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11	Babu MA, Shukla R, Nath C, Kaskhedikar SG. Synthesis and biological evaluation of ester derivatives of indomethacin as selective COX-2 inhibitors. <i>Med Chem Res</i> 2011; doi 10.1007/s00044-011-9747-5	25
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15	Chakravarthi S, HS Nagaraja. A comprehensive review of the occurrence and management of systemic candidiasis as an opportunistic infection. <i>Microbiol J</i> 2011; 1(1): 1-7; doi: 10.3923/mj.2011.1.7	28
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44	Hasan SS, Chew S Yong, Muneer GB, Cho Naing, Abdul Hameed, Mirza R Baig, Shahid M Iqbal, Therese Kairuz. Understanding, perceptions and self-use of complementary and alternative medicine (CAM) among Malaysian pharmacy students. <i>BMC Compl Alternat Med</i> 2011; 11: 95-103	55
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53	Jeevaratnam K, Tee SP, Zhang Y, Rewbury R, Guzadhur L, Duchmke R, Grace AA, Lei M, Huang CLH. Delayed conduction and its implications in murine <i>Scn5<sup>+/+</sup></i> hearts: independent and interacting effects of genotype, age, and sex. <i>Eur J Physiol</i> 2011; 461: 29-44	64
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65	Lai NM, Teng CL, Lee ML. Interpreting systemic reviews: are we ready to make our own conclusions? A cross-sectional study. <i>BMC Med</i> 2011; 9: 30-38	74-75
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73	Loh KY, Nazimah I. A still born baby with cranial vault defects. <i>Malaysian Fam Physician</i> 2011; 6(1): 1985-2274 (electronic)	*
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Abdulrazaq Bidemi Nafiu, Maung Maung Cho, Ni Ni Win. Beneficial effects of ginger (*Zingiber officinale*) on carbohydrate metabolism in streptozotocin-induced diabetic rats. *Brit J Nutr* 2011; doi: 10.1017/S0007114511006635

## **Beneficial effects of ginger (*zingiber officinale*) on carbohydrate metabolism in streptozotocin-induced diabetic rats**

Nafiu Bidemi Abdulrazaq<sup>1</sup>, Maung Maung Cho<sup>2</sup>, Ni Ni Win<sup>3</sup>, Rahela Zaman<sup>1</sup> and Mohammad Tariqur Rahman<sup>1</sup>

<sup>1</sup>Department of Biomedical Science, Faculty of Science, Jalan Istana, Bandar Indera Mahkota, 25200 Kuantan, Malaysia

<sup>2</sup>Department of Basic Medical Science, International Islamic University Malaysia, Jalan Istana, Bandar Indera Mahkota, Kuantan, Pahang 25200, Malaysia

<sup>3</sup>School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia.

### **Abstract**

*Zingiber officinale* (ZO), commonly known as ginger, has been traditionally used in the treatment of diabetes mellitus. Several studies have reported the hypoglycaemic properties of ginger in animal models. The present study evaluated the antihyperglycaemic effect of its aqueous extract administered orally (daily) in three different doses (100, 300, 500 mg/kg body weight) for a period of 30 d to streptozotocin (STZ)-induced diabetic rats. A dose-dependent antihyperglycaemic effect revealed a decrease of plasma glucose levels by 38 and 68% on the 15th and 30th day, respectively, after the rats were given 500 mg/kg. The 500 mg/kg ZO significantly ( $P<0.05$ ) decreased kidney weight (% body weight) in ZO-treated diabetic rats v. control rats, although the decrease in liver weight (% body weight) was not statistically significant. Kidney glycogen content increased significantly ( $P<0.05$ ) while liver and skeletal muscle glycogen content decreased significantly ( $P<0.05$ ) in diabetic controls v. normal controls. ZO (500 mg/kg) also significantly decreased kidney glycogen ( $P<0.05$ ) and increased liver and skeletal muscle glycogen in STZ-diabetic rats when compared to diabetic controls. Activities of glucokinase, phosphofructokinase and pyruvate kinase in diabetic controls were decreased by 94, 53 and 61 %, respectively, when compared to normal controls; and ZO significantly increased ( $P<0.05$ ) those enzymes' activities in STZ-diabetic rats. Therefore, the present study showed that ginger is a potential phytomedicine for the treatment of diabetes through its effects on the activities of glycolytic enzymes.

**Key words:** *Zingiber officinale*, Carbohydrate metabolism, Diabetic rats, Tissue glycogen

Achike FI, To NH, Wang H, Kwan CY. Obesity, metabolic syndrome, adipocytes and vascular function: a holistic viewpoint. *Clin Exp Pharmacol Physiol* 2011; 38(1); 1-10

## **Obesity, metabolic syndrome, adipocytes and vascular function: a holistic viewpoint**

Francis I Achike<sup>\*</sup>, Nim-Hin Peter To<sup>†</sup>, HuidiWang<sup>‡</sup> and Chiu-Yin Kwan<sup>†</sup>

<sup>\*</sup>International Medical University, Kuala Lumpur, Malaysia,

<sup>†</sup>Vascular Biology Research Group, China Medical University, Taichung, Taiwan, China

<sup>‡</sup>Brock University, St Catharines, Ontario, Canada

### **Abstract**

1. Obesity is a metabolic disease of pandemic proportions largely arising from positive energy balance, a consequence of sedentary lifestyle, conditioned by environmental and genetic factors. Several central and peripheral neurohumoral factors (the major ones being the anorectic adipokines leptin and adiponectin and the orexigenic gut hormone ghrelin) acting on the anorectic (pro-opiomelanocortin and cocaine- and amphetamine-regulated transcript) and orexigenic (neuropeptide Y and agouti related protein) neurons regulate energy balance. These neurons, mainly in the arcuate nucleus of the hypothalamus, project to parts of the brainmodulating functions such as wakefulness, autonomic function and learning. A tilt in the anorectic–orexigenic balance, perhaps determined genetically, leads to obesity.

2. Excess fat deposition requires space, created by adipocyte (hypertrophy and hyperplasia) and extracellular matrix (ECM) remodelling. This process is regulated by several factors, including several adipocyte-derived Matrix metalloproteinases and the adipokine cathepsin, which degrades fibronectin, a key ECM protein. Excess fat, also deposited in visceral organs, generates chronic low-grade inflammation that eventually triggers insulin resistance and the associated comorbidities of metabolic syndrome (hypertension, atherosclerosis, dyslipidaemia and diabetes mellitus).

3. The perivascular adipose tissue (PVAT) has conventionally been considered non-physiological structural tissue, but has recently been shown to serve a paracrine function, including the release of adipose-derived relaxant and contractile factors, akin to the role of the vascular endothelium. Thus, PVAT regulates vascular function *in vivo* and *in vitro*, contributing to the cardiovascular pathophysiology of the metabolic syndrome. Defining the mechanism of PVATregulation of vascular reactivity requires more and better controlled investigations than currently seen in the literature.

**Key words:** diabetes mellitus, metabolic syndrome, obesity, perivascular adipose tissue, vascular reactivity.

Acuin Cecilia S, Khor GL, Liabsuetrakul Tippawan, Achadi Endang L, Htay Thein Thein, Firestone Rebecca, Bhutta Zulfiqar. Maternal, neonatal, and child health in Southeast Asia: towards greater regional collaboration. *The Lancet* 2011; 377: 516-525

## **Maternal, neonatal, and child health in Southeast Asia: towards greater regional collaboration**

Cecilia S Acuin<sup>1</sup>, Geok Lin Khor<sup>2</sup>, Tippawan Liabsuetrakul<sup>3</sup>, Endang L Achadi<sup>4</sup>, Thein Thein Htay<sup>5</sup>, Rebecca Firestone<sup>6,7</sup>, Zulfiqar A Bhutta<sup>8</sup>

<sup>1</sup>Institute of Clinical Epidemiology, University of the Philippines, National Institutes of Health, Ermita, Manila, Philippines

<sup>2</sup>Faculty of Medicine and Health, International Medical University, Kuala Lumpur, Malaysia

<sup>3</sup>Epidemiology Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

<sup>4</sup>Faculty of Public Health, University of Indonesia and SEAMEO TROPMED, Regional Center for Community Nutrition, Jakarta, Indonesia

<sup>5</sup>Public Health Division, Department of Health, Ministry of Health, Myanmar

<sup>6</sup>China Medical Board, Cambridge, MA, USA

<sup>7</sup>Harvard Global Equity Initiative, Boston, MA, USA

<sup>8</sup>Department of Paediatrics and Child Health, Aga Khan University, Karachi, Pakistan

### **Abstract**

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

Ahmed SI, Hassali MA, Bukhari NI, Sulaiman SAA. A comparison of HIV/AIDS-related knowledge, attitudes and risk perceptions between final year medical and pharmacy students: A cross sectional study. HealthMED 2011; 5 (2): 317-326

## **A comparison of HIV/AIDS-related knowledge, attitudes and risk perceptions between final year medical and pharmacy students: a cross sectional study**

Syed Imran Ahmed<sup>1</sup>, Mohammad Azmi Hassali<sup>2</sup>, Nadeem Irfan Bukhari<sup>3</sup>, Siti Amrah Sulaiman<sup>4</sup>

<sup>1</sup> Lecture in Pharmacy Practice, School of Pharmaceutical and Health Sciences, International Medical University (IMU), Kuala Lumpur, Malaysia

<sup>2</sup> Lecture of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, University Sains Malaysia (USM), Penang, Malaysia.

<sup>3</sup> Department of Pharmaceutics, Faculty of Pharmacy, University of Punjab, Lahore, Pakistan

<sup>4</sup> Department of Pharmacology, School of Medical Sciences, University Sains Malaysia (USM), Malaysia

### **Abstract:**

Background:

Awareness about HIV/AIDS in future healthcare professionals is necessary to control growing epidemics of the above diseases.

Objective:

To evaluate and compare the knowledge, attitude and risk perceptions towards HIV/AIDS between the final year pharmacy and medical students at University Sains Malaysia.

Materials and Method:

In a cross sectional study, validated questionnaires were served to (130) pharmacy and (160) medical students in their final year of study. The data were analyzed to find differences at a p-value <0.05.

Results:

About 83% pharmacy and 65% medical students responded in this study. Though 36.1% pharmacy students showed confidence on their professional education, lesser number (9.2%) of pharmacy students demonstrated willingness to assist HIV patients. The majority (58.1%) of medical students were doubtful regarding their competency, 55.2% were willing to assist, while 50.5% were confident on their professional education. About 72 % of medical students feared of acquiring HIV in professional life compared 29.6% (p=0.000) pharmacy students. Student groups were having lower awareness levels about PEP (post exposure prophylaxis), 18.5% by pharmacy and 48.6% by medical students (p= 0.000). About 40% of both groups demonstrated lack of unawareness for the use of antivirals to treat HIV/AIDS. Pharmacy students showed lesser awareness about opportunistic infections (18.5%). Low agreement on competency to treat and counsel HIV/AIDS patients were reflected, 12.9% and 29.6% for pharmacy and medical students, respectively. The confidence on the education provided was lower in pharmacy (36.1%) and medical students (49.1%).

Conclusion:

Significant misconceptions, negative attitudes and risk perceptions were indicated by the pharmacy and medical students and should be addressed with educational and practical programs.

**Key words:** AIDS (Acquired Immunity Deficiency syndrome), HIV (Human Immunodeficient virus), PEP (Post exposure prophylaxis), HCP (Health care professionals)

Aisyah Ali, Vasudevan Ramachandran Patimah Ismail, Christoper Lim Thiam Seong, SChakravarthi S. Analysis of insertion/deletion polymorphism of angiotensin converting enzyme gene in Malaysian end stage renal disease patients. J Renin-Angiotensin-Aldosterone System 2011; doi: 10.1177/1470320310392096

## **Analysis of insertion/deletion polymorphisms of the angiotensin converting enzyme gene in Malaysian end-stage renal disease patients**

Aisyah Ali<sup>1</sup>, Ramachandran Vasudevan<sup>1</sup>, Patimah Ismail<sup>1</sup>, Christoper Lim Thiam Seong<sup>2</sup> and Srikumar Chakravarthi<sup>3</sup>

<sup>1</sup> Molecular Biology and Bioinformatics Lab, Department of Biomedical Sciences, Universiti Putra Malaysia, Malaysia

<sup>2</sup> Department of Medicine, Universiti Putra Malaysia, Malaysia

<sup>3</sup> Faculty of Medicine and Health Sciences, Department of Pathology, International Medical University, Malaysia

### **Abstract**

Introduction:

Insertion/deletion (I/D) polymorphisms found in the angiotensin converting enzyme (ACE) gene have been associated with hypertension, diabetes and renal disease. The present study sought to determine the association of I/D polymorphisms of the ACE gene with end-stage renal disease (ESRD) patients in Malaysia.

Materials and methods:

A total of 380 subjects were recruited to determine the genotypes of I/D polymorphisms of the ACE gene. Genotyping was performed using a PCR method. Statistical analyses were carried out using statistical software, and a level of  $p < 0.05$  was considered statistically significant.

Results:

The frequencies for II, ID and DD genotypes of the ACE gene were 24.7%, 65.80% and 9.47%, respectively, in ESRD patients, and in control subjects were 45.26%, 47.37% and 7.37% respectively. The frequency for the D allele was found to be higher (42.40%) in ESRD patients compared to control subjects (31.05%). The genotypic and allelic frequencies of I/D polymorphisms of the ACE gene differed significantly ( $p < 0.05$ ) between ESRD patients and control subjects in the Malaysian population.

Conclusion:

The findings of this study indicate that I/D polymorphisms of the ACE gene are a useful marker and are likely to play a major role in determining genetic susceptibility to ESRD in the Malaysian population.

**Key words:** Angiotensin converting enzyme, end-stage renal disease, insertion/deletion, PCR, polymorphism, Malaysia

Ambikaborthy J, Ibrahim H, Ambu S, Chakravathi S, Awang K, Vijayan J. Efficacy evaluations of *Mimosa pudica* tannin isolate (MPT) for its anti-ophidian properties. *J Ethnopharmacol* 2011; 137: 257-262

## **Efficacy evaluations of *Mimosa pudica* Tannin Isolate (MPT) for its anti-ophidian properties**

Jamunaa Ambikaborthy<sup>a</sup>, Halijah Ibrahim<sup>a</sup>, Stephen Ambu<sup>b</sup>, Srikumar Chakravarthi<sup>b</sup>, Khalijah Awang<sup>c</sup>, Jaya Vejjayan<sup>d</sup>

<sup>a</sup> Institute of Biological Sciences, University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>b</sup> International Medical University, 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>c</sup> Chemistry Department, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>d</sup> School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon Selatan, 46150 Bandar Sunway, Selangor, Malaysia

### **Abstract:**

Aim of the study:

Evaluations of the anti-snake venom efficacy of *Mimosa pudica* tannin isolate (MPT) obtained from root of the plant.

Materials and method:

MPT was investigated in vitro and in vivo for its efficacy against the venom of *Naja kaouthia* snake.

Results:

In vitro: (1) mice injected i.p. with MPT pre-incubated with *Naja kaouthia* venom at concentrations as low as 0.625 mg/ml showed 100% survival after a 24-h observation period. (2) In the proteomics study, mice injected with MPT pre-incubated with the *Naja kaouthia* venom showed down-regulation of five serum proteins. (3) In the protein-dye-binding study, the percentage of Bradford dye-protein binding showed a reduction relative to the decrease in MPT concentration used to incubate with the venom. In vivo: the results from the animal studies showed that MPT had no in vivo protection against the *Naja kaouthia* venom (0.875 mg/kg) in four different rescue modes and in an oral pre-treatment experiment.

Conclusion:

The study indicated the promising ability of MPT to neutralize the *Naja kaouthia* venom in in vitro experiments but fell short in its in vivo potential. As such, the use of *Mimosa pudica* (Mimosaceae) as therapeutics for snake bites is questionable as all the possible in vivo rescue studies and pre-treatment of the active constituents showed no protection against the affected mice.

**Key words:** Touch me not, Snake venom, Proteomics, Polyphenol, Plant

Appukutty M, Radhakrishnan AK, Ramasamy Kalavathy, Abu Bakar Abdul Majeed, Mohd Ismail Noor, Nik Shanita Safii, Karunthan Chinna, Poh bee Koon. Modulation of interferon gamma response through orally administered bovine colostrum in active adolescent boys. *Biomed Res* 2011; 22(1): 18-22

## **Modulation of interferon gamma response through orally administered bovine colostrum in active adolescent boys**

Mahenderan Appukutty<sup>1,2</sup>, Ammu Kutty Radhakrishnan<sup>3\*</sup>, Kalavathy Ramasamy<sup>4</sup>, Abu Bakar Abdul Majeed<sup>4</sup>, Mohd Ismail Noor<sup>1</sup>, Nik Shanita Safii<sup>1</sup>, Karuthan Chinna<sup>5</sup>, Poh Bee Koon<sup>1</sup>

<sup>1</sup>Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia, Malaysia

<sup>2</sup>Faculty of Sports Science and Recreation, Universiti Teknologi MARA, Malaysia

<sup>3</sup>Faculty of Medicine and Health, International Medical University, Malaysia

<sup>4</sup>Faculty of Pharmacy, Universiti Teknologi MARA, Malaysia

<sup>5</sup>Faculty of Computer and Mathematical Sciences, Universiti Teknologi MARA, Malaysia

### **Abstract**

Bovine colostrum (BC) is a rich source of bioactive components reported to have health promoting effects. The purpose of the present study was to determine the effects of six-week supplementation of BC on the production of gamma-interferon (IFN- $\gamma$ ) by mitogen-stimulated peripheral blood leucocytes (PBL) in active adolescent male. Subjects were recruited from the students who were undergoing regular athletics training. The subjects were randomly assigned into control and experimental groups. The control group (n=18) received daily supplementation of skim milk while the experimental group (n=18) received bovine colostrum (20 g/day). Fasting venous blood samples were collected on day-0 and day-42 for measurement of IFN- $\gamma$  produced by concanavalin A (Con A)-stimulated PBL. Interferon- $\gamma$  levels were quantified using ELISA. Changes in IFN- $\gamma$  levels from baseline to endpoints for both groups were compared and presented as mean ( $\pm$  SD). Although baseline levels of cytokine concentrations were similar in both groups, there was a decreasing trend in IFN- $\gamma$  production by the mitogen-stimulated PBL from subjects who received the bovine colostrum supplement compared to controls. The findings of the present study suggest that oral supplementation of bovine colostrum for a period of 6 weeks may modulate *in vitro* IFN- $\gamma$  concentration.

**Key words:** Bovine colostrum: Dietary intervention, Adolescent male, Immune response



Babu MA, Shukla R, Nath C, Kaskhedikar SG. Synthesis and biological evaluation of ester derivatives of indomethacin as selective COX-2 inhibitors. *Med Chem Res* 2011; doi 10.1007/s00044-011-9747-5

## **Synthesis and biological evaluation of ester derivatives of indomethacin as selective COX-2 inhibitors**

M. Arockia Babu<sup>1</sup>, Rakesh Shukla<sup>2</sup>, Chandishwar Nath<sup>2</sup> and S. G. Kaskhedikar<sup>3</sup>

<sup>1</sup>School of Pharmacy and Health Sciences, International Medical University, 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Division of Pharmacology, Central Drug Research Institute, Lucknow 226 001, India

<sup>3</sup>Department of Pharmacy, Shri G. S. Institute of Technology and Science, Indore 452003, India

### **Abstract**

The ester derivatives of indomethacin were prepared by condensing indomethacin with an equimolar quantity of an appropriate alcoholic compound in anhydrous dichloromethane in the presence of DCC and DMAP. Spectral studies comprising of IR, <sup>1</sup>H NMR, mass, and microanalysis were performed in order to confirm their structures. In vivo anti-inflammatory studies were carried out using carrageenan rat paw edema method and in vivo ulcerogenic studies by ulcer index method for the panel of synthesized compounds. Out of eleven compounds, the compound IIc displayed moderate anti-inflammatory activity with no observable ulcerogenic effect when compared to indomethacin. Furthermore, compound IIc, indomethacin and celecoxib were tested at a concentration of 20 μM against COX-1 and COX-2 enzymes by colorimetric COX inhibitor screening assay. Compound IIc was found to be active against COX-2 and COX-1 enzymes exhibiting 62.0 and 12.9% inhibition, respectively.

