and current diagnostic and therapeutic strategies are applied for the most effective and appropriate treatment for resuscitating the child in shock. A strong index of suspicion, early recognition, timely intervention and transfer to an intensive care unit are critical for successful outcomes in the management of paediatric shock.

**Keywords**: shock, child, aetiology, treatment, management.

Sivalingam N, Loh KY. Concepts in the management of the overactive bladder in women. *Medical Journal of Malaysia*, 2012; 67: 37-142.

### Concepts in the management of the overactive bladder in women

N Sivalingam<sup>1</sup>, K Y Loh<sup>2</sup>.

#### **Abstract**

The 'overactive bladder' is a common problem affecting the elderly female population especially after the menopause. Urgency with or without urge incontinence accompanied by frequency of micturition and nocturia are presenting symptoms. The diagnosis is established after excluding other diseases of the lower urinary tract which have similar presenting features. The aetiology is multifactorial and this problem often causes physical, psychological and emotional distress to the patient. Management can be provided by primary care physicians initiating behavioral changes which include life style interventions and bladder drills with or without antimuscarinic drugs. The recalcitrant patient not responding to conventional therapy should be referred for specialist care. Non–conventional treatment using acupressure, neuromodulation and surgical methods are only instituted in indicated cases.

**Keywords:** Overactive bladder, Urgency, Frequency, Non-pharmacological treatment, Antimuscarinincs.

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Suzana S, Kee CC, Jamaludin AR, Noor Safiza MN, Khor GL, Jamaiyah H, Geeta A, Rahmah R, Ruzita AT, Ahmad Fauzi Y. Overnutrition and abdominal obesity among Malaysian older people –NHMS3. *Asia-Pacific Journal of Public Health*, 2012; 24: 318-329.

# The Third National Health and Morbidity Survey: Prevalence of Obesity, and Abdominal Obesity among the Malaysian Elderly Population

Suzana S<sup>1</sup>, Kee CC<sup>2</sup>, Jamaludin AR<sup>3</sup>, Noor Safiza MN<sup>4</sup>, Khor GL<sup>5</sup>, Jamaiyah H<sup>6</sup>, Geeta A<sup>6</sup>, Ahmad Ali Z<sup>4</sup>, Rahmah R<sup>1</sup>, Ruzita AT<sup>1</sup>, Ahmad Fauzi Y<sup>4</sup>.

#### **Abstract**

Obesity is an emerging public health threat in the elderly population in developing countries. Hence, the Third National Health and Morbidity Survey has assessed 4746 individuals aged 60 years and older recruited through a household survey to determine the prevalence of adiposity using body mass index and waist circumference. The national's prevalence of overweight and obesity in men was 29.2% (95% confidence interval [CI] = 27.2-31.3) and 7.4% (95% CI = 6.4-8.6), respectively. However, the prevalence decreased with age. The figures in women were 30.3% (95% CI = 28.5-32.1) and 13.8% (95% CI = 12.5-15.2), respectively. The prevalence of abdominal obesity was 21.4% (95% CI = 20.2-22.6), with 7.7% (95% CI = 6.7-9.0) in men and 33.4% (95% CI = 31.4-35.3) in women. Predictors of adiposity include the following: Malay and Indian ethnicity, higher education level, higher household income, from urban area, and being married. In conclusion, adiposity affects about one third of the Malaysian elderly population, especially those of the younger age group, women, and those with higher socioeconomic status.

**Keywords**: nutrition assessment, elderly, obesity, abdominal obesity, socioeconomic status.

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Tan KL, Yadav H. Depression among the urban poor in Peninsular Malaysia: A community based cross-sectional study. *Journal of Health Psychology*, 2012; (in press).

# Depression among the urban poor in Peninsular Malaysia: A community based cross-sectional study

Kok Leong Tan<sup>1</sup>, Hematram Yadav<sup>1</sup>.

#### **Abstract**

This community based cross-sectional study examined the prevalence and factors associated with depression among urban poor in Peninsular Malaysia. The Patient Health Questionnaire (PHQ-9) was used to determine the presence or absence of depression. The prevalence of depression among the urban poor was 12.3%. Factors significantly associated with depression included respondents under 25 years old, male gender, living in the area for less than four years and those who do not exercise regularly. It is important to identify individuals with depression and its associated factors early because depression can severely affect the quality of life.