**Key words:** Indomethacin esters, COX-2 inhibitors, Colorimetric COX inhibitor screening assay

Bajuri Mohd Yazid, Maidin S, Rauf A, Baharuddin M, Harjeet S. Functional outcomes of conservatively treated clavicle fractures. Clinics 2011; 66(4): 635-639

## Functional outcomes of conservatively treated clavicle fractures

Mohd Yazid Bajuri<sup>I</sup>, S. Maidin<sup>I</sup>, A. Rauf<sup>II</sup>, M. Baharuddin<sup>III</sup>, S. Harjeet<sup>II</sup>

<sup>I</sup>Department of Orthopaedics and Traumatology, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia

<sup>II</sup>Department of Orthopaedics, Tuanku Ja'afar General Hospital, Seremban, Malaysia

<sup>III</sup>Pantai Medical Centre Batu Pahat, International Medical University, Seremban, Malaysia

### Abstract

#### Objective:

The main aim of the study was to analyze the outcomes of clavicle fractures in adults treated nonsurgically and to evaluate the clinical effects of displacement, fracture patterns, fracture location, fracture comminution, shortening and fracture union on shoulder function.

#### Methods:

Seventy clavicle fractures were non-surgically treated in the Orthopedics Department at the Tuanku Ja'afar General Hospital, a tertiary care hospital in Seremban, Malaysia, an average of six months after injury. The clavicle fractures were treated conservatively with an arm sling and a figure-eight splint for three weeks. No attempt was made to reduce displaced fractures, and the patients were allowed immediate free-shoulder mobilization, as tolerated. They were prospectively evaluated clinically and radiographically. Shoulder function was evaluated using the Constant scoring technique.

#### Results:

There were statistically significant functional outcome impairments in non-surgically treated clavicle fractures that correlated with the fracture type (comminution), the fracture displacement (21 mm or more), shortening (15 mm or more) and the fracture union (malunion).

#### Conclusion:

This article reveals the need for surgical intervention to treat clavicle fractures and improve shoulder functional outcomes.

**Key words:** clavicle, fracture, conservative surgical, functional.

Boo NY, Gan CY, Gian YW, Lim KSL, Krisna-Kumar H. Malaysian mothers' knowledge & practices on care of neonatal jaundice. *Mal Med J* 2011; 66(3): 239-243

## **Malaysian mothers' knowledge & practices on care of neonatal jaundice**

N Y Boo\*, C Y Gan\*, Y W Gian\*, K S L Lim\*, M W Lim\*, H Krishna-Kumar\*\*

\*Department of Paediatrics, Clinical School, International Medical University

\*\*Department of Obstetrics and Gynaecology, Hospital Tuanku Jaafar, Seremban, Negeri Sembilan, Malaysia

### **Abstract**

This study aimed to determine the gaps of knowledge and practices of care of neonatal jaundice among Malaysian mothers. It was a cross sectional study of 400 mothers who attended the obstetric clinics or were admitted to the obstetric wards of a general hospital. They were surveyed with a structured set of questionnaire. The results showed that a majority (93.8%) of them knew about neonatal jaundice, and 71.7% knew that jaundice lasting more than 2 weeks was abnormal. However, only 34.3% of them were aware that jaundice appearing during the first 36 hours of life was abnormal. Less than 20% knew about glucose-6-phosphate dehydrogenase deficiency and that fetal/maternal blood group differences could cause jaundice. Although 71.7% and 69.7%, respectively, of the mothers knew that severe jaundice could cause death and brain damage, only 38.4% of them were aware that severe jaundice could result in hearing impairment. A very low proportion (27.1%) of them was aware that putting jaundiced infants under the direct sun could result in dehydration and worsening of jaundice. Out of a maximum score of 15, the mean maternal knowledge score was 7.4 (95% confidence intervals: 7.1, 7.7). Majority (83.1%) of the multiparous mothers with a past history of having children developing neonatal jaundice (n=154) practiced placing their infants under the direct sun. This study revealed that there was a wide knowledge gap among Malaysian mothers on care of neonatal jaundice. Placing infants under the direct sun was still a common practice.

**Key words:** Maternal knowledge, Neonatal jaundice, Sunning

Chakravarthi S, Nagaraja HS. A comprehensive review of the occurrence and management of systemic candidiasis as an opportunistic infection. *Microbiol J* 2011; 1(1): 1-7; doi: 10.3923/mj.2011.1.7

## **A comprehensive review of the occurrence and management of systemic candidiasis as an opportunistic infection**

Srikumar Chakravarthi<sup>1</sup>, Nagaraja Haleagrahara<sup>2</sup>

<sup>1</sup>Department of Pathology, Faculty of Medicine, International Medical University, Malaysia

<sup>2</sup>Department of Human Biology, Faculty of Medicine, International Medical University, Malaysia

### **Abstract**

Candidiasis is a fungal infection which is prone to occur in people with immunosuppression due to debilitating diseases and nosocomial causes. The epidemiology of *Candida* fungal infections is on the rise and it is a common cause of systemic infections. Even though bloodstream infection is on the decline, the number of risk factors which could eventually lead to candidiasis has been increasing steadily. They include immunosuppression due to chemotherapy or corticosteroid therapy, diabetes mellitus, low birth weight in neonates, broad spectrum antibiotics, long term catheterization, haemodialysis and parenteral nutrition. However, it has generally been observed that 3 main groups of patients are associated with candidiasis, namely those with neutropenic cancer, organ or stem cell transplant patients and those undergoing intensive care procedures. Discussion of surveillances and reports will be useful to improve our understanding of the importance of systemic *Candida* infections and to facilitate the prioritization of the investigation as well as the prevention efforts.

**Key words:** Systemic candidiasis, *Candida albicans*, immunosuppression

Chakravathi S, Nagaraja HS, Choo Zhen Wei, Wong SF, Mak JW, Radhakrishnan AK. A histopathological study of cardiac candidiasis and its behaviour under immunosuppressive effect of disseminated breast carcinoma. *The Cardiology* 2011; 6(1): 1-7; doi: 10.3923/tcard.2011.1.7

## **A histopathological study of cardiac candidiasis and its behaviour under immunosuppressive effect of disseminated breast carcinoma**

Srikumar Chakravathi<sup>1</sup>, Nagaraja HS<sup>2</sup>, Choo Zhen Wei<sup>3</sup>, Wong SF<sup>1</sup>, Mak JW<sup>1</sup>, Radhakrishnan A<sup>1</sup>

<sup>1</sup>Department of Pathology, Faculty of Medicine, International Medical University, Malaysia

<sup>2</sup>Department of Human Biology, Faculty of Medicine, International Medical University, Malaysia

<sup>3</sup>Faculty of Medicine, University of Queensland, Australia

### **Abstract**

Candidiasis is a fungal infection which patients with solid malignancies are at high risk. While few studies have shown evidence of this disease co-existing with malignancy-induced immunosuppression disease, there never were any exclusive animal studies demonstrating this relationship, especially cardiac candidiasis with breast cancer. In fact, the exact causative mechanism of candidiasis is by and large still under much speculation. This study aims to demonstrate this relationship by observing the histopathological changes of the hearts harvested from female Balb/c mice which were experimentally induced with breast cancer and inoculated with candida. The mice were randomly assigned to 5 different groups (n = 12). The first group (group 1) was injected with Phosphate Buffer Solution (PBS), the second group (group 2) with candida, third group (Group 3) with breast cancer and the final two groups, fourth and fifth group (Group 4 and 5) having co-existence of candidiasis and breast cancer at 2 different doses of candidiasis, respectively. Inoculation of mice with candidiasis was done by intravenous injection of *Candida albicans* via the tail vein after successful culturing methods. Induction of mice with breast cancer is via injection of 4T1 cancer cells at the right axillary mammary fatpad after effective culturing methods. The prepared slides with the livers were stained with Haematoxylin and Eosin (H and E), Periodic Acidic Schiff (PAS) and Gomori Methenamine Silver (GMS) stains for histopathology analysis. Grading of primary tumour and identification of metastatic deposits were done. Scoring of inflammation and congestion in the liver was done. Statistical tests done to compare group 2 and 4 showed that group 4 exhibited a highly statistically significant increase in inflammation and congestion ( $p < 0.01$ ). The median severity of candidiasis was also increased in group 4 as compared to group 2. In conclusion, based on the above evidences, cardiac candidiasis was significantly increased in mice with breast cancer.

**Key words:** Cardiac candidiasis, breast cancer, *Candida albicans*, immunosuppression

Chan LL, Mak JW, Low Yoon Thong, Koh Thuan Tzen, Init Ithoi, Shar Mariam M. Isolation and characterization of *Acanthamoeba* spp. from air-conditioners in Kuala Lumpur, Malaysia. *Acta Trop* 2011; 117: 23-30

## **Isolation and characterization of *Acanthamoeba* spp. from air-conditioners in Kuala Lumpur, Malaysia**

Li-Li Chan<sup>a</sup>, Joon-Wah Mak<sup>a</sup>, Yoon-Tong Low<sup>a</sup>, Thuan-Tzen Koh<sup>a</sup>, Init Ithoi<sup>b</sup>, Shar Mariam Mohamed<sup>a</sup>

<sup>a</sup> Department of Postgraduate and Research, International Medical University, No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>b</sup> Department of Parasitology, University of Malaya, 50603 Kuala Lumpur, Malaysia

### **Abstract**

During a study on the quality of the indoor environment, *Acanthamoeba* spp. were detected in 20 out of 87 dust samples collected from air-conditioners installed in a four-story campus building located in Kuala Lumpur, Malaysia. Twenty-one cloned *Acanthamoeba* isolates designated as IMU1 to IMU21 were established from the positive primary cultures. Five species were identified from the 16 isolates according to the morphological criteria of Pussard and Pons; i.e. *A. castellanii*, *A. culbertsoni*, *A. griffini*, *A. hatchetti* and *A. polyphaga*. Species identities for the remaining five isolates (IMU4, IMU5, IMU15, IMU20 and IMU21), however, could not be determined morphologically. At genotypic characterization, these isolates were placed into T3 (IMU14); T5 (IMU16 and IMU17) and T4 (all the remaining isolates). To predict the potential pathogenicity of these *Acanthamoeba* isolates, thermo- and osmotolerance tests were employed; many isolates were predicted as potential human pathogens based on the outcome of these tests. This is the first time potentially pathogenic *Acanthamoeba* have been isolated from air-conditioners in Malaysia.

**Key words:** *Acanthamoeba*, Air-conditioners, Environmental isolates, Kuala Lumpur, Malaysia

Chew SC, Khor GL, Loh SP. Association between dietary folate intake and blood status of folate and homocysteine in Malaysian adults. *J Nutr Sci Vitaminol* 2011; 57: 150-155

## **Association between dietary folate intake and blood status of folate and homocysteine in Malaysian adults**

Siew-Choo Chew<sup>1</sup>, Geok-Lin Khor<sup>2</sup> and Su-Peng Loh<sup>1</sup>

<sup>1</sup>Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

<sup>2</sup>Department of Nutrition and Dietetics, Faculty of Medicine and Health, International Medical University, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Folate is of prime interest among investigators in nutrition due to its multiple roles in maintaining health, especially in preventing neural tube defects and reducing the risk of cardiovascular diseases. We investigated the effect of dietary folate intake on blood folate, vitamin B<sub>12</sub>, vitamin B<sub>6</sub> and homocysteine status. One hundred subjects consisting of Chinese and Malay subjects volunteered to participate in this cross-sectional study. Dietary folate intake was assessed by 24-h dietary recall and a food-frequency questionnaire (FFQ). Serum and red blood cell folate were analyzed using a microbiological assay, while serum vitamin B<sub>12</sub> was determined by electrochemiluminescence immunoassay (ECLIA), and high performance liquid chromatography (HPLC) was used for the determination of serum vitamin B<sub>6</sub> and homocysteine. The mean folate intake, serum folate, RBC folate, serum vitamin B<sub>12</sub> and B<sub>6</sub>, were higher in female subjects, with exception of serum homocysteine. The Chinese tended to have higher folate intake, serum folate, RBC folate and vitamin B<sub>12</sub>. A positive association was found between folate intake and serum folate while a negative association was found between folate intake and serum homocysteine. Stepwise linear regression of serum folate showed a significant positive coefficient for folate intake whilst a significant negative coefficient was found for serum homocysteine when controlling for age, gender and ethnicity. In conclusion, high dietary folate intake helps to increase serum folate and to lower the homocysteine levels.

**Key words:** microbiological assay, folate, homocysteine, ethnicity

Chew WK, Ignacio S. Simultaneous HPLC determination of metronidazole and spiramycin in plasma and brain of mouse. *Curr Pharmaceut Anal* 2011; 7(4): 262-267

## Simultaneous HPLC determination of metronidazole and spiramycin in plasma and brain of mouse

Chew W.Kit<sup>1</sup> and Ignacio Segarra<sup>2</sup>

<sup>1</sup>Department of Human Biology, School of Medicine, International Medical University, No 126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia.

<sup>2</sup>Department of Pharmaceutical Technology, School of Pharmacy and Health Sciences, International Medical University, No 126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia.

### Abstract

Treatments fail to eliminate *Toxoplasma gondii* due to low drug brain penetration. Spiramycin is an Mrp2, P-glycoprotein substrate, active in acute and chronic murine toxoplasmosis. Metronidazole is a CYP3A4 inhibitor and P-glycoprotein substrate. We developed a simple HPLC method to analyze spiramycin and metronidazole simultaneously. Male Balb/c mice were randomly selected in three groups and were dosed orally either 500 mg/kg metronidazole (group1, n=4) or 400 mg/kg spiramycin (group2, n=4) or coadministered 500 mg/kg metronidazole 30 min prior to 400mg/kg spiramycin (group3, n=4). Mice were euthanized 2 hours after spiramycin administration. Metronidazole and spiramycin brain and plasma concentrations were measured by HPLC using a Phenomenex® C-18 (150x3.8mm, 5µM) column and acetonitrile-phosphate buffer (pH2.5) gradient elution (20/80 to 30/70 in 3 min) at 1ml/min flow, 29°C and 232nm. The method was linear (0.25-50.0 µg/ml), the LLOQ was 0.25 µg/ml, intra- and interday variability, precision and accuracy were within 15%. Recoveries were above 75% and there was no matrix interference. Metronidazole eluted at 3 min and spiramycin at 5min. spiramycin did not affect plasma metronidazole concentration (6.93 ± 0.48 µg/ml in combination vs. alone 7.65 ± 0.55 µg/ml) or brain (2.96 ± 0.60 µg/g after coadministration vs. control, 4.02 ± 0.78 µg/g). Metronidazole did not change spiramycin plasma concentration (coadministration: 3.94 ± 1.30 µg/ml, control: 3.71 ± 0.94 µg/ml). However, spiramycin brain concentration increased 2-fold after metronidazole coadministration from 2.44 ± 0.33 µg/g to 4.83 ± 1.25 µg/g (P<0.05). Metronidazole increased spiramycin brain uptake, probably due to P-glycoprotein inhibition, which may improve toxoplasmosis encephalitis treatments.

**Key words:** Brain uptake, drug-drug interaction, metronidazole, spiramycin, *Toxoplasma Gondii*



Chitneni M, Kok Khiang Peh, Yusrida Darwis, Muthanna Abdulkarim, Ghassan Zuhair Abdullah, Mohammed Javed Q. Intestinal permeability studies of sulpiride incorporated into self-microemulsifying drug delivery system (SMEDDS). Pak J Pharm Sci 2011; 24(2): 113-21.

## **Intestinal permeability studies of sulpiride incorporated into self-microemulsifying drug delivery system (SMEDDS)**

Mallikarjun Chitneni<sup>1,2</sup>, Kok Khiang Peh<sup>2</sup>, Yusrida Darwis<sup>2</sup>, Muthanna Abdulkarim<sup>2</sup>, Ghassan Zuhair Abdullah<sup>2</sup>, Mohammed Javed Qureshi<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Technology, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Pharmaceutical Technology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia

### **Abstract**

The objective of the present study was to determine the intestinal absorption of sulpiride incorporated into SMEDDS by means of single-pass intestinal perfusion method (SPIP) in rat and to compare the effective permeability coefficient obtained with that of drug solution and micellar solution. The prepared SMEDDS and micelles formulations were investigated for droplets size. SPIP experiment was performed using the three formulations in three of the secluded regions of the small intestine (duodenum, jejunum, and ileum). The amount of the drug in the samples was estimated by HPLC and the effective permeability coefficients in rats were calculated. The human intestinal permeability was predicted based on rat effective permeability coefficient value. The dilution stability of the formulations was also determined. The average droplet size of SMEDDS and micelles was 9.27 nm and 7.20 nm respectively. The effective permeability coefficient of sulpiride was appreciably lower in the ileum weighed against jejunum and duodenum when administered as a solution ( $p < 0.05$ ). The estimated human absorption of sulpiride for the SMEDDS dilutions was superior to that from solution ( $p < 0.05$ ) and similar to micellar solution. The micellar dilutions were unstable whereas the SMEDDS dilutions were stable. Based on the above results, SMEDDS can be a potential candidate for improving the peroral absorption of the sulpiride.

**Key words:** Sulpiride, single-pass intestinal perfusion technique, SMEDDS, micellar solution, effective permeability coefficient

Chiu CK, Low TH, Tey YS, Singh VA, Shong HK. The efficacy and safety of intramuscular injections of Methylcobalamin in patients with chronic non-specific low back pain: a randomised controlled trial. Singapore Med J 2011; 52(12): 868-873

## **The efficacy and safety of intramuscular injections of Methylcobalamin in patients with chronic non-specific low back pain: a randomised controlled trial**

Chiu C K<sup>1</sup>, Low T H<sup>2</sup>, Tey Y S<sup>1</sup>, Singh V A<sup>2</sup>, Shong H K<sup>1</sup>

<sup>1</sup>Department of Orthopaedic Surgery, International Medical University, Clinical School, Seremban 70300, Malaysia

<sup>2</sup>Department of Orthopaedic Surgery, University of Malaya Medical Centre, Lembah Pantai, Kuala Lumpur 59100, Malaysia

### **Abstract**

#### **Introduction:**

Chronic, nonspecific low back pain is a difficult ailment to treat and poses an economic burden in terms of medical expenses and productivity loss. The aim of this study was to determine the efficacy and safety of intramuscular methylcobalamin in the treatment of chronic nonspecific low back pain.

#### **Methods:**

This was a double-blinded, randomised, controlled experimental study. 60 patients were assigned to either the methylcobalamin group or the placebo group. The former received intramuscular injections of 500 mcg parenteral methylcobalamin in 1ml solution three times a week for two weeks, and the placebo group received 1 ml normal saline. Patients were assessed with Oswestry Disability Index questionnaire Version 2.0 and Visual Analogue Scale pain score. They were scored before commencement of the injections and at two months interval.

#### **Results:**

Of the 60 patients, 27 received the placebo injections and 33 were given methylcobalamin injections. A total of 58 patients were available for review at two months (placebo: n is 26; methylcobalamin: n is 32). There was a significant improvement in the Oswestry Disability Index and Visual Analogue Scale pain scores in the methylcobalamin group as compared with the placebo group (p-value less than 0.05). Only minor adverse reactions such as pain and haematoma at the injection sites were reported by some patients.

#### **Conclusion:**

Intramuscular methylcobalamin is both an effective and safe method of treatment for patients with nonspecific low back pain, both singly or in combination with other forms of treatment.

**Key words:** methylcobalamin, nonspecific low back pain, vitamin B<sub>12</sub>

Cho Naing, Hasan SS, Kyan Aung. Do variations in allocation concealment methods influence the effects found in intervention reviews? *J Evidence-Based Med* 2011; 4: 255-258

## **Do variations in allocation concealment methods influence the effects found in intervention reviews?**

Cho Naing, Syed Shahzad Hasan and Kyan Aung

International Medical University, Kuala Lumpur 57000, Malaysia.

### **Abstract**

#### **Objective:**

(i) To explore any discrepancies in intervention effects between a set of Cochrane reviews that includes trials with liberal criteria and a set with restrictive criteria in which trials with liberal design have been removed from the review, and (ii) to suggest ways to improve the quality of evidence.

#### **Methods:**

A documentary analysis of three Cochrane reviews of intervention studies. The selection of the Cochrane reviews was based on a two-stage sampling. The stability of effect measures after removal of trials with liberal design was investigated.

#### **Results:**

In two of the three reviews, we found changes in the original effect measure of the intervention after removing the studies without allocation concealment. One of these reported an 87% greater relative risk when randomized trials with liberal design were included. In the other, the risk was 19.5% lower when randomized trials with liberal design were included.

#### **Conclusions:**

The instability of the effect measure indicates the importance of allocation concealment during recruitment for clinical trials. We recommend further research incorporating a large number of intervention reviews and factors other than allocation concealment.