**Keywords**: depression, Peninsular Malaysia, PHQ-9, urban poor.

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Tan W, Wazir NN, Chiu CK, Ko M. Chronic osteomyelitis secondary to human bite: A case report. *Malaysian Orthopaedic Journal*, 2012; 6(3): 40-41.

### Chronic osteomyelitis secondary to human bite: A case report

W Tan, NN Wazir, CK Chiu, M Ko.

Department of Orthopaedic Surgery, International Medical University, Seremban, Malaysia

#### **Abstract**

We report a case of a human bite that was initially inadequately treated and progressed to chronic osteomyelitis, finally resulting in digital amputation. Human bites are seemingly innocuous, but if neglected, may lead to subsequent infection and morbidity. Persistence of symptoms should alert the practitioner to the possibility of infection extending to the soft tissue or bone. Bacteriological studies commonly yield mixed aerobic and anaerobic flora. Early debridement and antibiotic treatment may prevent development of severe soft tissue or bone infection.

**Keywords**: human bite, osteomyelitis, amputation.

Tang LIC, Ling APK, Koh RY, Chye SM, Voon KGL. Screening of anti-dengue activity in methanolic extracts of medicinal plants. *BMC Complementary and Alternative Medicine*, 2012; 12: 3.

### Screening of anti-dengue activity in methanolic extracts of medicinal plants

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#### **Abstract**

#### Background:

Dengue fever regardless of its serotypes has been the most prevalent arthropod-borne viral diseases among the world population. The development of a dengue vaccine is complicated by the antibody-dependent enhancement effect. Thus, the development of a plant-based antiviral preparation promises a more potential alternative in combating dengue disease.

#### Methods:

Present studies investigated the antiviral effects of standardised methanolic extracts of *Andrographis paniculata*, *Citrus limon*, *Cymbopogon citratus*, *Momordica charantia*, *Ocimum sanctum* and *Pelargonium citrosum* on dengue virus serotype 1 (DENV-1).

#### Results:

O. sanctum contained 88.6% of total flavonoids content, an amount that was the highest among all the six plants tested while the least was detected in *M. charantia*. In this study, the maximum non-toxic dose (MNTD) of the six medicinal plants was determined by testing the methanolic extracts against Vero E6 cells in vitro. Studies also determined that the MNTD of methanolic extract was in the decreasing order of *M. charantia* > C. limon > P. citrosum, O. sanctum > A. paniculata > C. citratus. Antiviral assay based on cytopathic effects (CPE) denoted by degree of inhibition upon treating DENV1-infected Vero E6 cells with MNTD of six medicinal plants showed that *A. paniculata* has the most antiviral inhibitory effects followed by *M. charantia*. These results were further verified with an in vitro inhibition assay using MTT, in which 113.0% and 98.0% of cell viability were recorded as opposed to 44.6% in DENV-1 infected cells. Although methanolic extracts of *O. sanctum* and *C. citratus* showed slight inhibition effect based on CPE, a significant inhibition was not reflected in MTT assay. Methanolic extracts of *C. limon* and *P. citrosum* did not prevent cytopathic effects or cell death from DENV-1.

#### Conclusions:

The methanol extracts of *A. paniculata* and *M. charantia* possess the ability of inhibiting the activity of DENV-1 in in vitro assays. Both of these plants are worth to be further investigated and might be advantageous as an alternative for dengue treatment.

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# INTERNATIONAL MEDICAL UNIVERSITY (IMU)

Tang WM, Ghani MFA. Job satisfaction among the nurse educators in the Klang Valley, Malaysia. *International Journal of Nursing Science*, 2012; 2(4): 29-33.

### Job satisfaction among the nurse educators in the Klang Valley, Malaysia

Wai Mun Tang<sup>1</sup>, Muhammad Faizal A. Ghani<sup>2</sup>.

#### **Abstract**

The aims of this study were to identify the priority factors that contribute towards the job satisfaction and determine the relationship between the level of job satisfaction and salary earned by the nurse educators in the Klang Valley, Malaysia. The study had a cross-sectional design and included nurse educators (n = 66, response rate 82.5%) working in five higher educational institutions. Data collection was conducted with a questionnaire consisting of 56 items. The respondents reported that the three highest priority factors that determine their job satisfaction were salary, benefit entitlement and working conditions. Furthermore, the study also revealed that there was a significant relationship between the level of job satisfaction and salary earned among the nurse educators.

**Keywords**: Job Satisfaction, Nurse Educators, Nursing Shortage, Herzberg's Two-Factor Theory.

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Teoh ML, Phang SM, Chu WL. Response of Antarctic, temperate, and tropical microalgae to temperature stress. *Journal of Applied Phycology*, 2012: doi: 10.1007/s10811-012-9863-8.

## Response of Antarctic, temperate, and tropical microalgae to temperature stress

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#### **Abstract**

The global temperature increase has significant implications on the survival of microalgae which form the basis of all aquatic food webs. The aim of this study was to compare the response of similar taxa of microalgae from the Antarctic (Chlamydomonas UMACC 229, Chlorella UMACC 237, and Navicula glaciei UMACC 231), temperate (Chlamydomonas augustae UMACC 247, Chlorella vulgaris UMACC 248, and Navicula incerta UMACC 249), and tropical (C. augustae UMACC 246, C. vulgaris UMACC 001, and Amphiprora UMACC 239) regions to changing temperature. The Antarctic, temperate, and tropical strains were grown over specific temperature ranges of 4 °C to 30 °C, 4 °C to 32 °C, and 13 °C to 38 °C, respectively. The three Antarctic strains survived at temperatures much higher than their ambient regime. In comparison, the tropical strains are already growing at their upper temperature limits. The three Chlorella strains from different regions are eurythermal, with a large overlap on tolerance ranging from 4 °C to 38 °C. The specific growth rate ( $\mu$ ) of the Antarctic Navicula decreased (<0.34 day<sup>-1</sup>) at temperatures above 4 °C, showing it to be sensitive to temperature increase. If further warming of Earth occurs, N. glaciei UMACC 231 is likely to have the most deleterious consequences than the other two Antarctic microalgae studied. The percentage of polyunsaturated fatty acids (PUFA) decreased with increasing temperature in the Antarctic Navicula. As temperature increases, the growth and nutritional value of this commonly occurring diatom in the Antarctic may decrease, with consequences for the aquatic food web. Of the three Chlamydomonas strains, only the Antarctic strain produced predominantly PUFA, especially 16:3 (48.4–57.2 % total fatty acids).

**Keywords**: Antarctic microalgae, Temperature stress, *Chlamydomonas*, *Chlorella*, Diatoms.

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Tilakavati K, Chee WSS, Liew SY, Ng BK, Karuthan C. Dietary health behaviors of women living in high rise dwellings: A case study of an urban community in Malaysia. *Journal of Community Health*, 2012; doi: 10.1007/s10900-012-9597-1.

# Dietary health behaviors of women living in high rise dwellings: A case study of an urban community in Malaysia

Tilakavati Karupaiah<sup>1</sup>, Winnie Chee Siew Swee<sup>2</sup>, Siew Ying Liew<sup>1</sup>, Boon Koon Ng<sup>1</sup>, Karuthan Chinna<sup>3</sup>.

#### **Abstract**

Diet-related non-communicable disease (DRNCD) occurrence is a serious problem amongst Malaysian women and urbanization is probably a challenge to their achieving the nutritional environment conducive to healthy eating. This case study aimed to determine diet quality of an urban community using women respondents from high rise dwellings in Kuala Lumpur. The sample consisted of 135 households and a healthy eating index (HEI) scale was used to evaluate the women's diet quality. A total of 128 women (Malays = 45, Chinese = 56, Indian = 27) participated. Total HEI score was significantly different (P\0.05) within ethnicity (Indians =  $75.7 \pm 8.1$ \Malays =  $80.5 \pm 7.4$ \Chinese =  $80.1 \pm 8.1$ ) and affected by component scores for fruit (range 3.8-6.2, P = 0.044), sodium (range 7.8-9.0, P = 0.006) and food variety (range 9.3-9.9, P = 0.001). Dairy foods rated poorly (range 2.0-3.9, P = 0.05) regardless of ethnicity. Income strata (q = 0.159, P = 0.048) and eating out frequency (q -0.149, P = 0.046) also independently affected HEI scores. Income negatively correlated with sodium restriction score (q = -0.294, P = 0.001) but positively with cereals (q = 0.181; P =0.025), fruits (q = 0.178; P = 0.022), dairy products (q = 0.198; P = 0.013) and food variety (q = 0.219, P = 0.007). Decreased vegetable intake (q = -0.320; P\0.001) and sodium excess (q = -0.320; P\0.001) = -0.135, P = 0.065) were associated with eating out frequency and poor HEI scores. This case study suggests health promotion for DRNCD prevention is needed at the community level to improve diet quality of urban women.