Cho Naing, Pereira Joanne, Tatsuki Abe, Daniel Eh Zhen Wei, Ibrzah Abdul Rahman Bajera, Undugodage Heshan Kavida Perera. Predictors associated with the willingness to take human papilloma virus vaccination. J Com Hlth 2011; 37(2):288-293

## **Predictors associated with the willingness to take human papilloma virus vaccination**

Cho Naing, Joanne Pereira, Tatsuki Abe, Daniel Eh Zhen Wei, Ibrizah Binti Abdul Rahman Bajera and Undugodage Heshan Kavinda Perera

School of Medical Sciences, International Medical University, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Human papilloma virus vaccine is considered to be the primary form of cervical cancer prevention. The objectives were (1) to determine knowledge about, and perception of human papilloma virus infection in relation to cervical cancer, (2) to explore the intention of the community to be vaccinated with human papilloma virus vaccine, and (3) to identify variables that could predict the likelihood of uptake of the vaccine. A cross-sectional survey was carried out in a semi-urban Town of Malaysia, using a pre-tested structured questionnaire. Summary statistics, Pearson chi-square test and a binary logistic regression were used for data analysis. A total of 232 respondents were interviewed. Overall, only a few had good knowledge related to human papilloma virus (14%) or vaccination (8%). Many had misconceptions that it could be transmitted through blood transfusion (57%). Sixty percent had intention to take vaccination. In the binary logistic model, willingness to take vaccination was significant with 'trusts that vaccination would be effective for prevention of cervical cancer' ( $P = 0.001$ ), 'worries for themselves' ( $P < 0.001$ ) or 'their family members' ( $P = 0.003$ ) and 'being Indian ethnicity' ( $P = 0.024$ ). The model could fairly predict the likelihood of uptake of the vaccine (Cox & Snell  $R^2 = .415$ ; Nagelkerke  $R^2 = 0.561$ ). Results indicate that intensive health education dispelling misconception and risk perception towards human papilloma virus infection and cervical cancer would be helpful to increase the acceptability of vaccination program.

**Key words:** Human papilloma virus, Knowledge and perception, Willingness to take vaccination, Household survey

Cho Naing, Ren WY, Man CY, Fern KP, Qiqi C, Ning CN, Ee CW. Awareness of dengue and practice of dengue control among the semi-urban community: a cross sectional survey. J Com Hlth 2011; 36(6): 1044-1049

## **Awareness of dengue and practice of dengue control among the semi-urban community: a cross sectional survey**

Cho Naing, Wong Yih Ren, Chan Yuk Man, Koh Pei Fern, Chua Qiqi, Choo Ning Ning , Clarice Wong Syun Ee

School of Medical Sciences, International Medical University, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Primary prevention is the most effective measure in dengue prevention and control. The objectives were (i) to determine the level of knowledge and practice of dengue control amongst the study community, and (ii) to explore the factors affecting practice of dengue control in the study area. A cross-sectional study was conducted in a semi-urban Town of Malaysia, using a structured questionnaire covering sociodemography, knowledge related to dengue, knowledge related to *Aedes* mosquito and preventive measures against the disease. For comparison of survey responses, *chi*-square test was applied for categorical data. To explore the factors affecting the practice of dengue control, a linear regression model was introduced. Almost all of the respondents (95%) had heard about dengue. Overall, misconceptions of dengue transmission were identified and the practice of dengue control in the study population was insufficient. About half (50.5%) had misconceptions that *Aedes* can breed in dirty water and the preferred biting time is dusk or sunset (45.6%). Only 44.5% of the households surveyed had covered their water containers properly. Significant associations were found between knowledge scores of dengue and age ( $P = 0.001$ ), education level ( $P = 0.001$ ), marital status ( $P = 0.012$ ), and occupation ( $P = 0.007$ ). In regression analysis, only the knowledge of dengue was significantly and positively associated with practice on dengue control. A future study with larger samples and more variables to assess the knowledge, attitudes and practices of dengue control is recommended.

**Key words:** Knowledge on dengue, Practise of dengue control, Cross sectional survey

Cho Naing, Rachel Yi Ping Tan. Knowledge about the pandemic influenza A(H1N1), and willingness to accept vaccination: a cross-sectional survey. J Pub Hlth 2011; 19(6): 511-516

## **Knowledge about the pandemic influenza A (H1N1) and willingness to accept vaccination: a cross-sectional survey**

Cho Naing<sup>1</sup> and Rachel Yi Ping Tan<sup>2</sup>

<sup>1</sup>International Medical University, Kuala Lumpur 57000, Malaysia

<sup>2</sup>Melbourne Medical School, University of Melbourne, Victoria 3010, Australia

### **Abstract**

#### **Aims:**

(1) To determine undergraduate medical students' knowledge about and perceptions of influenza A (H1N1) infection, (2) to explore their willingness to be vaccinated, and (3) to identify variables that could predict the likelihood of taking the vaccination.

#### **Subject and methods:**

A cross-sectional survey with a convenience sample of 264 medical students was performed. Data were collected using a structured questionnaire. Summary statistics, Pearson *chi*-square test and logistic regression were used for data analysis.

#### **Results:**

A total of 264 undergraduate medical students were interviewed. All of them had heard of the influenza vaccine, but none had ever been vaccinated at the time of survey. Regarding mode of transmission, 38.3% had at least two misconceptions. Of them, 43% had willingness to be vaccinated. In the binary logistic model, willingness to be vaccinated was statistically significant with those who feared the resurgence of a pandemic influenza ( $p = 0.01$ ), those who trusted that vaccination would be effective for prevention of a pandemic influenza ( $p = 0.045$ ), and those who were worried for family ( $p = 0.03$ ) and if the vaccination would be freely provided ( $p = 0.04$ ).

#### **Conclusion:**

The findings may be helpful for decision makers and health care planners as baseline information for designing wider coverage of newly implemented vaccination programs.

**Key words:** Influenza A(H1N1), Knowledge, Willingness to be vaccinated, Survey

Chong GL, Chu WL, Rofina Yasmin Othman, Phang SM. Differential gene expression of an Antarctic *Chlorella* in response to temperature stress. *Polar Biol* 2011;34: 637-645

## Differential gene expression of an Antarctic *Chlorella* in response to temperature stress

G.L. Chong<sup>1</sup>, W.L. Chu<sup>2</sup>, R.Y. Othman<sup>1</sup>, S.M. Phang<sup>1</sup>

<sup>1</sup> Institute of Biological Sciences, University of Malaya, Kuala Lumpur, Malaysia

<sup>2</sup> International Medical University, Kuala Lumpur, Malaysia

### Abstract

Changes in gene expression are an indication of adaptation of Antarctic algae to temperature stress. The objective of the present study was to isolate and identify genes involved in the adaptation of an Antarctic *Chlorella* to temperature stress. The Antarctic alga *Chlorella* UMACC 234 was grown at 4°C (ambient), 20°C (optimum) and 30°C (heat stress) on a 12: 12 h light-dark cycle for 10 days. The mRNA from *Chlorella* UMACC 234 was extracted and converted to cDNA by reverse-transcription. Differentially expressed genes in response to the variation in temperatures were isolated and identified using the GeneFishing DEG Kit (Seegene), with 20 arbitrary annealing control primers (ACP). Some primers, for example ACP 6, ACP 9 and ACP 17 were useful in fishing out the genes which were over-expressed at different temperatures. The bands of interest were excised from the agarose gel and purified by gel extraction kit. The DNA fragments were cloned and sequenced. The gene coding for the 42 kDa protein of Photosystem II was found to be over-expressed at 4 °C.

Chu WL. Potential applications of antioxidant compounds derived from algae. *Curr Topics Nutraceut Res* 2011; 9(3): 83-98

## **Potential applications of antioxidant compounds derived from algae**

Wan-Loy Chu

International Medical University, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Algae produce a variety of antioxidant compounds ranging from  $\beta$ -carotene, astaxanthin, fucoxanthin, phycocyanin to sulfated polysaccharides. The commercial microalgae *Spirulina*, *Chlorella*, *Dunaliella* and *Haematococcus*, currently consumed as nutritional supplements, are rich in antioxidant compounds. For instance, astaxanthin from green alga *Haematococcus* is known to be a very powerful antioxidant while the hypersaline alga *Dunaliella salina* is being mass-cultured for the commercial production of natural  $\beta$ -carotene. The health benefits of antioxidant compounds such as sulfated polysaccharides and fucoxanthin from seaweeds (macroalgae) have also received much interest. Algae have great potential for nutraceuticals and functional food ingredients as studies have shown that antioxidants from algae may have preventive effects against diseases such as diabetes, atherosclerosis and cancers. However, the therapeutic potential of antioxidant compounds from algae is yet to be fully explored. In addition, the antioxidant extracts and compounds from algae may have applications in prolonging the shelf life of food products by retarding oxidation and peroxidation processes, as well as functional ingredient in the food industry. In this review, the potential applications of antioxidant compounds from the four commercial microalgae *Spirulina*, *Chlorella*, *Haematococcus* and *Dunaliella*, as well as those from seaweeds are highlighted.

**Key words:** Algae, Antioxidants, *Chlorella*, *Dunaliella*, *Haematococcus*, *Spirulina*



Daood U, Bandey N, Qasim SB, Omar H, Khan SA. Surface characterization analysis of failed dental implants using scanning electron microscopy. Acta Odontol Scand 2011; 69(6): 367-373

## Surface characterization analysis of failed dental implants using scanning electron microscopy

UMER DAOOD<sup>1</sup>, NINETTE BANDEY<sup>2</sup>, SAAD BIN QASIM<sup>3</sup>, HANAN OMAR<sup>1</sup> & SAAD A. KHAN<sup>1</sup>

<sup>1</sup>International Medical University, Malaysia,

<sup>2</sup>UAE Health Authority, United Arab Emirates

<sup>3</sup>King Saud University, Riyadh

### Abstract

Objective:

To investigate the failure of 15 dental implants (Paragon/Zimmer) in relation to their surface quality.

Materials and methods:

The study comprised of 15 dental implants (7 mm D Advent Implant, 3.9 mm D apex design implant), which were followed from surgery to completion of prosthetic restorations. The implants were placed during a 6-year period from 2003-2009 in non-smoking patients (male; 7, females; 5). There were eight upper and seven lower implants. Surface characterization after immersion in SBF of these failed implants was investigated using SEM and EDS compared to that of an unused implant of the same brand.

Results:

Results revealed that, following immersion in SBF, the implant surfaces showed new components like Ca<sup>+</sup>, Na<sup>+</sup> and Cl<sup>-</sup>, but in trace quantities.

Conclusions:

After SEM observation and EDS analysis, it was concluded that the apatite layer formation could not be verified.

**Key words:** titanium implants, dental implants, surface morphology

DMani Sheba. The grotesque female in Malaysian poems: shaping the migrant's psyche. *J Med Humanit* 2011; *J Med Humanit*, 2011, 32:4:305-313

## **The grotesque female in Malaysian poems: shaping the migrant's psyche**

Sheba DMani

Department of Language, Communication and Culture, International Medical University, No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

The works of Malaysian poet, Wong Phui Nam's *Against the Wilderness* (vii) *China bride* and *Variations on a Birthday Theme* (iv) *Kali*, illustrate a bride and a mother in terrifying images. Wong's stylistic form of representing the female body through startling images of inversion and degradation evoke feelings of unease. The suspension between the known and the unknown causes a bewildering reality verging on madness. Interpreted through the lens of the carnivalesque, specifically, the grotesque body, festive language and parody, I attempt to reconstruct the psyche of the Chinese migrant which underpins these poems. The migrant who arrived in Malaya during the colonial era in the early nineteenth century faced political and social struggles in adapting to a new land. In the poems, the migrant juxtaposes his position to a female and uses the female body as a site of contention to intensify the torment of the psyche and to reflect the despair of the Chinese in Malaysia.

**Key words:** Humanities, Body, Literature, Interdisciplinary studies

Dolatian M, Hasanpour A, Montazeri Sh, Heshmat R, Alavi Majd H. The effect of reflexology on pain intensity and duration of labor on primiparas. Iranian Red Crescent Med J 2011; 13(7): 475-479

## **The effect of reflexology on pain intensity and duration of labor on primiparas**

M Dolatian<sup>1</sup>, A Hasanpour<sup>1</sup>, Sh Montazeri<sup>2</sup>, R Heshmat<sup>3</sup>, H Alavi Majd<sup>4</sup>

<sup>1</sup>Department of Midwifery, Shahid Beheshti University of Medical Sciences, Tehran

<sup>2</sup>Department of Medicine and Health, International Medical University (IMU), Bukit, Jalil, Kuala Lumpur, Malaysia

<sup>3</sup>Acupuncture and Reflexology Specialist, Tehran

<sup>4</sup>Department of Biostatistics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

### **Abstract**

#### **Background:**

Reflexology is an ancient, mild and non-invasive technique, used widely as one of the nonpharmacological methods for pain relief. The aim of this research was to determine the effect of reflexology on pain intensity as well as to determine the duration of labor in primiparas.

#### **Methods:**

In 2008, a randomized clinical trial study was conducted randomly enrolling 120 parturient women with low risk pregnancy into three groups in Shahid Akbarabadi Hospital, Tehran, Iran. The first group received 40 minutes of reflexology at the beginning of active phase (4-5 cm cervical dilatation). Emotional support was offered for the second group in the same stage of pregnancy and with the same duration. The third group received only routine care during labor. Pain severity was evaluated with visual analogue scale (0 to 10 cm). In all groups, pregnant women were asked to evaluate the severity of pain experienced before and after intervention and also at cervical dilatations of 6-7 cm and 8-10 cm respectively. Data were collected through the numerical pain scale.

#### **Results:**

Pain intensity at all the three stages of cervical dilatation was significantly lower in the reflexology group. During the 4-5 cm dilatation stage, women in the supported group reported less severe pain compared to those receiving routine care, but no significant differences at the later stages of labor. This indicates that reflexology could decrease the duration of first, second and third stages of labor.

#### **Conclusion:**

Our findings showed that reflexology can be useful to decrease the pain intensity as well as duration of labor.

**Key words:** Reflexology; Primiparas; Pain intensity; Duration of labor

Dua K, Pabreja K, Lather Vinny. Molecular modeling of inclusion complex of aceclofenac with  $\beta$ -cyclodextrins. Indian J Novel Drug Delivery 2011; 3(1): 58-60

## **Molecular modeling of inclusion complex of aceclofenac with $\beta$ -cyclodextrins**

Kamal Dua<sup>1\*</sup>, Kavita Pabreja<sup>2</sup>, Vinny Lather<sup>3</sup>

<sup>1</sup>Department of Pharmaceutical Technology, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, MALAYSIA-57000

<sup>2</sup>Department of Life Sciences, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, MALAYSIA-57000

<sup>3</sup>Centro de Quimica da Madeira, Universidade da Madeira, Campus da Penteada, Funchal 9000390, Madeira, PORTUGAL

### **Abstract**

Aceclofenac (AF) is a new generational non-steroidal anti-inflammatory drug showing effective anti-inflammatory and analgesic properties with a good tolerability profile in a variety of painful conditions like ankylosing spondylitis, rheumatoid arthritis and osteoarthritis. Aceclofenac is very slightly soluble in water and therefore an attempt has been made to prepare inclusion complexes of aceclofenac with  $\beta$ -cyclodextrin ( $\beta$ -CD) and to explore the possibility of its molecular arrangement using molecular modeling and structural designing. The results indicated the relative energetic stability of the  $\beta$ -CD dimer-AF complex as compared to  $\beta$ -CD monomer-AF. Such molecular-modeling studies can be employed as an additional tool to support the formation of stable molecular inclusion complexation of any water insoluble drug complexed with cyclodextrins.

**Key words:** Aceclofenac,  $\beta$ -cyclodextrin, Molecular, Modeling

Dua K, Pabreja K, M.V. Ramana. Enhancement of dissolution behavior of Aceclofenac by complexation with b-Cyclodextrin-Choline Dichloride Coprecipitate. J of Dispersion Science and Tech 2011; 32:1477-84

## Enhancement of dissolution behavior of Aceclofenac by complexation with b-Cyclodextrin-Choline Dichloride Coprecipitate

Kamal Dua<sup>1</sup>, Kavita Pabreja<sup>2</sup>, and M. V. Ramana<sup>3</sup>

<sup>1</sup>Department of Pharmaceutical Technology, School of Pharmacy and Health Sciences, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Life Sciences, School of Pharmacy and Health Sciences, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>3</sup>Department of Pharmaceutical Chemistry, School of Science and Humanities, VIT University, Vellore, Tamil Nadu, India

### Abstract

The objective of the present investigation was to study the effect of presence of choline dichloride (CDC) in b-cyclodextrin (b-CD) on in vitro dissolution of aceclofenac (AF) from molecular inclusion complexes. The molecular inclusion complexes of AF with b-CD coprecipitated with CDC in 1:1 and 1:2M ratio were prepared using kneading method. In vitro dissolution of pure drug, physical mixtures, and cyclodextrin inclusion complexes (AF-b-CD-CDC) were carried out. Molecular inclusion complexes of aceclofenac with coprecipitated b-CD showed considerable increase in the dissolution rate in comparison with physical mixture and pure drug in 0.1N HCl, pH 1.2 and phosphate buffer, pH, 7.4. Inclusion complexes with 1:2M ratio showed maximum dissolution rate in comparison to other ratios. FTIR spectroscopy and differential scanning calorimetry studies indicated no interaction between AF and b-CD-CDC in complexes in solid state. Dissolution enhancement was attributed to the formation of water soluble inclusion complexes with the precipitated form of b-CD. The in vitro release from all the formulations was best described by first order kinetics ( $R^2=0.9354$  and  $0.9268$  in 0.1N HCl and phosphate buffer, respectively) followed by Higuchi release model ( $R^2=0.9029$  and  $0.9578$  in 0.1N HCl and phosphate buffer, respectively). In conclusion, dissolution of aceclofenac can be enhanced by using the b-CD-CDC coprecipitate as a host molecule.

**Key words:** Aceclofenac, b-CD, CDC, complexes, solubility

Dua K, Pabreja K, M.V. Ramana, Bukhari NI. Preparation, characterization and in vitro evaluation of Aceclofenac PVP-solid dispersions. J Dispersion Sci Technol 2011; 32(8): 1151-1157

## **Preparation, characterization, and in vitro evaluation of Aceclofenac PVP-solid dispersions**

Kamal Dua<sup>1</sup>, Kavita Pabreja<sup>1</sup>, M. V. Ramana<sup>2</sup>, and N. I. Bukhari<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Technology, Faculty of Medicine & Health Sciences, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup>Vellore Institute of Technology, Vellore, Tamilnadu, India

### **Abstract**

The objective of the present investigation was to study the effect of polyvinylpyrrolidone (PVP) on in vitro dissolution of aceclofenac from solid dispersions. Aceclofenac binary solid dispersions (SD) with different drug loadings were prepared using the melting or fusion method. In vitro dissolution of pure drug, physical mixtures, and solid dispersions were carried out. Solid dispersion of aceclofenac with PVP showed considerable increase in the dissolution rate in comparison with physical mixture and pure drug in 0.1N HCl, pH 1.2 and phosphate buffer, pH 7.4. Solid dispersions in 1:2 ratio showed maximum dissolution rate in comparison to other ratios. The amorphous nature of the drug in solid dispersion was confirmed by scanning electron microscopy and a decrease in enthalpy of drug melting in solid dispersion compared to the pure drug. FTIR spectroscopy and differential scanning calorimetry studies indicated no interaction between aceclofenac and PVP in solid dispersions in solid state. Dissolution enhancement was attributed to decreased crystallinity of the drug and to the wetting, eutectic formation, and solubilizing effect of the carrier from the solid dispersions of aceclofenac. In conclusion, dissolution of aceclofenac can be enhanced by the use of hydrophilic carriers like PVP.

**Key words:** Aceclofenac, dissolution, PVP

Ghassan Z Abdullah, Muthanna F Abdulkarim, Ibrahim M Salman, Omar Z Ameer, Mun F Yam, Ahmed F Mutee, Chitneni M, Elrashid S Mahdi, Mahiran Basri, Munavvar A Sattar, Azmin M Noor. In vitro permeation and in vivo anti-inflammatory and analgesic properties of nanoscaled emulsions containing ibuprofen for topical delivery. *Intl J Nanomed (New Zealand)* 2011; 6: 387-396

## **In vitro permeation and in vivo anti-inflammatory and analgesic properties of nanoscaled emulsions containing ibuprofen for topical delivery**

Ghassan Z Abdullah<sup>1\*</sup>, Muthanna F Abdulkarim<sup>1</sup>, Ibrahim M Salman<sup>1</sup>, Omar Z Ameer<sup>1</sup>, Mun F Yam<sup>1,2</sup>, Ahmed F Mutee<sup>1</sup>, Mallikarjun Chitneni<sup>3</sup>, Elrashid S Mahdi<sup>1</sup>, Mahiran Basri<sup>4</sup>, Munavvar A Sattar<sup>1</sup>, Azmin M Noor<sup>1</sup>

<sup>1</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia;

<sup>2</sup>Faculty of Medicine and Health Science, Universiti Putra Malaysia, Selangor, Malaysia;

<sup>3</sup>School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia;

<sup>4</sup>Faculty of Science, Universiti Putra Malaysia, Selangor, Malaysia

### **Abstract**

Introduction:

As a topical delivery system, a nanoscaled emulsion is considered a good carrier of several active ingredients that convey several side effects upon oral administration, such as nonsteroidal anti-inflammatory drugs (NSAIDs).

Objective: We investigated the in vitro permeation properties and the in vivo pharmacodynamic activities of different nanoscaled emulsions containing ibuprofen, an NSAID, as an active ingredient and newly synthesized palm olein esters (POEs) as the oil phase.

Methodology:

A ratio of 25:37:38 of oil phase:aqueous phase:surfactant was used, and different additives were used for the production of a range of nanoscaled emulsions. Carbopol® 940 dispersion neutralized by triethanolamine was employed as a rheology modifier. In some circumstances, menthol and limonene were employed at different concentrations as permeation promoters. All formulae were assessed in vitro using Franz diffusion cell fitted with full-thickness rat skin. This was followed by in vivo evaluation of the anti-inflammatory and analgesic activities of the promising formulae and comparison of the effects with that of the commercially available gel.

Results and discussion:

Among all other formulae, formula G40 (Carbopol® 940-free formula) had a superior ability in transferring ibuprofen topically compared with the reference. Carbopol® 940 significantly decreased the amount of drug transferred from formula G41 through the skin as a result of swelling, gel formation, and reduction in drug thermodynamic activity. Nonetheless, the addition of 10% w/w of menthol and limonene successfully overcame this drawback since, relative to the reference, higher amount of ibuprofen was transferred through the skin. By contrast, these results were relatively comparable to that of formula G40. Pharmacodynamically, the G40, G45, and G47 formulae exhibited the highest anti-inflammatory and analgesic effects compared with other formulae.

Conclusion:

The ingredients and the physical properties of the nanoscaled emulsions produced by using the newly synthesized POEs succeeded to deliver ibuprofen competently.

**Key words:** in vivo analgesic, anti-inflammatory effects



Gillani SW, Sulaiman SAS, Sundram S, Sari YO, Baig M, Iqbal MS. Factors associated with infections in diabetic population. *Afr J Pharm Pharmacol (Nigeria)* 2011; 5(11): 1414-1421

## Factors associated with infections in diabetic population

Syed Wasif Gillani<sup>1\*</sup>, Syed Azhar Syed Sulaiman<sup>1</sup>, Shameni Sundram<sup>2</sup>, Yelly Oktavia Sari<sup>3,4</sup>, Mirza Baig<sup>5</sup> and Muhammad Shahid Iqbal<sup>6</sup>

<sup>1</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia, Pulau Pinang, Malaysia.

<sup>2</sup>Hospital Pulau Pinang, 10990, Residential Street, Penang, Malaysia.

<sup>3</sup>Faculty of Pharmacy, Andalas University, Padang 25163, Indonesia.

<sup>4</sup>Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia.

<sup>5</sup>Department of Clinical Pharmacy, Aimst University, Kedah, Malaysia.

<sup>6</sup>School of Pharmacy and Health Sciences, International Medical University, Malaysia.

### Abstract

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

**Key words:** Diabetes mellitus, infections, factors association, clinical management, metabolic disorder, endocrinology

Gomez Edmund Luke, Gun Suk Chyn, Somnath SD, D'Souza, Beryl, Lim Ai Lee, Chinna Karuthan, Radhakrishnan AK. The prevalence of rheumatoid factor isotypes and anti-cyclic citrullinated peptides in Malaysian rheumatoid arthritis patients. *Intl J Rheumatic Dis (UK)* 2011; 14: 12-17

## **The prevalence of rheumatoid factor isotypes and anti-cyclic citrullinated peptides in Malaysian rheumatoid arthritis patients**

Edmund Luke Gomez<sup>1</sup>, Suk Chyn Gun<sup>2</sup>, Sushela Devi Somnath<sup>1</sup>, Beryl D'souza<sup>2</sup>, Ai Lee Lim<sup>2</sup>, Karuthan Chinna<sup>3</sup> and Ammu K. Radhakrishnan<sup>1</sup>

<sup>1</sup>Pathology Division, Faculty of Medicine and Health, International Medical University, Kuala Lumpur, <sup>2</sup>Department of Medicine, Hospital Tuanku Ja'afar, Negeri Sembilan and <sup>3</sup>Faculty of Mathematics and Computer Science, University Technology MARA, Selangor, Malaysia

### **Abstract**

**Aim:**

The purpose of this study is to compare the prevalence of rheumatoid factor (RF) isotypes and second generation anti-cyclic citrullinated peptides (anti-CCP) in Malaysian rheumatoid arthritis (RA) patients.

**Methods:**

In this cross-sectional study, 147 established RA patients from three ethnic groups were recruited from a major rheumatology clinic in Malaysia. Enzyme-linked immunosorbent assays (ELISA) for serum RF isotypes IgA, IgG and IgM as well as second-generation anti-CCP were performed and the prevalence of each auto-antibody was compared in the three ethnic groups.

**Results:**

The anti-CCP was the most prevalent auto-antibody in each of the ethnic groups, followed closely by RF IgM and RF IgG. Rheumatoid factor IgA was the least prevalent across all three ethnic groups. The anti-CCP–RF IgM combination provided the best test sensitivity. Seroprevalence of anti-CCP was strongly associated with the presence of each of the RF isotypes. The seroprevalence of RF and anti-CCP did not increase or decrease with advancing age, age at onset and disease duration.

**Conclusion:**

When used alone, anti-CCP provides a diagnostic advantage over RF IgM on the basis of test sensitivity. Considering the high cost of the anti-CCP assay, step-wise serum testing with IgM RF followed by anti-CCP may provide a more economically sensible option to optimize test sensitivity for RA.

**Key words:** anti-cyclic citrullinated peptides, auto-antibodies, rheumatoid arthritis, rheumatoid factor, rheumatoid factor isotypes.

Gorajana A, Wong Yuen Nee. Physicochemical characterization and in vitro evaluation of solid dispersions of Nimodipine with PEG 8000. Asian J Chem 2011; 23 (7): 2857-2859

## **Physicochemical characterization and in vitro evaluation of solid dispersions of Nimodipine with PEG 8000**

Adinarayana Gorajana<sup>1</sup>, Nalamolu Koteswara Rao<sup>2</sup> and Wong Yuen Nee<sup>1</sup>.

<sup>1</sup>Department of Pharmaceutics, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>School of Medicine, Taylor's University, Taylor's Lakeside Campus, No.1, Jalan Taylor's, 47500 Subang Jaya, Malaysia

### **Abstract**

Solid dispersions of nimodipine were prepared in an attempt to enhance solubility and dissolution rate. Solid dispersions of nimodipine were prepared with polyethylene glycol (PEG8000) using melting method. Solid dispersions were characterized using differential scanning calorimetric and X-ray powder diffraction analysis. Dissolution characteristics were determined by using pH4.5 acetate buffer containing 0.3% SDS. Differential scanning calorimetric and X-ray powder diffraction studies reflected that no chemical incompatibility between the drug and polymeric. It is also indicated that crystallinity of the drug in solid dispersions was significantly decreased and the possibility of existence of amorphous entities of the drug in solid dispersions. The solid dispersions and physical mixtures showed higher solubility and dissolution rate than nimodipine due to improved wettability and dispersibility of nimodipine. It is concluded that the solid dispersions of nimodipine in PEG 8000 considerably enhanced the dissolution rate of nimodipine.

**Key words:** Nimodipine, PEG8000, differential scanning calorimetry, X-ray powder diffraction study, dissolution enhancement.

Gupta SK, Kumar B, Nag TC, Agrawal SS, Agrawal R, Agrawal P, Saxena R, Srivastava S. Curcumin prevents experimental diabetic retinopathy in rats through its hypoglycemic, antioxidant, and anti-inflammatory mechanisms. *J Ocul Pharmacol Therapeutics* 2011; 27(2): 123-130

## **Curcumin prevents experimental diabetic retinopathy in rats through its hypoglycemic, antioxidant, and anti-inflammatory mechanisms**

Suresh Kumar Gupta<sup>1</sup>, Binit Kumar<sup>1</sup>, Tapas Chandra Nag<sup>2</sup>, Shyam Sunder Agrawal<sup>1</sup>, Renu Agrawal<sup>3</sup>, Puneet Agrawal<sup>4</sup>, Rohit Saxena<sup>5</sup>, and Sushma Srivastava<sup>1</sup>

<sup>1</sup>Department of Pharmacology, Delhi Institute of Pharmaceutical Sciences and Research, New Delhi, India

<sup>2</sup>Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India

<sup>3</sup>Faculty of Medicine, Universiti Teknologi MARA, Shah Alam, Malaysia

<sup>4</sup>Department of Ophthalmology, International Medical University, IMU Clinical School, Jalan Rasah, Seremban, Malaysia

<sup>5</sup>Dr. R.P. Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

### **Abstract**

#### **Purpose:**

The purpose of this study was to evaluate the therapeutic potential of oral curcumin (1 g/kg body weight of rat) in the prevention and treatment of streptozotocin-induced diabetic retinopathy in Wistar albino rats.

#### **Methods:**

The treatment was carried out for a period of 16 weeks in diabetic rats and evaluated for hyperglycemic, antioxidant (superoxide dismutase, catalase, and glutathione), and inflammatory parameters (tumor necrosis factor- $\alpha$ , vascular endothelial growth factor). Rat fundus was observed weekly to see any visible changes in the retina, such as tortuosity and dilation of retinal vessels. Histological changes were evaluated by transmission electron microscopy.

#### **Results:**

Treatment with curcumin showed significant hypoglycemic activity compared with the diabetic group. Retinal glutathione levels were decreased by 1.5 fold, and antioxidant enzymes, superoxide dismutase and catalase, showed >2-fold decrease in activity in the diabetic group; on the other hand, curcumin positively modulated the antioxidant system. Proinflammatory cytokines, tumor necrosis factor  $\alpha$  and vascular endothelial growth factor, were elevated >2-fold in the diabetic retinae, but prevented by curcumin. Transmission electron microscopy showed degeneration of endothelial cell organelles and increase in capillary basement membrane thickness in diabetic retina, but curcumin prevented the structural degeneration and increase in capillary basement membrane thickness in the diabetic rat retinae.

#### **Conclusion:**

Based on the above results, it may be concluded that curcumin may have potential benefits in the prevention of retinopathy in diabetic patients.

Haneline M. A primer on evidence-based practice for chiropractors. *Chiropractic J Aust* 2011; 41(3): 78-80

## **A primer on evidence-based practice for chiropractors**

Haneline, Michael<sup>1</sup>

<sup>1</sup>Department of Chiropractic, School of Pharmacy and Health Sciences, International Medical Univeristy

### **Abstract**

Evidence-based practice (EBP) has existed for more than 20 years and has been adopted on a global level by representatives from virtually every health care profession, including chiropractic. EBP was conceived by a group of medical educators at McMaster's University when they began training physicians about the importance of integrating research evidence into their clinical practices. Pertaining to chiropractic, EBP has been defined as: Actively seeking support for and improvement of chiropractic clinical practice through the integration of the best available research evidence, combined with clinical expertise and patient preferences.

EBP is taught in some form at every chiropractic educational institution in the world and many chiropractors utilise it in their practices. Nevertheless, it is misunderstood and criticized by some chiropractors and at times it is misused. The purpose of this article is therefore to briefly inform chiropractors about the steps involved in EBP, how it can be of benefit to patients as well as practitioners, and how it can be mastered by all chiropractors.

Hasan SS, Willian CW Loon, Keivan A, Ahmed SI, Bukhari NI. Reasons, perceived efficacy and factors associated with complementary and alternative medicine use among Malaysian patients with diabetes mellitus. *Brit J Diabetes Vascular Dis* 2011; 11(2): 92-98

## **Reasons, perceived efficacy and factors associated with complementary and alternative medicine use among Malaysian patients with diabetes mellitus**

Shahzad S Hasan, William CW Loon, Keivan Ahmadi, Syed I Ahmed, Nadeem I Bukhari

Department of Pharmacy Practice, School of Pharmacy and Health Sciences, International Medical University, No 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia, Diabetes Health Clinics, Outpatient Department, Hospital Tuanku Jaa'far, Seremban, Malaysia.

### **Abstract**

This study aimed to evaluate complementary and alternative medicine (CAM) use among Malaysian diabetic patients. Subjects for this case-control study were randomly selected from the pool of patients who were attending diabetes clinics, at the Hospital Tuanku Jaa'far, Seremban, Malaysia. Perceived effect of CAM use, reasons for starting CAM, and socio-demographic factors were collected from patients (n=230). Blood glucose levels were also recorded. Almost half of the study population (49.6%, 114/230) were using CAM together with conventional treatment for diabetes. Thirteen different types of CAM were utilised by the 114 CAM users and herbal medicine (64.9%) was found to be the most commonly used CAM modality. The majority of patients reported quality and safety of CAM (63.2%) and an additional treatment for diabetes (53.5%) as two main reasons for using CAM. About 44% of patients reported that their condition had improved by using CAM ( $R^2=0.512$ ,  $p=0.004$ ), which was evident by their lowered fasting blood glucose ( $p=0.045$ , 7.171 versus 8.767). About 18% perceived their health condition as poor compared to 56% who perceived it as good after commencing CAM use.

**Key words:** diabetes, complementary and alternative medicine, plant remedies, traditional treatments

Hasan SS, Chew S Yong, Muneer GB, Cho Naing, Abdul Hameed, Mirza R Baig, Shahid M Iqbal, Therese Kairuz. Understanding, perceptions and self-use of complementary and alternative medicine (CAM) among Malaysian pharmacy students. *BMC Compl Alternat Med* 2011; 11: 95-103

## **Understanding, perceptions and self-use of complementary and alternative medicine (CAM) among Malaysian pharmacy students**

Syed S Hasan<sup>1\*</sup>, Chew S Yong<sup>2</sup>, Muneer G Babar<sup>2</sup>, Cho M Naing<sup>2</sup>, Abdul Hameed<sup>3</sup>, Mirza R Baig<sup>4</sup>, Shahid M Iqbal<sup>2</sup> and Therese Kairuz<sup>1</sup>

<sup>1</sup>School of Pharmacy, The University of Queensland, 20 Cornwall Street, Woolloongabba, 4102, Brisbane, Australia

<sup>2</sup>International Medical University, Jalan Jalil Perkasa 19, Bukit Jalil, Kuala Lumpur, 57000, Malaysia

<sup>3</sup>Faculty of Pharmacy, University Technology Mara, Bandar Puncak Alam, 42300, Selangor, Malaysia

<sup>4</sup>Faculty of Pharmacy, AIMST University, Jalan Bedong, Semeling, 08100, Bedong, Kedah, Malaysia

### **Abstract**

#### **Background:**

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

#### **Methods:**

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

#### **Results:**

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

#### **Conclusions:**

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

Hasan SS, R Shamala, Ahmed SI, N. Basariah, Chong DWK , Teh KM, Chin OH. Factors affecting warfarin-related knowledge and INR control of patients attending Physician- and Pharmacist- Managed Anticoagulation Clinics. J Pharm Practice 2011; 24(5):485-493

## **Factors affecting warfarin-related knowledge and INR control of patients attending Physician- and Pharmacist- Managed Anticoagulation clinics**

Syed S. Hasan<sup>1</sup>, R. Shamala<sup>1</sup>, Imran A. Syed<sup>1</sup>, N. Basariah<sup>2</sup>, David W. K. Chong<sup>1</sup>, Teh K. Mei<sup>1</sup>, and Ong H. Chin<sup>1</sup>

<sup>1</sup> Department of Pharmacy Practice, School of Pharmacy and Health Sciences, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup> Department of Pharmacy, General Hospital Kuala Lumpur, Jalan Pahang Kuala Lumpur, Malaysia

### **Abstract**

#### **Objectives:**

To assess the anticoagulation knowledge and international normalized ratio (INR) control among patients on warfarin.

#### **Methods:**

A cross-sectional study with 156 randomly sampled patients from physician- (non medication therapy adherence clinic [non-MTAC]) and pharmacist (MTAC)-run anticoagulation clinics using a validated interviewer-administered questionnaire. Patients' INR readings from 2008 to 2010 were recorded.

#### **Results:**

Patients on warfarin scored an average of 66.5% + 36.0% for their knowledge on how warfarin works, 42.9% + 44.9% for interaction between warfarin and alcohol, and 49.2% + 21.1% for adverse effects. No significant differences were found between MTAC and non-MTAC patients on their knowledge. There was a negative correlation between patients' knowledge and age ( $P \leq .001$ ,  $r = -.293$ ) and a positive correlation between patients' knowledge and education level ( $P \leq .001$ ,  $r = .365$ ). MTAC patients were found to have better INR control than non MTAC when compared for mean percentage days in range (63.4% + 18.9% vs 52.5% + 18.2%;  $P \leq .006$ ) and mean percentage visits in range (58.8%+17.9% vs 46.8% +18.6%;  $P \leq .001$ ).

#### **Conclusions:**

MTAC patients were found to have better INR control compared to non-MTAC patients. A joint cooperation between physicians, pharmacists, and nurses should exist to achieve desired therapeutic outcomes.

**Key words:** factors, knowledge, warfarin, INR control, anticoagulation, clinics



Hasan SS, Keong SC, Christopher LKC, Ahmed SI, Ching TW, Mudassir A, Keivan A, Muneer GB. Patient-reported adverse drug reactions and drug-drug interactions: a cross-sectional study on Malaysian HIV/AIDS patients. *Med Princ Pract* 2011; 20:265-270

## **Patient-reported adverse drug reactions and drug-drug interactions: a cross-sectional study on Malaysian HIV/AIDS patients**

Syed S. Hasan<sup>1\*</sup>, See C. Keong<sup>1</sup>, Christopher L.K. Choong<sup>2</sup>, Syed I. Ahmed<sup>1</sup>, Ting W. Ching<sup>2</sup>, Mudassir Anwar<sup>1</sup>, Keivan Ahmadi<sup>1</sup>, Muneer G. Babar<sup>1</sup>

\*Department of Pharmacy Practice and Community Oral Health, School of Pharmacy and Dentistry, International Medical University, Kuala Lumpur, and b Department of Infectious Diseases, Hospital Sungai Buloh, Jalan Hospital, Sungai Buloh, Malaysia

### **Abstract**

#### **Objective:**

This study aimed to explore the adverse drug reactions (ADRs) reported by patients and to identify drug-drug interactions (DDIs) among human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients.

#### **Subjects and methods:**

This cross-sectional study was conducted at the Medication Therapy Adherence Clinic, Hospital Sungai Buloh, an HIV/AIDS referral centre. The patients were randomly selected and were encouraged to describe ADRs caused specifically by any of the prescribed antiretroviral drugs (ARDs). Sociodemographic characteristics were recorded from the patients' medical records. In addition data on antiretroviral treatment (ART), DDIs and other conventional medication were also documented.

#### **Results:**

A total of 325 randomly selected HIV/AIDS patients with a mean age of 22.94 years participated in the study. The most frequently prescribed ARDs were lamivudine (64.6%), zidovudine (40.6%) and efavirenz (42.5%). Commonly reported ADRs were fatigue (54.8%), allergic reactions (41.5%), weight loss (41.5%), dry mouth (35.1%) and memory loss (35.1%). Female (87.8%), non-complementary and alternative medicine (CAM) users (87.3%) and participants below 50 years old (81.1%) were identified as having a higher prevalence of ADRs compared to males (79.6%), CAM users (78.7%) and participants aged 50 years or more (77.5%). Patient age was found to be significantly associated ( $p = 0.048$ ) with the ADRs. In addition, a total of 44 cases of DDIs belonging to category D were also found in this study.

#### **Conclusions:**

This study enabled us to identify the most common ADRs and DDIs associated with the use of ART. Safe and effective treatment depends on the healthcare providers' knowledge of the same.