**Keywords**: Urban women, High rise dwelling, Ethnicity, Income, Diet quality, HEI.

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Veettil SK, Salmiah MA, Rajiah K, Kumar SBR. Cost of acute exacerbation of COPD in patients attending government hospital in Kerala, India. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2012; 4(3): 659-661.

# Cost of acute exacerbation of COPD in patients attending government hospital in Kerala, India

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#### **Abstract**

Although exacerbations are the major cause of hospitalizations and financial burden in patients with COPD, little information is available on the costs of their management in different settings. The study objective was to provide an estimate of cost of acute exacerbation of COPD in patients attending tertiary level government hospitals in South India. This study is a prospective observational study aimed at identifying different costs in the treatment of acute exacerbation of COPD for seven days under non-experimental conditions using a total number of 120 eligible consenting patients. Cost data were based on existing information on cost of the hospital and Government rates for drugs and investigations. The mean total cost calculated for COPD exacerbation for 7day stay was found out to be \$ 89.75 (INR 4128. 36/). The distribution of the total costs in the present study was 93% direct costs, and 7% indirect costs. Direct medical costs contribute 80% of the total cost. Although the drug cost contribution in total cost was only 9.1%. The total treatment cost was highly correlated with the disease severity (p<0.01). Costs of management of acute exacerbation of COPD are exceptionally low in government hospitals in India compared to data obtained from developed countries.

Keywords: COPD, Exacerbation, Cost, Government, Kerala, India.

Velayudhan M. Managing diabetes during the Muslim fasting month of Ramadan. *Medical Journal of Malaysia*, 2012; 67(3): 353-354.

### Managing diabetes during the Muslim fasting month of Ramadan

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#### **Abstract**

Target blood sugar levels in diabetes are achieved through manipulation of diet, exercise and medication. A change in any one of these three things can skew blood sugar levels and create complications associated with hyperglycemia or hypoglycemia. Fasting during the month of Ramadan is a religious activity that devout Muslims practice whether they are diabetic or not. Since such fasting involves abstinence from food and water for twelve hours or more during the day from dawn to dusk, it is evident that advice regarding exercise and medication will have to be modified during this period.

Velayudhan M. Using a Facebook group for interactive clinical learning. *International e-Journal of Science, Medicine and Education (IeSJME)*, 2012; 6(1): 21-23.

### Using a Facebook group for interactive clinical learning

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#### **Abstract**

#### Background:

Facebook is a popular social networking site with more than five hundred million users. This study assessed whether Facebook Groups can be used to teach clinical reasoning skills.

#### Methods:

Sixty-seven final year medical students from the International Medical University, Malaysia, were exposed to interactive online learning through a Facebook Group for a period of six months in this study. The purpose was to determine if supervised interactive online learning could be used to augment the deep learning that comes from learning medicine at the bedside of patients. The interactive online discussions were entirely triggered by clinical problems encountered in the medical wards of the general hospital to which these students were attached.

#### Results:

A total of 10 topics were discussed in this forum during the duration of this study and an example of one such discussion is provided to illustrate the informal nature of this kind of learning. The results showed a high degree of student involvement with 76 percent of students actively participating in the discussions.

#### Conclusion:

The high degree of voluntary participation in the clinical discussions through the Facebook Group in this study tells us that Facebook Groups are a good way of engaging students for learning and can be used in medical education to stimulate creative clinical thinking.