**Key words:** Patient-reported adverse drug reactions · Drug-drug interactions · HIV/AIDS, Malaysians

Ho CCK, Tong SF, Low WY, Ng CJ, Khoo EM, Lee VKM, Zulkifli MZ, Tan HM. A randomized, double-blind, placebo-controlled trial on the effect of long-acting testosterone treatment as assessed by the Aging Male Symptoms scale. *Brit J Urology Intl* 2011; 110:260-265

## **A randomized, double-blind, placebo-controlled trial on the effect of long-acting testosterone treatment as assessed by the Aging Male Symptoms scale**

Christopher C.K. Ho<sup>1</sup>, Seng Fah Tong<sup>2</sup>, Wah Yun Low<sup>3</sup>, Chirk Jenn Ng<sup>4</sup>, Ee Ming Khoo<sup>4</sup>, Verna K.M. Lee<sup>5</sup>, Zulkifli Md Zainuddin<sup>1</sup> and Hui Meng Tan<sup>3,6</sup>

<sup>1</sup> Departments of Surgery Universiti Kebangsaan Malaysia Medical Centre, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur, Malaysia

<sup>2</sup> Family Medicine, Universiti Kebangsaan Malaysia Medical Centre

<sup>3</sup> Medical Research and Development Unit

<sup>4</sup> Department of Primary Care Medicine, Faculty of Medicine, University of Malaya

<sup>5</sup> Department of Family Medicine, Faculty of Medicine, International Medical University, Kuala Lumpur

<sup>6</sup> Sime Darby Medical Centre, Selangor, Malaysia

### **Abstract**

Objective:

- To evaluate the effect of i.m. injection of testosterone undecanoate 1000 mg over 12 months on the Aging Male Symptom (AMS) scale scores in men with testosterone deficiency syndrome (TDS).

Patients and methods:

- A total of 120 men > 40 years old with TDS (total testosterone < 12 nmol/L and total AMS scores  $\geq$  27) were randomized into i.m. injection of either placebo or testosterone undecanoate 1000 mg.
- In all, 56 and 58 participants from the active treatment and placebo groups, respectively completed the study.
- An i.m. injection of either placebo or testosterone undecanoate 1000 mg was given at weeks 0, 6, 18, 30 and 48.
- Self-administered AMS questionnaires were completed at weeks 0, week 18 and week 48.

Results:

- Improvement in the total AMS score was significantly greater in the treatment group than in the placebo group (F: 4.576,  $P = 0.017$ ) over the 48-week period.
- The mean (SD) total AMS score was 38.46 (11.85) at baseline and 33.59 (1.69) at 48 weeks for the placebo group, and 41.73 (12.73) at baseline and 32.61 (9.67) at 48 weeks for the treatment group.
- The mean change in the total AMS score was -12.6% in the placebo group and -21.9% in the treatment group.
- The mean psychological and somatovegetative domain scores decreased significantly more in the treatment group than in the placebo group (-2.8 vs -1.2,  $P = 0.03$ ; and -3.2 vs -1.8,  $P = 0.016$ ).
- The difference in change between the randomized groups for the sexual domain scores followed the same trend, though the difference was not significant.

Conclusion:

- Long-acting testosterone is effective in improving health-related quality of life as assessed by the AMS scale in men with TDS.

**Key words:** testosterone deficiency, hypogonadism, testosterone undecanoate, injectable, long-acting, AMS scale

Huang YC, Hung WC, Chye SM, Chen WT, Chai CY. para-phenylenediamine-induced autophagy in human uroepithelial cell line mediated mutant p53 and activation of ERK signaling pathway. *Toxicology in Vitro (Netherlands)* 2011; 25(8): 1630-1637

## **para-Phenylenediamine-induced autophagy in human uroepithelial cell line mediated mutant p53 and activation of ERK signaling pathway**

Ya-Chun Huang <sup>1,2</sup>, Wen-Chun Hung <sup>3,4</sup>, Soi-Moi Chye <sup>5</sup>, Wan-Tzu Chen <sup>6</sup>, Chee-Yin Chai <sup>1,2,3,4,6\*</sup>

<sup>1</sup> Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>2</sup> Department of Pathology, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>3</sup> Institute of Biomedical Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan

<sup>4</sup> National Sun Yat-Sen University–Kaohsiung Medical University Joint Research Center, Kaohsiung, Taiwan

<sup>5</sup> Department of Human Biology, School of Medicine, International Medical University, Malaysia

<sup>6</sup> Department of Pathology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

### **Abstract**

para-Phenylenediamine (p-PD) is a major aromatic amine that is a widely used commercial oxidativetype hair dye. Some epidemiologic studies have suggested that the use of p-PD based hair dyes might be related to increased risk of human malignant tumors including bladder cancer. However, the effects of p-PD on autophagy in human uroepithelial cells (SV HUC-1) is still unclear. In this study, we demonstrate that p-PD can activate the extracellular signaling-regulated protein kinase 1/2 (ERK1/2) signaling pathway in SV-HUC-1 cells. In addition, we observed that autophagosomes increased in p-PD-treated SVHUC-1 cells as shown by electron microscopy. Our results showed incremental increase of the concentrations, Beclin-1 and microtubule-associated protein light chain 3B (LC3B), which are important regulators of autophagosomes. In contrast, the MEK inhibitor (U0126) was suppressed autophagy and the effect of p-PD on ERK1/2, Beclin-1 and LC3B proteins expression, except for mutant p53. In this study, we demonstrated that inactivation of p53 induces a potent autophagy response. Finally, our results suggest that p-PD can activate the ERK1/2 signaling pathway and mutant p53, leading to the stimulation of autophagy in SV HUC-1 cells. These results provide us with new insights for the understanding of the mechanism of p-PD-induced cell death in urothelial cells.

**Key words:** para-Phenylenediamine, SV-HUC-1 cells, Autophagy, Mutant p53, Beclin-1

Init Ithoi, Arine-Fadzlun Ahmad, Mak JW, Veeranoot Nissapatorn, Yee Ling Lau, Rohela Mahmud. Morphological characteristics of developmental stages of Acanthamoeba and Naegleria species before and after staining by various techniques. Southeast Asian J Trop Med Pub Hlth (Thailand) 2011; 44(6): 1-12

## **Morphological characteristics of developmental stages of Acanthamoeba and Naegleria species before and after staining by various techniques**

Init Ithoi<sup>1</sup>, Arine-Fadzlun Ahmad<sup>1</sup>, JW Mak<sup>2</sup>, Veeranoot Nissapatorn<sup>1</sup>, Yee-Ling Lau<sup>1</sup> and Rohela Mahmud<sup>1</sup>

<sup>1</sup>Department of Parasitology, Faculty of Medicine, University of Malaya, Kuala Lumpur

<sup>2</sup>School of Postgraduate and Research, International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

Seven stains were studied to determine the best color and contrast for staining the developmental stages of free living pathogenic Acanthamoeba and Naegleria species. The acid-fast bacilli stain (AFB) produced a blue color without contrast; trichrome-eosin and modified-Field's showed various color contrasts; Giemsa, iron-haematoxylin, modified-AFB and Gram produced only one color which distinguished the nucleus, nucleolus, cytoplasm, food- and water-vacuoles. The motile organs (acanthopodia, pseudopodia, lobopodia and flagella) were also clearly differentiated but produced a similar color as the cytoplasm. These motile organelles were first induced by incubating at 37°C for at least 15 minutes and then fixing with methanol in order to preserve the protruding morphology prior to staining. The trichrome-eosin and iron-hematoxylin stains showed good color contrast for detecting all three stages, the trophozoite, cyst and flagellate; Giemsa and Gram stained the trophozoite and flagellate stages; the modified-Field's and modified-AFB stains stained only the trophozoite stage. Depending on the purpose, all these stains (except the AFB stain) can be used to identify all of the developmental stages of Acanthamoeba and Naegleria for clinical, epidemiological or public health use.

**Key words:** Acanthamoeba, Naegleria, stains, developmental stages

Init Ithoi, Arine Fadzlun Ahmad, Veeranoot Nissapatorn, Yee Ling Lau, Rohela Mahmud, Joon Wah Mak. Detection of *Naegleria* species in environmental samples from Peninsular Malaysia. PLoS ONE (US) 2011; 6(9): e24327

## Detection of *Naegleria* species in environmental samples from Peninsular Malaysia

Init Ithoi<sup>1\*</sup>, Arine Fadzlun Ahmad<sup>1</sup>, Veeranoot Nissapatorn<sup>1</sup>, Yee Ling Lau<sup>1</sup>, Rohela Mahmud<sup>1</sup>, Joon Wah Mak<sup>2</sup>

<sup>1</sup> Department of Parasitology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

<sup>2</sup> School of Postgraduate Studies and Research, International Medical University, Kuala Lumpur, Malaysia

### Abstract

Background:

In Malaysia, researchers and medical practitioners are unfamiliar with *Naegleria* infections. Thus little is known about the existence of pathogenic *Naegleria fowleri*, and the resultant primary amoebic meningoencephalitis (PAM) is seldom included in the differential diagnosis of central nervous system infections. This study was conducted to detect the presence of *Naegleria* species in various environmental samples.

Methods/Findings:

A total of 41 *Naegleria*-like isolates were isolated from water and dust samples. All these isolates were subjected to PCR using two primer sets designed from the ITS1-ITS2 regions. The *N. fowleri* species-specific primer set failed to produce the expected amplicon. The *Naegleria* genus-specific primers produced amplicons of 408 bp (35), 450 bp (2), 457 bp (2) or 381 bp (2) from all 41 isolates isolated from aquatic (33) and dust (8) samples. Analysis of the sequences from 10 representative isolates revealed that amplicons with fragments 408, 450 and 457 bp showed homology with nonpathogenic *Naegleria* species, and 381 bp showed homology with *Vahlkampfia* species. These results concurred with the morphological observation that all 39 isolates which exhibited flagella were *Naegleria*, while 2 isolates (AC7, JN034055 and AC8, JN034056) that did not exhibit flagella were *Vahlkampfia* species.

Conclusion:

To date, pathogenic species of *N. fowleri* have not been isolated from Malaysia. All 39 isolates that produced amplicons (408, 450 and 457 bp) from the genus-specific primers were identified as being similar to nonpathogenic *Naegleria*. Amplicon 408 bp from 5 representative isolates showed 100% and 99.7% identity to *Naegleria philippinensis* isolate RJTM (AM167890) and is thus believed to be the most common species in our environment. Amplicons 450 bp and 457 bp were respectively believed to be from 2 new species of *Naegleria*, since representative isolates showed lower homology and had a longer base pair length when compared to the reference species in the Genbank, *Naegleria schusteri* (AJ566626) and *Naegleria laresi* (AJ566630), respectively.

Init Ithoi, Azman Jali, J.W.Mak, Wan Yusoff Wan Sulaiman, and Rohela Mahmud. Occurrence of Blastocystis in water of two rivers from recreational areas in Malaysia. *J Parasitol Res* 2011; doi:10.1155/2011/123916

## **Occurrence of Blastocystis in water of two rivers from recreational areas in Malaysia**

Init Ithoi<sup>1</sup>, Azman Jali<sup>2</sup>, J.W.Mak<sup>3</sup>, Wan Yusoff Wan Sulaiman<sup>1</sup>, and Rohela Mahmud<sup>1</sup>

<sup>1</sup>Department of Parasitology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>2</sup>Department of Biology, Faculty of Science, Putra Malaysia University, 43400 Serdang, Selangor, Malaysia

<sup>3</sup>School of Postgraduate Studies and Research, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

This study reports the occurrence of Blastocystis in water from two rivers, Sungai Congkak and Sungai Batu, located in recreational areas in Malaysia. This protozoan was detected in samples from both rivers with an average of 33.3% and 22.1%, respectively. It was detected highest at the downstream (73.8% and 33.8%) followed by midstream (17.5% and 25.0%) and upstream (8.8% and 7.5%) stations, with additionally higher detection during holidays (with average 47.5% and 30.8%) than week days (with average 19.2% and 13.3%), in both rivers, respectively. There was a strong association with the daily activities of locals and visitors, who came for water recreational activities, mainly located between midstream and downstream and was observed to be higher at Sungai Congkak. The detection of Blastocystis in these rivers' water implies that this protozoan could potentially be transmitted to humans by the waterborne route. Pearson correlation analysis showed that their occurrence was significantly correlated with faecal coliforms count; inconsistent correlation with dissolved oxygen, temperature and turbidity and no correlation with pH, conductivity and rainfall for both rivers. The correlation of coliforms and Blastocystis suggests the source of the Blastocystis in the water body is likely to be faecal.

Jeevaratnam K, Tee SP, Zhang Y, Rewbury R, Guzadhur L, Duchmke R, Grace AA, Lei M, Huang CLH. Delayed conduction and its implications in murine Scn5<sup>+/-</sup> hearts: independent and interacting effects of genotype, age, and sex. *Eur J Physiol* 2011; 461: 29-44

## **Delayed conduction and its implications in murine Scn5a<sup>+/-</sup> hearts: independent and interacting effects of genotype, age, and sex**

Kamalan Jeevaratnam<sup>1,2,5</sup>, Sui Poh Tee<sup>1</sup>, Yanmin Zhang<sup>1,4</sup>, Rebecca Rewbury<sup>1</sup>, Laila Guzadhur<sup>1,2</sup>, Rudolf Duehmke<sup>1,2</sup>, Andrew A. Grace<sup>2</sup>, Ming Lei<sup>3</sup>, Christopher L.H. Huang<sup>1,2</sup>

<sup>1</sup>Physiological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 3EG, UK

<sup>2</sup>Cardiovascular Research, Department of Biochemistry, Hopkins Building, University of Cambridge, Cambridge CB2 1QW, UK

<sup>3</sup>Cardiovascular Group, School of Clinical & Laboratory Sciences, University of Manchester Core Technology Facility (3rd floor), University of Manchester, Manchester M13 9NT, UK

<sup>4</sup>Department of Paediatrics, First Affiliated Hospital, Cardiovascular Ion Channel Disease Laboratory, Xi'an Jiaotong University, Xi'an 710061, People's Republic of China

<sup>5</sup>Department of Human Biology, Faculty of Medicine, International Medical University, Bukit Jalil, 57000, Kuala Lumpur, Malaysia

### **Abstract**

We explored for relationships between SCN5A haploinsufficiency, implicated in clinical arrhythmogenicity, and right ventricular (RV) conduction disorders in Langendorff-perfused, male and female, and young (3 months) and old (>12 month old) Scn5a<sup>+/-</sup> and wild type (WT) hearts. The investigated conditions of genotype, age, and sex affected latencies but not repolarization time courses of RV monophasic action potentials. This prompted examination of the patterns of RV epicardial activation, its dispersion, and their interrelationships as possible arrhythmic mechanisms using a 64-channel, multi-electrode array. Mean ventricular activation times (T\*MEAN), spatial dispersions (D\*S) between recording channels/cardiac cycle, and maximum activation times (T\*MAX) representing the slowest possible conduction in any given heart were all higher in old male Scn5a<sup>+/-</sup> compared with young male and old female Scn5a<sup>+/-</sup> and old male WT. Temporal dispersions (D\*T) of recording channels were similarly higher in old male Scn5a<sup>+/-</sup> compared with old male WT. All groupings of D\*T, D\*S, and T\*MAX nevertheless linearly correlated with T\*MEAN, with indistinguishable slopes. The variates explored thus influence D\*T, D\*S, and T\*MAX through actions on T\*MEAN. These findings in turn correlated with increased levels of fibrosis in young male, young female, and old male Scn5a<sup>+/-</sup> compared with the corresponding WTs. We thus demonstrate for the first time independent and interacting effects of genotype, age, and sex on epicardial conduction and its dispersions at least partially attributable to fibrotic change, resulting in the greatest effects in old male Scn5a<sup>+/-</sup> in an absence of alterations in repolarization time courses. This directly implicates altered depolarization in the clinical arrhythmogenicity associated with Scn5a<sup>+/-</sup>.

**Key words:** Multi-array, Biophysics, Conduction, Dispersion, Depolarization, Repolarization



Kee CC, Jamaiyah H, Geeta A, Ahmad Ali Z, Noor Safiza MN, Suzana S, Khor GL, Rahmah R, Jamalludin AR, Sumarni MG, Lim KH, Ahmad Faudzi Y, Amal NM. Sensitivity and specificity of waist circumference as a single screening tool for identification of overweight and obesity among Malaysian adults. *Med J Malaysia* 2011; 66: 460-465

## **Sensitivity and specificity of waist circumference as a single screening tool for identification of overweight and obesity among Malaysian adults**

C C Kee<sup>1</sup>, H Jamaiyah<sup>2</sup>, A Geeta<sup>3</sup>, Z Ahmad Ali<sup>4</sup>, M N Noor Safiza<sup>4</sup>, S Suzana<sup>5</sup>, G L Khor<sup>6</sup>, R Rahmah<sup>7</sup>, A R Jamalludin<sup>8</sup>, M G Sumarni<sup>1</sup>, K H Lim<sup>1</sup>, Y Ahmad Faudzi<sup>1</sup>, N M Amal<sup>1</sup>

<sup>1</sup>Institute for Medical Research, Kuala Lumpur

<sup>2</sup>Clinical Research Centre, Kuala Lumpur

<sup>3</sup>Universiti Putra Malaysia, Serdang

<sup>4</sup>Institute for Public Health, Kuala Lumpur

<sup>5</sup>Universiti Kebangsaan Malaysia, Kuala Lumpur

<sup>6</sup>International Medical University, Kuala Lumpur

<sup>7</sup>Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur

<sup>8</sup>International Islamic University, Kuantan

### **Abstract**

Generalised obesity and central obesity are risk factors for Type II diabetes mellitus and cardiovascular diseases. Waist circumference (WC) has been suggested as a single screening tool for identification of overweight or obese subjects in lieu of the body mass index (BMI) for weight management in public health program. Currently, the recommended waist circumference cut-off points of  $\geq 94$ cm for men and  $\geq 80$ cm for women (waist action level 1) and  $\geq 102$ cm for men and  $\geq 88$ cm for women (waist action level 2) used for identification of overweight and obesity are based on studies in Caucasian populations. The objective of this study was to assess the sensitivity and specificity of the recommended waist action levels, and to determine optimal WC cut-off points for identification of overweight or obesity with central fat distribution based on BMI for Malaysian adults. Data from 32,773 subjects (14,982 men and 17,791 women) aged 18 and above who participated in the Third National Health Morbidity Survey in 2006 were analysed. Sensitivity and specificity of WC at waist action level 1 were 48.3% and 97.5% for men; and 84.2% and 80.6% for women when compared to the cut-off points based on BMI  $\geq 25$ kg/m<sup>2</sup>. At waist action level 2, sensitivity and specificity were 52.4% and 98.0% for men, and 79.2% and 85.4% for women when compared with the cut-off points based on BMI ( $\geq 30$  kg/m<sup>2</sup>). Receiver operating characteristic analyses showed that the appropriate screening cut-off points for WC to identify subjects with overweight ( $\geq 25$ kg/m<sup>2</sup>) was 86.0cm (sensitivity=83.6%, specificity=82.5%) for men, and 79.1cm (sensitivity=85.0%, specificity=79.5%) for women. Waist circumference cut-off points to identify obese subjects (BMI  $\geq 30$  kg/m<sup>2</sup>) was 93.2cm (sensitivity=86.5%, specificity=85.7%) for men and 85.2cm (sensitivity=77.9%, specificity=78.0%) for women. Our findings demonstrated that the current recommended waist circumference cut-off points have low sensitivity for identification of overweight and obesity in men. We suggest that these newly identified cut-off points be considered.

**Key words:** Waist circumference, Obesity, Overweight, Sensitivity, Specificity

Khor GL, Chee WSS, Zalilah M Shariff, Poh BK, Arunmugam Mohan, Rahman Jamilludin A, Theobald Hannah E. High prevalence of vitamin D insufficiency and its association with BMI-for-age among primary school children in Kuala Lumpur, Malaysia. BMC Pub Hlth (UK) 2011; 11: 95-102

## High prevalence of vitamin D insufficiency and its association with BMI-for-age among primary school children in Kuala Lumpur, Malaysia

Geok L Khor<sup>1\*</sup>, Winnie SS Chee<sup>1</sup>, Zalilah M Shariff<sup>2</sup>, Bee K Poh<sup>3</sup>, Mohan Arumugam<sup>4</sup>, Jamalludin A Rahman<sup>5</sup>, Hannah E Theobald<sup>6</sup>

<sup>1</sup>Department of Nutrition and Dietetics, School of Pharmacy & Health Sciences, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Department of Nutrition and Dietetics, Faculty of Medicine & Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Malaysia

<sup>3</sup>Department of Nutrition and Dietetics, Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia, 50300 Kuala Lumpur, Malaysia

<sup>4</sup>Department of Medicine, Serdang Hospital, 43000 Kajang, Malaysia

<sup>5</sup>Department of Community Health and Family Medicine, Faculty of Medicine, International Islamic University Malaysia, 25200 Kuantan, Malaysia

<sup>6</sup>GlaxoSmithKline Nutritional Healthcare, 980 Great West Road, Brentford, TW8 9GS, UK

### Abstract

#### Background:

Deficiencies of micronutrients can affect the growth and development of children. There is increasing evidence of vitamin D deficiency world-wide resulting in nutritional rickets in children and osteoporosis in adulthood. Data on the micronutrient status of children in Malaysia is limited. The aim of this study was to determine the anthropometric and micronutrient status of primary school children in the capital city of Kuala Lumpur.

#### Methods:

A cross sectional study of primary aged school children was undertaken in 2008. A total of 402 boys and girls aged 7-12 years, attending primary schools in Kuala Lumpur participated in the study. Fasting blood samples were taken to assess vitamin D [as 25(OH)D], vitamin B12, folate, zinc, iron, and ferritin and haemoglobin concentrations. Height-for-age and body mass index for age (BMI-for-age) of the children were computed.

#### Results:

Most of the children had normal height-for-age (96.5%) while slightly over half (58.0%) had normal BMI-for-age. A total of 17.9% were overweight and 16.4% obese. Prevalence of obesity was significantly higher among the boys (25%) than in the girls (9.5%) ( $\chi^2 = 22.949$ ;  $P < .001$ ). Most children had adequate concentrations of haemoglobin, serum ferritin, zinc, folate and vitamin B12. In contrast, 35.3% of the children had serum 25(OH)D concentrations indicative of vitamin D deficiency ( $\leq 37.5$  nmol/L) and a further 37.1% had insufficiency concentrations ( $> 37.5 - \leq 50$  nmol/L). Among the boys, a significant inverse association was found between serum vitamin D status and BMI-for-age ( $\chi^2 = 5.958$ ;  $P = .016$ ).

Conclusions:

This study highlights the presence of a high prevalence of sub-optimal vitamin D status among urban primary school children in a tropical country. In light of the growing problem of obesity in Malaysian children, these findings emphasize the important need for appropriate interventions to address both problems of obesity and poor vitamin D status in children.

Khor Yen Haw, Chakravarthi S, Nagaraja HS, Pichika MR. Effects of *Etlingera elatior* extracts on lead acetate-induced testicular damage: a morphological and biochemical study. *Exp Therap Med* 2011; 3: 99-104

## Effects of *Etlingera elatior* extracts on lead acetate-induced testicular damage: A morphological and biochemical study

Khor Yen Haw<sup>1</sup>, Srikumar Chakravarthi<sup>2</sup>, Nagaraja Haleagrahara<sup>3</sup> And Mallikarjuna Rao<sup>4</sup>

<sup>1</sup>Department of Post Graduate Studies, Research Laboratory; Departments of

<sup>2</sup>Pathology

<sup>3</sup>Human Biology, Faculty of Medicine

<sup>4</sup>Department of Pharmacy, International Medical University, Kuala Lumpur, Malaysia

### Abstract

Lead causes damage to the whole body by inducing oxidative stress. This includes the testis, in which spermatogenesis is affected. *Etlingera elatior*, a consumable plant that is being extensively studied for its high anti-oxidant properties, was tested against the effect of lead acetate in experimental rats. Rats were divided into groups consisting of a control, lead acetate only, *Etlingera elatior* treatment only, concurrent treatment of lead acetate and *Etlingera elatior*, post-treatment of lead acetate followed by *Etlingera elatior* and preventive group of *Etlingera elatior* followed by lead acetate. The substances were administered for 14 days and the effects were measured by protein carbonyl content (PCC), superoxide dismutase (SOD) activity, glutathione peroxidase (GPx) activity in the testis, as well as the testosterone level in the serum. Histological changes in the testis were also observed. Results showed that *Etlingera elatior* induced a significant reduction in the testis PCC activity, while at the same time it significantly increased the activities of SOD and GPx in the testis, and the testosterone level in the serum. *Etlingera elatior* also improved the histology of the testis when compared to the lead acetate-treated group. On the whole, *Etlingera elatior* is effective against oxidative damage caused by lead acetate in the testis.

**Key words:** lead, *Etlingera elatior*, oxidative stress, spermatogenesis, testis

Koh KC, A Kamarulzaman. Profiles of men-who-have-sex-with-men seeking anonymous voluntary HIV counseling and testing at a community-based centre in Malaysia. Med J Malaysia 2011; 489-492

## **Profiles of men-who-have-sex-with-men seeking anonymous voluntary HIV counseling and testing at a community-based centre in Malaysia**

K C Koh<sup>1</sup>, A Kamarulzaman<sup>2</sup>

<sup>1</sup>Department of Medicine, Clinical School, International Medical University, Seremban, Negeri Sembilan, Malaysia

<sup>2</sup>Centre of Excellence for Research in AIDS (CERIA), University Malaya, Kuala Lumpur

### **Abstract**

Community-based HIV voluntary counseling and testing (VCT) services is an effective alternative for mapping the local demographics of at-risk populations for HIV as well as provide an acceptable and reliable means of early detection of HIV. We describe the profiles of men-who-have-sex-with men (MSM) who sought VCT services in a community based centre in Kuala Lumpur.

**Key words:** HIV, Voluntary counseling and testing, MSM

Kok YY, Chu WL, Phang SM, Shar Mariam M, Naidu R, Lai PJ, Ling SN, Mak JW, Lim PKC, Balraj P, Khoo ASB. Inhibitory activities of microalgal extracts against Epstein-Barr virus DNA release from lymphoblastoid cells. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)* (China) 2011; 12(5): 335-345

## **Inhibitory activities of microalgal extracts against Epstein-Barr virus DNA release from lymphoblastoid cells**

Yih-Yih Kok<sup>1</sup>, Wan-Loy Chu<sup>1</sup>, Siew-Moi Phang<sup>2</sup>, Shar Mariam Mohamed<sup>1</sup>, Rakesh Naidu<sup>3,4</sup>, Pey-Jiun Lai<sup>3</sup>, Shui-Nyuk Ling<sup>1</sup>, Joon-Wah Mak<sup>1</sup>, Patricia Kim-Chooi Lim<sup>5</sup>, Pauline Balraj<sup>5</sup>, Alan Soo-Beng Khoo<sup>5</sup>

<sup>1</sup>Division of Human Biology, International Medical University, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Institute of Biological Sciences, Faculty of Science, and Institute of Ocean and Earth Sciences IOES

University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>3</sup>Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>4</sup>School of Medicine and Health Sciences, Monash University, 46150 Petaling Jaya, Selangor, Malaysia

<sup>5</sup>Molecular Pathology Unit, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia

### **Abstract**

This study aimed to assess the inhibitory activities of methanol extracts from the microalgae *Ankistrodesmus convolutus*, *Synechococcus elongatus*, and *Spirulina platensis* against Epstein-Barr virus (EBV) in three Burkitt's lymphoma (BL) cell lines, namely Akata, B95-8, and P3HR-1. The antiviral activity was assessed by quantifying the cell-free EBV DNA using real-time polymerase chain reaction (PCR) technique. The methanol extracts from *Ankistrodesmus convolutus* and *Synechococcus elongatus* displayed low cytotoxicity and potent effect in reducing cell-free EBV DNA ( $EC_{50} < 0.01$   $\mu\text{g/ml}$ ) with a high therapeutic index ( $> 28\ 000$ ). After fractionation by column chromatography, the fraction from *Synechococcus elongatus* (SEF1) reduced the cell-free EBV DNA most effectively ( $EC_{50} = 2.9$   $\mu\text{g/ml}$ , therapeutic index  $> 69$ ). Upon further fractionation by high performance liquid chromatography (HPLC), the sub-fraction SEF1'a was most active in reducing the cell-free EBV DNA ( $EC_{50} = 1.38$   $\mu\text{g/ml}$ , therapeutic index  $> 14.5$ ). This study suggests that microalgae could be a potential source of antiviral compounds that can be used against EBV.

**Key words:** Microalgae, *Ankistrodesmus convolutus*, *Synechococcus elongatus*, *Spirulina platensis*, Lymphoblastoid cells, Epstein-Barr virus (EBV)

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. *J Neural Transm (Germany)* 2011; doi: 10.1007/s00702-011-0715-5

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

K. Krishnan<sup>1</sup>, N. K. Mitra<sup>2</sup>, L. S. Yee<sup>1</sup>, H. M. Yang<sup>1</sup>

<sup>1</sup>School of Pharmacy and Health Science, International Medical University, No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Department of Human Biology, School of Medicine, International Medical University, No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **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  $\frac{1}{2}$  LD<sub>50</sub> 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<sup>2</sup> 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.

**Key words:** Chlorpyrifos, Dermal toxicity, Cerebellum, GFAP

Kumarappan C, Albert Jaswanth, Karpagam Kumarasunden. Antihaemolytic and snake venom neutralizing effect of some Indian medicinal plants. *Asian Pacific J Trop Med (China)* 2011; 4(9): 743-747

## **Antihaemolytic and snake venom neutralizing effect of some Indian medicinal plants**

Chidambaram Kumarappan<sup>1\*</sup>, Albert Jaswanth<sup>2</sup>, Karpagam Kumarasunderi<sup>2</sup>

<sup>1</sup>Department of Life Sciences, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Pharmacology, Periyar College of Pharmaceutical Sciences, Tamilnadu, India

### **Abstract**

**Objective:** To validate traditional claims of usefulness of the Indian plants in management of poisonous snakebite and evaluate the antivenom properties displayed by the alcoholic extracts of *Andrographis paniculata* (*A. paniculata*), *Crateva magna* (*C. magna*), *Gloriosa superba* (*G. superba*) and *Hydrocotyle javanica* (*H. javanica*). **Methods:** These plants were collected, identified and the extracts were prepared by using conventional Soxhlet ethanol extraction technique. The venom neutralization activity was assessed in mice (20-25g) and number of mortalities was observed against clinically important snake (*Naja nigricollis*) venom. Present study also deals with in vitro membrane stabilizing activity of these plants against hyposaline induced human red blood corpuscles (HRBC). **Results:** Extracts of *H. javanica* and *G. superba* gave 80 % and 90 % protection to mice treated with minimum lethal dose of venom (LD<sub>50</sub>). These two plants showed significant neutralization effect against the venoms of *Naja nigricollis* venom. *H. javanica* and *G. superba* (25-100 mg/mL) produced significant changes of membrane stabilization of human red blood cells (HRBC) exposed to hyposaline-induced haemolysis. **Conclusions:** We conclude that probably due to presence of various phytochemicals plays an important role in the anti-venom potential of these Indian medicinal plants against *Naja nigricollis* venom. The above observations confirmed that *A. paniculata*, *C. magna*, *G. superba* and *H. javanica* plant extracts possess potent snake venom neutralizing capacity and could potentially be used as an adjuvants for antivenin therapy in case of snakebite envenomation, especially against the local effects of cobra venoms.

**Key words:** Antivenom activity, *Naja nigricollis*, hemolysis, neutralization, Indian medicinal plants



Kumarappan C, Madhavan Vijayakumar, Ellappan Thilagam, Manikam Balamurugan, Madheswaran Thiagarajan, Siddan Senthil, Sunil C Das, Subbash C Mandal. Protective and curative effects of polyphenolic extracts from *Ichnocarpus frutescense* leaves on experimental hepatotoxicity by carbon tetrachloride and tamoxifen. *Ann Hepatol (Mexico)* 2011; 10(1): 63-72

## **Protective and curative effects of polyphenolic extracts from *Ichnocarpus frutescense* leaves on experimental hepatotoxicity by carbon tetrachloride and tamoxifen**

Chidambaram Kumarappan<sup>1,2\*</sup>, Madhavan Vijayakumar<sup>2</sup>, Ellappan Thilagam<sup>3</sup>, Manikam Balamurugan<sup>4</sup>, Madheswaran Thiagarajan<sup>5</sup>, Siddan Senthil<sup>3</sup>, Sunil C. Das<sup>6</sup>, Subhash C. Mandal<sup>1</sup>

<sup>1</sup>Division of Pharmacognosy, Pharmacognosy and Phytotherapy Research Laboratory, Department of Pharmaceutical Technology, Faculty of Engineering and Technology, Jadavpur University, Kolkata, India

<sup>2\*</sup>Department of Life sciences, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia

<sup>3</sup>Ethnopharmacology Laboratory, National Botanical Research Institute, India

<sup>4</sup>Department of Phytochemistry and Pharmacognosy, J.K.K.M.M.R.F/ College of Pharmacy, B. Komarapalayam, India

<sup>5</sup>Department of Pharmaceutics, University of Nizwa, Birkat Al Mouz, Nizwa, Sultanate of Oman.

<sup>6</sup>Thuagarajan M, Clinical Pharmacy Lab, College of Pharmacy, Yeungnam University, South Korea

<sup>7</sup>Department of Plant Molecular Biology and Biotechnology, Loyola College (Autonomous), India.

### **Abstract**

The aim of this study was to investigate prophylactic and curative effect of polyphenolic extract of *Ichnocarpus frutescense* against carbon tetrachloride and tamoxifen induced hepatotoxicity in rats. Carbon tetrachloride and tamoxifen caused liver damage in rats manifested by significant rise in serum enzymes levels. Models of carbon tetrachloride and tamoxifen intoxication elicited significant declines in the reduced glutathione concomitant with significant elevations in malondialdehyde levels. The oral administration of polyphenolic extract to carbon tetrachloride and tamoxifen intoxicated rats, produced significant increments in the reduced glutathione concomitant with significant decrements in malondialdehyde and liver transaminases levels. Prophylactic and curative treatments with the polyphenolic extract generally resulted in a relatively good protection against both carbon tetrachloride and tamoxifen intoxicated rats. The histopathological changes of liver sections showed an improved histological appearance. The extract inhibits CYP monooxygenases aminopyrine-N-demethylase and aniline hydroxylase, suggesting a plausible hepatoprotective mechanism. However prophylactic treatment with the polyphenolic extract exhibited a higher activity compared to curative treatment. The normalization of phenobarbitone induced sleeping time suggests the restoration of liver CYP enzymes. The study shows that hepatoprotective activity of polyphenol extract is by regulating the levels of hepatic microsomal drug metabolising enzymes. These results supported the use of this plant for the treatment of hepatitis in oriental traditional medicine.

**Key words:** *Ichnocarpus frutescens*, Hepatoprotection, Carbon tetrachloride, Tamoxifen, Polyphenolic extract, Phase 1 enzymes.

Lai NM, Teng CL, Lee ML. Interpreting systemic reviews: are we ready to make our own conclusions? a cross-sectional study. *BMC Med* 2011; 9: 30-38

## **Interpreting systemic reviews: are we ready to make our own conclusions? a cross-sectional study**

Lai NM<sup>1</sup>, Teng CL<sup>2</sup>, Lee ML<sup>3</sup>

<sup>1</sup>Department of Paediatrics, Monash University Sunway Campus, Jeffrey Cheah School of Medicine and Health Sciences, JKR 1235, Bukit Azah, 80100, Johor Bahru, Johor, Malaysia

<sup>2</sup>Department of Family Medicine, International Medical University, Jalan Rasah, 70000, Seremban, Negeri Sembilan, Malaysia

<sup>3</sup>Clinical Research Centre, Hospital Tuanku Jaafar, Jalan Rasah, 70000, Seremban, Negeri Sembilan, Malaysia

### **Abstract**

#### **Background:**

Independent evaluation of clinical evidence is advocated in evidence-based medicine (EBM). However, authors' conclusions are often appealing for readers who look for quick messages. We assessed how well a group of Malaysian hospital practitioners and medical students derived their own conclusions from systematic reviews (SRs) and to what extent these were influenced by their prior beliefs and the direction of the study results.

#### **Methods:**

We conducted two cross-sectional studies: one with hospital practitioners (n = 150) attending an EBM course in June 2008 in a tertiary hospital and one with final-year medical students (n = 35) in November 2008. We showed our participants four Cochrane SR abstracts without the authors' conclusions. For each article, the participants chose a conclusion from among six options comprising different combinations of the direction of effect and the strength of the evidence. We predetermined the single option that best reflected the actual authors' conclusions and labelled this as our best conclusion. We compared the participants' choices with our predetermined best conclusions. Two chosen reviews demonstrated that the intervention was beneficial ("positive"), and two others did not ("negative"). We also asked the participants their prior beliefs about the intervention.

#### **Results:**

Overall, 60.3% correctly identified the direction of effect, and 30.1% chose the best conclusions, having identified both the direction of effect and the strength of evidence. More students (48.2%) than practitioners (22.2%) chose the best conclusions (P < 0.001). Fewer than one-half (47%) correctly identified the direction of effect against their prior beliefs. "Positive" SRs were more likely than "negative" SRs to change the participants' beliefs about the effect of the intervention (relative risk (RR) 1.8, 95% confidence interval 1.3 to 2.6) and "convert" those who were previously unsure by making them choose the appropriate direction of effect (RR 1.9, 95% confidence interval 1.3 to 2.8).

Conclusions:

The majority of our participants could not generate appropriate conclusions from SRs independently. Judicious direction from the authors' conclusions still appears crucial to guiding our health care practitioners in identifying appropriate messages from research. Authors, editors and reviewers should ensure that the conclusions of a paper accurately reflect the results. Similar studies should be conducted in other settings where awareness and application of EBM are different.

Lai NM, Teng CL. Self-perceived competence correlates poorly with objectively measured competence in Evidence Based Medicine among medical students. BMC Med Edu (UK) 2011; 11: 25

## **Self-perceived competence correlates poorly with objectively measured competence in Evidence Based Medicine among medical students**

Lai NM<sup>1</sup>, Teng CL<sup>2</sup>

<sup>1</sup>Department of Paediatrics, Monash University Sunway Campus, Jeffrey Cheah School of Medicine and Health Sciences, JKR 1235, Bukit Azah, 80100, Johor Bahru, Johor, Malaysia

<sup>2</sup>Department of Family Medicine, International Medical University, Jalan Rasah, 70000, Seremban, Negeri Sembilan, Malaysia

### **Abstract**

#### **Background:**

Previous studies report various degrees of agreement between self-perceived competence and objectively measured competence in medical students. There is still a paucity of evidence on how the two correlate in the field of Evidence Based Medicine (EBM). We undertook a cross-sectional study to evaluate the self-perceived competence in EBM of senior medical students in Malaysia, and assessed its correlation to their objectively measured competence in EBM.

#### **Methods:**

We recruited a group of medical students in their final six months of training between March and August 2006. The students were receiving a clinically-integrated EBM training program within their curriculum. We evaluated the students' self-perceived competence in two EBM domains ("searching for evidence" and "appraising the evidence") by piloting a questionnaire containing 16 relevant items, and objectively assessed their competence in EBM using an adapted version of the Fresno test, a validated tool. We correlated the matching components between our questionnaire and the Fresno test using Pearson's product-moment correlation.

#### **Results:**

Forty-five out of 72 students in the cohort (62.5%) participated by completing the questionnaire and the adapted Fresno test concurrently. In general, our students perceived themselves as moderately competent in most items of the questionnaire. They rated themselves on average 6.34 out of 10 (63.4%) in "searching" and 44.41 out of 57 (77.9%) in "appraising". They scored on average 26.15 out of 60 (43.6%) in the "searching" domain and 57.02 out of 116 (49.2%) in the "appraising" domain in the Fresno test. The correlations between the students' self-rating and their performance in the Fresno test were poor in both the "searching" domain ( $r = 0.13$ ,  $p = 0.4$ ) and the "appraising" domain ( $r = 0.24$ ,  $p = 0.1$ ).

#### **Conclusions:**

This study provides supporting evidence that at the undergraduate level, self-perceived competence in EBM, as measured using our questionnaire, does not correlate well with objectively assessed EBM competence measured using the adapted Fresno test.

**Key words:** Evidence Based Medicine assessment, undergraduate

Lee Choy Sin, Lee Song Cang. Preparation of polyester polyol from epoxidized palm olein. Chin J Chem (China) 2011; 29: 2421-2427

## Preparation of polyester polyol from epoxidized palm olein

Lee Choy Sin<sup>1</sup>, Lee Song Cang<sup>2</sup>

<sup>1</sup>Pharmaceutical Chemistry Department, International Medical University, No 126, Jalan 19/155B, Bukit Jalil, 57000 KL, Malaysia

<sup>2</sup>Biomedical Engineering Department, Faculty of Engineering, University of Malaya, 50603 KL, Malaysia

### Abstract

In this work, polyester polyols with high weight average molecular weight ( $M_w$ ) ( $M_w = 10000\text{--}15000$ ) were prepared from epoxidized palm olein (EPOo) and a series of dicarboxylic acids (C6—C12) at elevated temperature under non-catalyzed condition. The optimal reaction conditions were determined as 180 °C for 4 h. Longer carbon chain length of dicarboxylic acids was more reactive when reacted with EPOo. The physical appearance of the product was observed as liquid at room temperature. This palm oil-based polyester polyol is proposed as starting material for flexible polyurethane. For reaction monitoring purposes, FTIR was used while <sup>1</sup>H NMR analysis was carried out to characterize the important functional groups of the products. The effects of reaction time and temperature on the  $M_w$  of the reaction mixture were also studied by GPC.