**Keywords:** e-learning, interactive learning, online learning, medical students.

Wong RSY, Radhakrishnan AK. Tocotrienols: Past into present. *Nutrition Reviews*, 2012; (in press).

### **Tocotrienols: Past into present**

Rebecca SY Wong<sup>1</sup>, Ammu K Radhakrishnan<sup>2</sup>.

#### **Abstract**

The vitamin E family consists of eight isomers known as alpha-, beta-, gamma-, and delta-tocopherols and alpha-, beta-, gamma-, and delta-tocotrienols. Numerous studies focused on the health benefits of these isomers have been performed since the discovery of vitamin E in 1922. Recent discoveries on the potential therapeutic applications of tocotrienols have revolutionized vitamin E research. Nevertheless, despite the abundance of literature, only 1% of vitamin E research has been conducted on tocotrienols. Many new advances suggest that the use of tocotrienols for health improvement or therapeutic purposes is promising. Although the mechanisms of action of tocotrienols in certain disease conditions have been explored, more detailed investigations into the fundamentals of the health-promoting effects of these molecules must be elucidated before they can be recommended for health improvement or for the treatment or prevention of disease. Furthermore, many of the studies on the effects of tocotrienols have been carried out using cell lines and animal models. The effects in humans must be well established before tocotrienols are used as therapeutic agents in various disease conditions, hence the need for more evidence-based human clinical trials.

**Keywords:** health-promoting benefits, therapeutic applications, tocotrienols, vitamin E.

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Wong RSY, Radhkrishnan AK, Tengku Azmi Tengku Ibrahim, Cheong SK. Delta- and gamma-tocotrienols induce classical ultrastructural apoptotic changes in human T lymphoblastic leukaemic cells. *Microscopy and Microanalysis*, 2012; (in press).

# Delta- and gamma-tocotrienols induce classical ultrastructural apoptotic changes in human T lymphoblastic leukaemic cells

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#### **Abstract**

Tocotrienols are isomers of the vitamin E family, which have been reported to exert cytotoxic effects in various cancer cells. Although there have been some reports on the effects of tocotrienols in leukemic cells, ultrastructural evidence of tocotrienol-induced apoptotic cell death in leukemic cells is lacking. The present study investigated the effects of three isomers of tocotrienols (alpha, delta, and gamma) on a human T lymphoblastic leukemic cell line (CEM-SS). Cell viability assays showed that all three isomers had cytotoxic effects (p < 0.05) on CEM-SS cells with delta-tocotrienol being the most potent. Transmission electron microscopy showed that the cytotoxic effects by delta- and gamma-tocotrienols were through the induction of an apoptotic pathway as demonstrated by the classical ultrastructural apoptotic changes characterized by peripheral nuclear chromatin condensation and nuclear fragmentation. These findings were confirmed biochemically by the demonstration of phosphatidylserine externalization via flow cytometry analysis. This is the first study showing classical ultrastructural apoptotic changes induced by delta- and gamma-tocotrienols in human T lymphoblastic leukemic cells.

**Keywords**: tocotrienols, T lymphoblastic leukemia, phosphatidylserine externalization, peripheral chromatin condensation, nuclear fragmentation, apoptosis.

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Wu JC, Chye SM, Shih MK, Chen CH, Yang HL, Chen SC. Genotoxicity of dicrotophos, an organophosphorous pesticide, assessed with different assays in vitro. *Environmental Toxicol*ogy, 2012; 27(5): 307-315.

# Genotoxicity of dicrotophos, an organophosphorous pesticide, assessed with different assays in vitro

Jong-C. Wu<sup>1</sup>, Soi M. Chye<sup>2</sup>, Ming–K. Shih<sup>3</sup>, Chin-H. Chen<sup>4</sup>, Hsin-L. Yang<sup>5</sup>, Ssu C. Chen<sup>6</sup>.