**Key words:** dicarboxylic acids, epoxidized palm olein, polyester polyol

Lim Kian Long, Tay A, Nadarajah VD, Mitra NK. The effect of consequent exposure of stress and dermal application of low doses of chlorpyrifos on the expression of glial fibrillary acidic protein in the hippocampus of adult mice. *J Occupational Med Toxicol (UK)* 2011; 6: 4-9

## **The effect of consequent exposure of stress and dermal application of low doses of chlorpyrifos on the expression of glial fibrillary acidic protein in the hippocampus of adult mice**

Lim Kian Long, Annie Tay, Vishna Devi Nadarajah, Nilesh Kumar Mitra

<sup>1</sup>Postgraduate & Research Department, International Medical University, No.126, Jalan 19/155B, Bukit Jalil, 57000, Kuala Lumpur, Malaysia

<sup>2</sup>Pathology Department, International Medical University, No.126, Jalan 19/155B, Bukit Jalil, 57000, Kuala Lumpur, Malaysia

<sup>3</sup>Human Biology Department, International Medical University, No.126, Jalan 19/155B, Bukit Jalil, 57000, Kuala Lumpur, Malaysia

### **Abstract**

#### **Background:**

Chlorpyrifos (CPF), a commonly used pesticide worldwide, has been reported to produce neurobehavioural changes. Dermal exposure to CPF is common in industries and agriculture. This study estimates changes in glial fibrillary acidic protein (GFAP) expression in hippocampal regions and correlates with histomorphometry of neurons and serum cholinesterase levels following dermal exposure to low doses of CPF with or without swim stress.

#### **Methods:**

Male albino mice were separated into control, stress control and four treatment groups (n = 6). CPF was applied dermally over the tails under occlusive bandage (6 hours/day) at doses of 1/10th (CPF 0.1) and 1/5<sup>th</sup> dermal LD50 (CPF 0.2) for seven days. Consequent treatment of swim stress followed by CPF was also applied. Serum cholinesterase levels were estimated using spectrofluometric methods. Paraffin sections of the left hippocampal regions were stained with 0.2% thionin followed by the counting of neuronal density. Right hippocampal sections were treated with Dako Envision GFAP antibodies.

#### **Results:**

CPF application in 1/10th LD50 did not produce significant changes in serum cholinesterase levels and neuronal density, but increased GFAP expression significantly (p < 0.001). Swim stress with CPF 0.1 group did not show increase in astrocytic density compared to CPF 0.1 alone but decreased neuronal density.

#### **Conclusions:**

Findings suggest GFAP expression is upregulated with dermal exposure to low dose of CPF. Stress combined with sub-toxic dermal CPF exposure can produce neurotoxicity.

Lim FCP, Ling APK, Hii SL, Hussein S. Towards understanding of physiological changes in cell culture of recalcitrant woody plant - *Eurycoma longifolia* in response to carbon and nitrogen sources. *J Med Plant Res* 2011; 5(14): 3200-3209

## **Towards understanding of physiological changes in cell culture of recalcitrant woody plant - *Eurycoma longifolia* in response to carbon and nitrogen sources**

Lim FCP<sup>1</sup>, Ling APK<sup>2</sup>, Hii SL<sup>3</sup>, Hussein S<sup>4</sup>

<sup>1</sup>Department of Science, Faculty of Engineering and Science, University of Tunku Abdul Rahman, Setapak, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Human Biology, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>3</sup>Department of Chemical Engineering, Faculty of Engineering and Science, University of Tunku Abdul Rahman, Setapak, Kuala Lumpur, Malaysia

<sup>4</sup>Agrotechnology and Bioscience Division, Malaysian Nuclear Agency, Bangi, Kajang, Selangor, Malaysia

### **Abstract**

*Eurycoma longifolia* possesses high medicinal and economical values owing mainly to its aphrodisiac properties claimed by the local communities in Southeast Asia regions. However, the long cultivation period, low successful rate of seed propagation and susceptibility towards pests and diseases have affected the supply of *E. longifolia* to meet the high market demand. Thus, the large scale production of *E. longifolia* using cell suspension technique is tantalizing. In this study, the *E. longifolia* cells cultivated in shake flask system were subjected to different carbon and nitrogen sources treatments. The cells treated with glucose gave the highest increment of fresh weight ( $0.4386 \pm 0.0120$  g/mL), with increment of total soluble protein content,  $0.71 \pm 3.05$  mg/g FW and increment of specific activity of peroxidase,  $5410.04 \pm 1221.43$  U/mg. Glucose-treated cells also achieved the highest carbon source utilization rate ( $2.81 \pm 0.31$  mg/mL/Day). For the cells treated with different nitrogen sources, the potassium nitrate (KNO<sub>3</sub>) treatment gave the highest increment of fresh weight ( $0.2601 \pm 0.0387$  g/mL), with increment of total soluble protein content,  $0.62 \pm 0.00$  mg/g and increment of specific activity of peroxidase,  $-3691.57 \pm 2717.18$  U/mg. The cells also had the highest sucrose utilization rate ( $2.92 \pm 0.02$  mg/mL/Day).

**Key words:** Carbon utilization rate, cell suspension culture, *Eurycoma longifolia*, specific activity of peroxidases, total soluble protein content

## **Leptospirosis: a re-emerging infection**

Lim VKE

Division of Pathology, Faculty of Medicine and Health, International Medical University, Malaysia

### **Abstract**

Leptospirosis is a re-emerging zoonotic infection. In developing countries large outbreaks have occurred in urban slums and following floods. Individuals from developed nations are also now more frequently exposed to the infection as a result of international travel and greater participation in certain outdoor recreational activities. Leptospirosis remains a diagnostic challenge since it often presents as a non-specific febrile event and laboratory diagnosis is still currently inadequate. Rapid tests may not be sufficiently sensitive in early disease and culture facilities are not widely available. A severe pulmonary haemorrhagic form of the infection is increasingly being encountered in many countries including Malaysia. The control of leptospirosis is largely dependent on general hygienic measures and rodent control. An effective human vaccine is still not available. There remains much that is unknown about this disease and there is scope and opportunity for good quality research.

**Key words:** leptospirosis, re-emerging infection, zoonosis, Weil



Lim Yee Lyn, Huan Wen Sze, Gorajana A, Rajendran A, Dua K, Sanjay Garg.  
Crystal modifications and dissolution rate of piroxicam. *Acta Pharmaceutica*  
2011; 61: 391-402

## Crystal modifications and dissolution rate of piroxicam

Lim Yee Lyn<sup>1</sup>, Huan Wen Sze<sup>1</sup>, Adinarayana Gorajana<sup>1</sup>, Adhiyaman Rajendran<sup>1</sup>, Kamal Dua<sup>1</sup>, Sanjay Garg<sup>2</sup>

<sup>1</sup>School of Pharmacy and Health Sciences, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup>AnQual Laboratories, School of Pharmacy, University of Auckland Auckland, New Zealand

### Abstract

Piroxicam is a nonsteroidal anti-inflammatory drug with low aqueous solubility which exhibits polymorphism. The present study was carried out to develop polymorphs of piroxicam with enhanced solubility and dissolution rate by the crystal modification technique using different solvent mixtures prepared with PEG 4000 and PVP K30. Physicochemical characteristics of the modified crystal forms of piroxicam were investigated by X-ray powder diffractometry, FT-IR spectrophotometry and differential scanning calorimetry. Dissolution and solubility profiles of each modified crystal form were studied and compared with pure piroxicam. Solvent evaporation method (method I) produced both needle and cubic shaped crystals. Slow crystallization from ethanol with addition of PEG 4000 or PVP K30 at room temperature (method II) produced cubic crystal forms. Needle forms produced by method I improved dissolution but not solubility. Cubic crystals produced by method I had a dissolution profile similar to that of untreated piroxicam but showed better solubility than untreated piroxicam. Cubic shaped crystals produced by method II showed improved dissolution, without a significant change in solubility. Based on the XRPD results, modified piroxicam crystals obtained by method I from acetone/benzene were cube shaped, which correlates well with the FTIR spectrum; modified needle forms obtained from ethanol/methanol and ethanol/ acetone showed a slight shift of FTIR peak that may be attributed to differences in the internal structure or conformation.

**Key words:** piroxicam, polymorphism, crystallization, polymer, dissolution

Ling APK, Ong SL, Hussein S. Strategies in enhancing secondary metabolites production in plant cell cultures. *Medicinal Aromatic Plant Sci Biotechnol* 2011; 5(2): 94-101

## **Strategies in enhancing secondary metabolites production in plant cell cultures**

Ling APK<sup>1</sup>, Ong SL<sup>2</sup>, Hussein S<sup>3</sup>

<sup>1</sup>Department of Human Biology, International Medical University (IMU), Kuala Lumpur, Malaysia

<sup>2</sup>Department of Science, Faculty of Engineering and Science, Tunku Abdul Rahamn University (UTAR), Setapak, Kuala Lumpur, Malaysia

<sup>3</sup>Agrotechnology and Bioscience Division, Malaysia Nuclear Agency, Bangi, 43000 Kajang, Selangor, Malaysia

### **Abstract**

Conventionally, pharmaceutically important secondary metabolites such as flavonoids were excreted directly from whole plants collected from the wild. This conventional method is not cost effective and could even lead to extinction of some endangered plant species. Furthermore, the production of uniform quantity and quality secondary metabolites will be affected as their production is greatly influenced by geographical, seasonal and environmental variations. Biotechnological approaches, specifically, plant tissue culture techniques, have been considered as an attractive solution to the problems of extracting secondary metabolites for industrial applications. Nevertheless, the commercial implementation of pilot scale plant cell suspensions for chemical production is still in the development stage with a few exceptional cases. The major setback is the failure of cell cultures to accumulate significant amounts of secondary metabolites compared to whole plants or organ cultures. Even so, several strategies can be applied in order to substantially increase the yields of secondary metabolites in plant cell cultures. This paper discussed the strategies of nutrient manipulation, precursor feeding and elicitation in enhancing the production of secondary metabolites.

**Key words:** callus culture, cell suspension culture, plant biotechnology, secondary metabolites

Mahalingam D, Radhakrishnan AK, Amom Z, Ibrahim N, Nesaretnam K. Effects of supplementation with tocotrienol-rich fraction on immune response to tetanus toxoid immunization in normal healthy volunteers. *Eur J Clin Nutr (UK)* 2011; 65: 63-69

## **Effects of supplementation with tocotrienol-rich fraction on immune response to tetanus toxoid immunization in normal healthy volunteers**

Mahalingam D<sup>1,2</sup>, Radhakrishnan AK<sup>2</sup>, Amom Z<sup>3</sup>, Ibrahim N<sup>2</sup>, Nesaretnam K<sup>1</sup>

<sup>1</sup>Malaysian Palm Oil Board, Selangor, Malaysia

<sup>2</sup>International Medical University, Kuala Lumpur, Malaysia

<sup>3</sup>University Putra Malaysia, Selangor, Malaysia

### **Abstract**

#### **Background/Objectives:**

Vitamin E is an essential fat-soluble vitamin that has been shown to induce favorable effects on animal and human immune systems. The objective of this study was to assess the effects of tocotrienol-rich fraction (TRF) supplementation on immune response following tetanus toxoid (TT) vaccine challenge in healthy female volunteers.

#### **Subjects/Methods:**

In this double-blinded, placebo-controlled clinical trial, participants were randomly assigned to receive either placebo (control group) or 400mg of TRF (study group) supplementation daily. Over the 2-month period of the study, volunteers were asked to attend three clinical sessions (that is, on days 0, 28 and 56) and blood samples were obtained from the volunteers during the follow-up. On day 28, all volunteers were also vaccinated with the TT vaccine (20 Lf) intramuscularly.

#### **Results:**

The results from the clinical trial showed that TRF supplementation significantly increased the total vitamin E level in the plasma of the TRF-supplemented volunteers compared with the placebo group, indicating overall compliance. Volunteers supplemented with TRF showed a significantly ( $P < 0.05$ ) enhanced production of interferon- $\gamma$  and interleukin (IL)-4 by the mitogen or TT-stimulated leukocytes compared with the control group. Volunteers from the TRF group produced significantly ( $P < 0.05$ ) lower amounts of IL-6 compared with the placebo group. Anti-TT IgG production was also significantly ( $P < 0.05$ ) augmented in the TRF-supplemented group compared with the placebo group.

#### **Conclusions:**

We conclude that TRF has immunostimulatory effects and potential clinical benefits to enhance immune response to vaccines.

**Key words:** tocotrienol-rich fraction; tetanus toxoid; immunostimulatory

Mathew T. The loading and unloading properties of various arch wires as a function of cross sectional dimension and inter bracket span width. *Mal Dent J* 2011; 32(1); 29-41

## **The loading and unloading properties of various arch wires as a function of cross sectional dimension and inter bracket span width**

Mathew T

Faculty of Dentistry, International Medical University

### **Abstract**

It is the aim of all clinicians to accomplish biological tooth movement, which implies the use of low, continuous force. Constant unrelented search for a better wire, which can deliver optimal orthodontic force, has led to the invention of a lot of orthodontic wires such as Stainless steel, Beta Titanium, Nickel Titanium and multi stranded wires. In this study, the loading and unloading properties of 0.016 inch, 0.016x0.022 inch and 0.017x0.025 inch dimensions of stainless steel, conventional NiTi, Super elastic NiTi, and TMA arch wires were determined by means of a modified three point bending test for two inter bracket widths of 5 mm and 6.5 mm for deflection of 1 to 3 mm. The applied forces dependence on cross-sectional size differs from the linear-elastic prediction in super elastic NiTi wires. The stainless steel wires had the highest force values on all the three dimensions and cross section. On loading and unloading, TMA wires had force values in-between stainless steel, conventional NiTi and super elastic NiTi. The conventional NiTi had much lower force values compared to stainless steel and TMA and were linearly progressing compared to Super elastic NiTi. On loading and unloading the super elastic NiTi had force values in the range of conventional NiTi and had constant forces on higher deflection. The studies showed that the force value was comparatively higher in 5 mm inter bracket width than the 6.5 mm inter bracket width for all the cross section and dimension of wires.

**Key words:** Optimal Orthodontic force, Inter bracket span, Cross sectional dimension

Mathews L, Nagaraja HS, Chakravarthi S. Insulin-like growth factor-1 (IGF-1) reduces ischemic changes and increases circulating angiogenic factors in experimentally-induced myocardial infarction in rats. *Vascular Cell* 2011; 3: 13; doi: 10.11186/2045-824X-3-13

## **Insulin-like growth factor-1 (IGF-1) reduces ischemic changes and increases circulating angiogenic factors in experimentally-induced myocardial infarction in rats**

Mathews Lisa<sup>1</sup>, Haleagraha N<sup>1</sup>, Srikumar Chakravarthi<sup>2</sup>

<sup>1</sup>Division of Human Biology, Faculty of Medicine, International Medical University, Kuala Lumpur, 57000, Malaysia

<sup>2</sup>Division of Pathology, International Medical University, Kuala Lumpur, 57000, Malaysia

### **Abstract**

#### **Background:**

Coronary artery disease is a global health concern in the present day with limited therapies. Extensive efforts have been devoted to find molecular therapies to enhance perfusion and function of the ischemic myocardium. Aim of the present study was to look into the effects of insulin like growth factor -1 (IGF-1) on circulating angiogenic factors after myocardial ischemia in rats.

#### **Methods:**

Adult male Sprague-Dawley rats were randomly divided into 10-days control, myocardial infarction, IGF-1 alone (2 µg/rat/day) and ISO+IGF-1 groups. Isoproterenol (ISO), a synthetic catecholamine was used to induce myocardial infarction. Serum transforming growth factor-b (TGF-b) and vascular endothelial growth factor (VEGF) levels were checked after 10-days of IGF-1 administration.

#### **Results:**

There was a significant increase in heart weight after IGF-1 treatment. A significant increase in cardiac enzyme level (CK-MB and LDH) was seen in isoproterenol treated rats when compared to control group. IGF-1 treatment induced a significant increase in serum angiogenic factors, IGF-1, VEGF and TGF beta levels. IGF-1 also reduced the ischemic changes in the myocardium when compared to the isoproterenol alone treated group.

#### **Conclusions:**

In conclusion, treatment with insulin-like growth factor-1 (IGF-1) in myocardial infarction significantly increased circulating angiogenic growth factors like IGF-1, VEGF and TGF beta thus, protecting against myocardial ischemia.

Mimi O, Tong SF, Nordin S, Teng CL, Khoo EM, Abdul-Rahman A, Zailinawati AH, Lee VKM, Chen WS, Shihabudin WM, Noridah MS, Fauziah ZE. A comparison of morbidity patterns in public and private primary care clinics in Malaysia. *Mal Fam Physician* 2011; 6(1): 19-25

## **A comparison of morbidity patterns in public and private primary care clinics in Malaysia**

Mimi O<sup>1</sup>, Tong SF<sup>2</sup>, Nordin S<sup>3</sup>, Teng CL<sup>4</sup>, Khoo EM<sup>5</sup>, Abdul-Rahman A<sup>3</sup>, Zailinawati AH<sup>6</sup>, Lee VKM<sup>4</sup>, Chen WS<sup>7</sup>, Shihabudin WM<sup>3</sup>, Noridah MS<sup>8</sup>, Fauziah ZE<sup>8</sup>

<sup>1</sup>Klinik Kesihatan Kelana Jaya

<sup>2</sup>Department of Family Medicine, Universiti Kebangsaan Malaysia

<sup>3</sup>Institute for Health System Research

<sup>4</sup>International Medical University

<sup>5</sup>Department of Primary Care, University of Malaya

<sup>6</sup>Klinik Keluarga Wangsa Maju

<sup>7</sup>Klinik Alam Medic

<sup>8</sup>Ministry of Health

### **Abstract**

#### **Objectives:**

To compare the morbidity patterns in public and private primary care clinics; determine patients' reasons for encounter (RFE) and diagnoses using the ICPC-2, and compare ten commonest diagnoses and RFEs.

#### **Methods:**

A cross-sectional study on randomly selected clinics was conducted nationwide. Doctors completed the Patient Encounter Record (PER) for systematically selected encounters for a week.

#### **Results:**

Response rate was 82.0% (public clinic) and 33% (private clinic) with 4262 encounters and 7280 RFE. Overall, the three commonest disease categories encountered were respiratory (37.2%), general and unspecified (29.5%), and cardiovascular diseases (22.2%). Public and private clinics handled 27% versus 50% acute cases and 20.0% versus 3.1% chronic cases i.e.

33.7 and 5.6 chronic diseases per 100 RFE respectively.

#### **Conclusion:**

Doctors in public clinics saw more chronic and complex diseases as well as pregnancy related complaints and follow-up cases while in private clinics more acute and minor illnesses were seen. Health services should be integrated and support given to co-manage chronic diseases in both sectors.

**Key words:** Primary practice, morbidity pattern, delivery of health care, reasons for encounter, Malaysia

Muayad S Rahma, Ni Ni Win, Rafidah HM, Ailin Razali. The effects of noise on biochemical parameters using rat's hearts. Eur J Sci Res 2011; 56 (1): 93-96

## **The effects of noise on biochemical parameters using rat's hearts**

Muayad S Rahma<sup>1</sup>, Ni Ni Win<sup>2</sup>, Rafidah HM<sup>3</sup>, Ailin Razali<sup>4</sup>

<sup>1</sup>International Islamic University Malaysia College of Dentistry, Malaysia

<sup>2</sup>International Medical University Malaysia

<sup>3</sup>University Sains Islam Malaysia

<sup>4</sup>International Islamic University Malaysia

### **Abstract**

The present study was undertaken to evaluate the effect of acute and chronic high intensity noise on plasma blood glucose concentration and lipid profile of rats. The rats were divided into four groups and they include exposure to noise of intensity 80-100 dBA on duration of 12 hours exposure (acute effect), 8 hours daily for 20 days (chronic effect), 20 days into 3 days exposure and 2 days without 8 hours per day (intermittent effect) and the control group. Noise of 80-100 dBA was found to cause significant increase in plasma glucose for the acute and chronic continuous groups as compared to no noise exposure. The cholesterol, triglycerides (TG) and high density lipoprotein (HDL) had no significant difference compared to control. HDL level revealed significant elevation in case of chronic continuous and intermittent noise exposure ( $p < 0.05$ ) when compared to control group. In conclusion the present study determined that high intensity noise may have an adverse effect on biochemical values and thus noise exposure should be well monitored.

**Key words:** Acute, intermittent and chronic noise

Muneer GB, Hasan SS, Cho Naing, Nur Hidayah Binti Hamzah. Perceptions and self-use of complementary and alternative medicine (CAM) among Malaysian dental students. *Eur J Integrative Med* 2011; doi: 10.1016/j.ujim.2011.11.001

## **Perceptions and self-use of complementary and alternative medicine (CAM) among Malaysian dental students**

Muneer Gohar Babar<sup>1</sup>, Shahzad H Syed<sup>2</sup>, Cho Min Naing<sup>1</sup>, Nur Hidayah Binti Hamzah<sup>1</sup>

<sup>1</sup>International Medical University, No. 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>University of Queensland, 20 Cornwall Street, Woolloongabba, 4102 Brisbane, Australia

### **Abstract**

#### **Introduction:**

A high self-use of CAM by medical students has been reported however, studies of CAM use among dental students is limited. The present study assesses the perceptions and self-use of CAM among dental students in Malaysia.