#### **Abstract**

Dicrotophos is a systemic insecticide with a wide range of applications. We investigated the genotoxicity of dicrotophos using the Ames test, the chromosome aberration test in CHO-K1 cells, and the comet assay in the Hep G2 cells, while this chemicals' toxicity to both the cell lines was evaluated with the MTT assay. Results showed that dicrotophos did not show any cytotoxicity to CHO-K1 cells, whereas it was cytotoxic to HepG2 cells incubated for 24 h but not for 2 h. For genotoxicity of dicrotophos, a significant change in the numbers of bacterial reverants using *Salmomella typhimurium* TA97a, TA98, TA100, TA102, and TA1535 as the tester strains, an increase in the frequencies of chromosome aberration in CHO-K1 cells, and an induced DNA damage in HepG2 cells were observed, indicating that dicrotophos was genotoxic in these three performed assays. From this study, we provide further evidence towards of genotoxic effects of dicrotophos.

**Keywords**: dicrofotos, Ames test, chromosome aberration, comet assay.

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Yadav H. A review of maternal mortality in Malaysia. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S142-S151.

### A review of maternal mortality in Malaysia

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#### **Abstract**

There has been a significant decline in maternal mortality from 540 per 100,000 live births in 1957 to 28 per 100,000 in 2010. This decline is due to several factors. Firstly the introduction of the rural health infrastructure which is mainly constructing health centres and midwife clinics for the rural population. This provided the accessibility and availability of primary health care and specially, antenatal care for the women. This also helped to increase the antenatal coverage for the women to 98% in 2010 and it increased the average number of antenatal visits per women from 6 in 1980 to 12 visits in 2010 for pregnant women. Along with the introduction of health centres, another main feature was the introduction of specific programmes to address the needs of the women and children. In the 1950s the introduction of Maternal and Child Health (MCH) programme was an important step. Later in the late 1970s there was the introduction of the High Risk Approach in MCH care and Safe Motherhood in the 1980s. In 1990, an important step was the introduction of the Confidential Enguiry into Maternal Deaths (CEMD). Another significant factor in the reduction is the identification of high risk mothers and this is being done by the introduction of the colour coding system in the health centres. Other factors include the increase in the number of safe deliveries by skilled personnel and the reduction in the number of deliveries by the Traditional Birth Attendants (TBAs). The reduction in fertility rate from 6.3 in 1960 to 3.3 in 2010 has been another important factor. To achieve the 2015 Millennium Development Goals (MDG) to further reduce maternal deaths by 50%, more needs to be done especially to identify maternal deaths that are missed by omission or misclassification and also to capture the late maternal deaths.

**Keywords**: Maternal mortality, Risk Approach in MCH Care, Confidential Enquiry, Malaysia.

Yeoh PN. Growing professionalism in pharmacy students. *International e-Journal of Science, Medicine and Education (IeJSME)*, 2012; 6(Suppl. 1): S152-S154.

### **Growing professionalism in pharmacy students**

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#### **Abstract**

IMU is one of 17 institutions of higher learning conducting the Bachelor of Pharmacy course in Malaysia. The White paper on pharmacy student professionalism by the Task Force of the American Pharmaceutical Association Academy of Students of Pharmacy together with the American Association of Colleges of Pharmacy Council of Deans mentioned 10 essential traits of a professional, recommending their early development. Since the beginning of the IMU Bachelor of Pharmacy (BPharm) (Hons) course in July 2004 on Registration Day, IMU has adopted the concept of developing professionalism in the pharmacy student from the very first day of university, by having the White Coat Ceremony where the entire class takes the Pledge of Professionalism (adapted from the Task Force) against the "Code of Conduct for Pharmacists and Bodies Corporate" by the Pharmacy Board of Malaysia in the presence of the Senior Director of the Pharmaceutical Services Division of the Ministry of Health, Malaysia and the President of the Malaysian Pharmaceutical Society (MPS). Throughout their 4 years in IMU, the pharmacy students are exposed to various aspects of professionalism in different subjects in their curriculum. On 23rd April 2012, when the fifth cohort of BPharm students received their final examination results, "Pharmacy Professional Day" was launched. The graduating students took the Oath of a Pharmacist (adapted from the American Association of Colleges of Pharmacy's Oath with slight amendment). Talks by alumni and speakers from MPS aimed to facilitate the transition of the new graduate to working life as a pharmacist.

**Keywords**: Pharmacy, White-Coat-Ceremony, Professionalism, Oath of a Pharmacist.