#### **Methods:**

A cross-sectional study of the perceptions and self-use of CAM among 267 randomly sampled dental students from 1 public and 2 private universities in Malaysia was undertaken using a validated self-administered questionnaire. Descriptive and inferential statistics were calculated using SPSS® version 18.

#### **Results:**

Seventy-six percent of the sample reported using CAM at the time of the survey. Of these, 21.7% (58) reported using Complementary Medicine (CM) and 16.5% (44) reported using Traditional Chinese Medicine (TCM). More than half (204, 76.4%) of the participants were currently using CAM while 95.8% (256) had used it previously. Students perceived all types of CAM as effective (mean score  $\leq 3$ ). Lack of trained professionals was reported by 64% of the sample as the main barrier to the use of CAM. A majority of students (58.4%,  $n = 156$ ) reported that friends and family members were their main source of information about CAM. Students supported the integration of CAM education into their dental curriculum (mean score  $\leq 3$ ).

#### **Conclusions:**

Data from this study adds to the understanding of dental students' current and previous self-use of CAM. The dental students in this study agreed that CAM knowledge is necessary to be a well-rounded professional and supported the integration of CAM education in the dental curriculum.

**Key words:** Perception; Self-use; Complementary; Alternative; Dental students; Malaysia



Mustafa Emienour-Muzalina, Phang SM, Chu WL. Use of an algal consortium of five algae in the treatment of landfill leachate using the high-rate algal pond system. J Appl Phycol 2011; doi 10.1007/s10911-011-9716-x

## Use of an algal consortium of five algae in the treatment of landfill leachate using the high-rate algal pond system

Mustafa Emienour-Muzalina<sup>1</sup>, Phang SM<sup>1</sup>, Chu WL<sup>2</sup>

<sup>1</sup>Institute of Biological Sciences, Faculty of Science and Institute of Ocean and Earth Sciences, University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>2</sup>International Medical University, Plaza Komanwel, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### Abstract

Five species of microalgae *Chlorella vulgaris*, *Scenedesmus quadricauda*, *Euglena gracilis*, *Ankistrodesmus convolutus* and *Chlorococcum oviforme*, were screened for their ability to grow in treated landfill leachate (TL) using shake flask cultures. The treated leachate had undergone previous treatment through mechanical aeration in treatment ponds at the landfill site. The five algae, except for *C. oviforme*, were able to grow in medium containing up to 50% TL. Two high-rate algal ponds (HRAP) equipped with paddlewheel were used for the semi-continuous cultures. A mixture of the five algae was used to inoculate one of two HRAPs for secondary treatment of TL. The other HRAP was filled with natural lake water containing mixed populations of algae. A volume of 400 mL (1%) from both ponds were removed daily and replaced with TL. The leachate loading rate was increased to 2% (0.8 L day<sup>-1</sup>) on day 197 and then to 4% (1.6 L day<sup>-1</sup>) on day 309, providing hydraulic retention time of 100, 50 and 25 days, respectively. Although higher biomass was obtained in the HRAP containing the consortium of five algae, there was no significant difference in reduction of pollutants between the two ponds. The HRAPs produced algal biomass ranging from 2.00 to 5.54 g dry weight L<sup>-1</sup> with significant reduction in chemical oxygen demand (91.0%), ammoniacal nitrogen (99.9%) and orthophosphate (86.0%) contents. The HRAP offers a potential treatment system for TL which is simple, low cost, flexible in use and requiring low maintenance.

**Key words:** Microalgae, Landfill leachate, High-rate algal pond (HRAP), Bioremediation

Nagarajah HS, Cheng Jun Siew, Mitra NK, Kumari M. Neuroprotective effect of bioflavonoid quercetin in 6-hydroxydopamine-induced oxidative stress biomarkers in the rat striatum. *Neuroscience Letters (Netherlands)* 2011; 500(2): 139-143

## **Neuroprotective effect of bioflavonoid quercetin in 6-hydroxydopamine-induced oxidative stress biomarkers in the rat striatum**

Nagarajah Haleagrahara, Cheng Jun Siew, Nilesh Kumar Mitra, Mangala Kumari

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

### **Abstract**

An increasing large body of research on Parkinson's disease (PD) has focused on the understanding of the mechanisms behind the potential neuro protection offered by antioxidants and iron chelating agents. In this study, the protective effect of the bioflavonoid quercetin on 6-hydroxydopamine (6-OHDA)-induced model of PD was investigated. PD was induced by a single intracisternal injection of 6-hydroxydopamine (300 µg) to male Sprague-Dawley rats. Quercetin treatment (30 mg/kg body weight) over 14 consecutive days markedly increased the striatal dopamine and antioxidant enzyme levels compared with similar measurements in the group treated with 6-OHDA alone. There was a significant decrease in protein carbonyl content in the striatum compared with that of rats that did not receive quercetin. A significant increase in neuronal survivability was also found with quercetin treatment in rats administered 6-OHDA. In conclusion, treatment with quercetin defended against the oxidative stress in the striatum and reduced the dopaminergic neuronal loss in the rat model of PD.

**Key words:** 6-Hydroxydopamine, Quercetin, Dopamine, Corpus striatum, Oxidative

Nagaraja HS, Chakravathi S, Anupama Bangra Kulu, Radhakrishnan AK. Effects of chronic lead acetate exposure on bone marrow lipid peroxidation and antioxidant enzyme activities in rats. *Afr J Pharm Pharmacol* 2011; 5(7): 923-929

## **Effects of chronic lead acetate exposure on bone marrow lipid peroxidation and antioxidant enzyme activities in rats**

Nagaraja Haleagrahara<sup>1</sup>, Srikumar Chakravathi<sup>2</sup>, Anupama Bangra Kulu<sup>3</sup>, Ammu Radhakrishnan<sup>2</sup>

<sup>1</sup>Human Biology Division, School of Medicine, International Medical University, Kuala Lumpur, 57000, Malaysia

<sup>2</sup>Pathology Division, School of Medicine, International Medical University, Kuala Lumpur, 57000, Malaysia

<sup>3</sup>Faculty of Medicine, MAHSA University College, Petaling Jaya, Kuala Lumpur, 46200, Malaysia

### **Abstract**

Occupational and environmental exposure of lead (Pb) is a serious health problem in developing and industrialized countries around the world. Toxic effect of lead is closely related to its accumulation in important tissues after its absorption into the blood. Present study looked into the effect of lead toxicity on bone marrow oxidative biomarkers in Sprague-Dawley rats. Rats were divided into four groups and in three experimental groups, they were given lead acetate in drinking water for 21 days in three different doses (200, 400 and 600 ppm). Effect of lead acetate on bone marrow lipid peroxidation and antioxidant enzymes were examined. Lead exposure for 21 days resulted in a significant increase ( $P < 0.05$ ) in lipid hydroperoxides and protein carbonyl contents of bone marrow and there was significant decrease ( $P < 0.05$ ) in bone marrow total antioxidants and superoxide dismutase, glutathione peroxidase and catalase enzyme levels. More significant increase ( $P < 0.05$ ) in lipid peroxidation and a decrease in antioxidant enzymes level were recorded with 600 ppm dose of lead. There was also a significant level of perturbations ( $P < 0.05$ ) in bone marrow antioxidant enzyme levels with low level of lead exposure for 21 days. Thus, the study confirms that exposure to lead will result in significant amount of toxic effect in the bone marrow, resulting in increased lipid peroxidation and depletion of antioxidant enzymes.

**Key words:** Lead acetate, Lead toxicity, oxidative stress, bone marrow, lipid peroxidation

Nagaraja HS, Chakravarthi S, Mathews L. Insulin like growth factor-1 (IGF-1) causes overproduction of IL-8, an angiogenic cytokine and stimulates neovascularization in isoproterenol-induced myocardial infarction in rats. *Intl J Mol Sci* 2011; 12: 8562-8574

## **Insulin like growth factor-1 (IGF-1) causes overproduction of IL-8, an angiogenic cytokine and stimulates neovascularization in isoproterenol-induced myocardial infarction in rats**

Nagaraja Haleagrahara<sup>1</sup>, Srikumar Chakravarthi<sup>2</sup>, Lisa Mathews<sup>3</sup>

<sup>1</sup>Faculty of Medicine, Health and Molecular Sciences, James Cook University, Townsville 4811, Queensland, Australia

<sup>2</sup>Division of Pathology, International Medical University, Kuala Lumpur 57000, Malaysia

<sup>3</sup>Division of Human Biology, International Medical University, Kuala Lumpur 57000, Malaysia

### **Abstract**

Angiogenesis factors are produced in response to hypoxic or ischemic insult at the site of pathology, which will cause neovascularization. Insulin like growth factor-1 (IGF-1) exerts potent proliferative, angiogenic and anti-apoptotic effects in target tissues. The present study was aimed to evaluate the effects of IGF-1 on circulating level of angiogenic cytokine interleukin-8 (IL-8), in experimentally-induced myocardial ischemia in rats. Male Sprague-Dawley rats were divided into control, IGF-1 treated (2 µg/kg/day subcutaneously, for 5 and 10 days), isoproterenol (ISO) treated (85 mg/kg, subcutaneously for two days) and ISO with IGF-1 treated (for 5 and 10 days). Heart weight, serum IGF-1, IL-8 and cardiac marker enzymes (CK-MB and LDH) were recorded after 5 and 10 days of treatment. Histopathological analyses of the myocardium were also done. There was a significant increase in serum cardiac markers with ISO treatment indicating myocardial infarction in rats. IGF-1 level increased significantly in ISO treated groups and the level of IGF-1 was significantly higher after 10 days of treatment. IL-8 level increased significantly after ISO treatment after 5 and 10 days and IGF-1 concurrent treatment to ISO rats had significantly increased IL-8 levels. Histopathologically, myocyte necrosis and nuclear pyknosis were reduced significantly in IGF-1 treated group and there were numerous areas of capillary sprouting suggestive of neovascularization in the myocardium. Thus, IGF-1 protects the ischemic myocardium with increased production of circulating angiogenic cytokine, IL-8 and increased angiogenesis.

**Key words:** IGF-1; isoproterenol; myocardial ischemia; angiogenesis; interleukin-8

Nagaraja HS, Tan Jackie, Chakravarthi S, Anupama Bangra Kulur. Protective effect of alpha-lipoic acid against lead acetate-induced oxidative stress in the bone marrow of rats. Intl J Pharmacol 2011; doi:10.3923/ijp.2011

## **Protective effect of alpha-lipoic acid against lead acetate-induced oxidative stress in the bone marrow of rats**

Nagaraja Haleagrahara<sup>1</sup>, Tan Jackie<sup>2</sup>, Srikumar Chakravarthi<sup>3</sup>, Anupama Bangra Kulur<sup>4</sup>

<sup>1</sup>Division of Human Biology, School of Medicine, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>Division of Postgraduate Studies, International Medical University, Kuala Lumpur, Malaysia

<sup>3</sup>Division of Pathology, School of Medicine, International Medical University, Kuala Lumpur, Malaysia

<sup>4</sup>Faculty of Medicine, MAHSA University College, Kuala Lumpur, Malaysia

### **Abstract**

The present study was designed to investigate the effects of alpha Lipoic Acid (LA) against lead acetate induced changes in free radical scavenging enzymes and lipid hydroperoxides in bone marrow of rats. Rats were exposed to lead acetate in their drinking water (500 ppm) for 14 days and alpha lipoic acid was given concurrently (25, 50 and 100 mg kg<sup>-1</sup>). Blood lead levels, lipid hydroperoxides, protein carbonyl contents and oxidative marker enzymes were estimated. Lead acetate in drinking water had elicited a significant ( $p < 0.05$ ) increase in bone marrow lipid hydroperoxides (LPO) ( $p < 0.05$ ) and Protein-Carbonyl-Contents (PCC). There was a significant ( $p < 0.05$ ) decrease in total antioxidants, superoxide dismutase ( $p < 0.05$ ), glutathione peroxidase ( $p < 0.05$ ), glutathione S-transferase ( $p < 0.05$ ) and catalase levels with lead ingestion. Supplementation of alpha lipoic acid was associated with reduced serum LPO and PCC and a significant ( $p < 0.05$ ) increase in total antioxidants and antioxidant enzyme levels. There was more significant protective effect of bone marrow with 100 mg kg<sup>-1</sup> b.wt. LA. The potency of alpha lipoic acid on the reversal of lead induced changes in oxidative biomarkers in bone marrow confirms the importance of lead induced oxidative stress in bone and suggests a therapeutic approach.

**Key words:** Lead acetate, lipid peroxidation, bone marrow, oxidative stress, alpha lipid lipoic acid

Nagaraja HS, Varkkey Julian, Chakravarthi S. N-acetylcysteine offers cardioprotection by decreasing cardiac lipid hydroperoxides and 8-isoprostane level in isoproterenol-induced cardiotoxicity in rats. *Cardiovascular Toxicol (USA)* 2011; doi: 10.1007/s12012-9132-0

## **N-acetylcysteine offers cardioprotection by decreasing cardiac lipid hydroperoxides and 8-Isoprostane level in isoproterenol-induced cardiotoxicity in rats**

Nagaraja HS<sup>1</sup>, Varkkey Julian<sup>2</sup>, Chakravarthi S<sup>3</sup>

<sup>1</sup>Human Biology Division, School of Medicine, International Medical University, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Division of Postgraduate Studies, International Medical University, 57000 Kuala Lumpur, Malaysia

<sup>3</sup>Pathology Division, School of Medicine, International Medical University, 57000 Kuala Lumpur, Malaysia

### **Abstract**

This study investigated the cardioprotective effect of N-acetylcysteine (NAC) on isoproterenol (ISO)- induced cardiotoxicity in rats. Male Sprague–Dawley rats were divided into control, NAC alone (100 mg/kg BW orally for 14 days), ISO-control (85 mg/kg BW), and ISO with NAC (for 14 days). Serum creatine kinase-MB and Lactate dehydrogenase were measured. From the heart homogenate lipid hydroperoxides (LPO), superoxide dis- mutase (SOD), total glutathione (GSH), and 8-isoprostane (IP) were measured. Histopathological examination of the heart was also carried out. There was a significant increase ( $P \leq 0.05$ ) in LPO and IP levels in ISO-control group and NAC treatment reduced these changes. Antioxidant enzyme, SOD and GSH, level decreased significantly ( $P \leq 0.05$ ) in ISO-control group, and treatment with NAC was able to reverse these changes significantly ( $P \leq 0.05$ ). Histopathologically, ISO-control group showed morpho- logical changes suggestive of cardiotoxicity with large areas of coagulative necrosis, with diffused interstitial edema. NAC treatment successfully reduced these histo- pathological changes. In conclusion, the study proves that NAC has a strong cardioprotective effect against isopro- terenol-induced cardiac changes. NAC decreases isoproterenol-induced LPO and IP levels in the heart tissue and prevented free radicals–induced damage to the myocardium.

**Key words:** Cardiotoxicity, N-acetylcysteine, Isoproterenol, Lipid hydroperoxides, Isoprostane

Nagarajah HS, Varkkey Julian, Chakravarthi S. Cardioprotective effects of glycyrrhizic acid against isoproterenol- induced myocardial ischemia in rats. Intl J Mol Sci 2011; 12, 7100-7113

## **Cardioprotective effects of glycyrrhizic acid against isoproterenol- induced myocardial ischemia in rats**

Nagarajah H<sup>1</sup>, Varkkey Julian<sup>2</sup>, Chakravarthi Srikumar<sup>3</sup>

<sup>1</sup>Human Biology Division, School of Medicine, International Medical University, Kuala Lumpur 57000, Malaysia

<sup>2</sup>Division of Postgraduate Studies, International Medical University, Kuala Lumpur 57000, Malaysia

<sup>3</sup>Pathology Division, School of Medicine, International Medical University, Kuala Lumpur 57000, Malaysia

### **Abstract**

The aim of the present study was to look into the possible protective effects of glycyrrhizic acid (GA) against isoproterenol-induced acute myocardial infarction in Sprague-Dawley rats. The effect of three doses of glycyrrhizic acid in response to isoproterenol (ISO)-induced changes in 8-isoprostane, lipid hydroperoxides, super oxide dismutase and total glutathione were evaluated. Male Sprague-Dawley rats were divided into control, ISO-control, glycyrrhizic acid alone (in three doses-5, 10 and 20 mg/kg BW) and ISO with glycyrrhizic acid (in three doses) groups. ISO was administered at 85 mg/kg BW at two consecutive days and glycyrrhizic acid was administered intraperitoneally for 14 days. There was a significant increase in 8-isoprostane (IP) and lipid hydroperoxide (LPO) level in ISO-control group. A significant decrease in total superoxide dismutase (SOD) and total glutathione (GSH) was seen with ISO-induced acute myocardial infarction. Treatment with GA significantly increased SOD and GSH levels and decreased myocardial LPO and IP levels. Histopathologically, severe myocardial necrosis and nuclear pyknosis and hypertrophy were seen in ISO-control group, which was significantly reduced with GA treatment. Glycyrrhizic acid treatment proved to be effective against isoproterenol-induced acute myocardial infarction in rats and GA acts as a powerful antioxidant and reduces the myocardial lipid hydroperoxide and 8-isoprostane level.

**Key words:** oxidative stress; isoproterenol; glycyrrhizic acid; lipid hydroperoxides; 8-isoprostane

Nalliah S, Lionel W, Subramani V. Issues in management of acute appendicitis in pregnancy. *IeJSME* 2011; 5(1): 2-9

## Issues in management of acute appendicitis in pregnancy

Sivalingam Nalliah<sup>1</sup>, Lionel W<sup>2</sup>, Subramani V<sup>3</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, International Medical University, Malaysia

<sup>2</sup>Department of Surgery, International Medical University, Malaysia

<sup>3</sup>Department of Imaging and Radiology, Tuanku Jaafar Hospital, Seremban, Malaysia

### Abstract

Acute appendicitis is an infrequent yet the commonest surgical emergency in pregnancy occurring in about 1:1500 pregnancies. The classical abdominal pain in the right lower quadrant of the abdomen is the only reliable clinical sign. Delay in diagnosis is attributed to presence of symptoms commonly seen in pregnancy like nausea and vomiting and difficulty in localizing abdominal pain due to displacement of the appendix with advancing gestation. Perforated appendix and generalized peritonitis impacts adversely on pregnancy contributing to increases in miscarriage, pre-term delivery, fetal loss and even maternal mortality. Imaging studies like abdominal ultrasonogram, helical computerized tomography and magnetic imaging have been utilized to complement clinical suspicion and decrease 'negative appendectomies' but robust data on their routine use is awaited. Although the laparoscopic approach is a useful diagnostic and therapeutic tool in early pregnancy, its use as the primary approach for appendicectomy in pregnancy requires further evaluation as increases in the incidence of fetal loss of 5.6% has been reported compared to 3.1% in open access surgery.

**Key words:** Acute appendicitis in pregnancy, diagnosis, imaging, surgical approaches, perinatal outcome



Nazimah I, Aznal SS, Chin SP, Ahmad WAW, Rosman A, Sinnadurai J, Ismail O, Zambahari R, Kui HS. Acute coronary syndrome in women of reproductive age. *Int J Women's Hlth (New Zealand)* 2011; 3: 375-380

## Acute coronary syndrome in women of reproductive age

Nazimah I<sup>1</sup>, Aznal SS<sup>1</sup>, Chin SP<sup>1</sup>, Ahmad WAW<sup>2</sup>, Rosman A<sup>3</sup>, Sinnadurai J<sup>4</sup>, Ismail O<sup>5</sup>, Zambahari R<sup>3</sup>, Kui HS<sup>6</sup>

<sup>1</sup>International Medical University, Seremban

<sup>2</sup>University Malaya Medical Centre, PJ

<sup>3</sup>Institut Jantung Negara, KL

<sup>4</sup>Hospital Kuala Lumpur, KL

<sup>5</sup>Hospital Pulau Pinang

<sup>6</sup>Hospital Umum Sarawak, Malaysia

### Abstract

#### Background:

There is scarce or no data on prevalence and presentation of acute coronary syndrome (ACS) among women of reproductive age. Furthermore, whether women of reproductive age presenting with ACS have the same risk factors as men and older women is not known.

#### Objective:

To analyze factors associated with ACS in women of reproductive age in comparison with older women and men of a similar age group.

#### Methodology:

A total of 9702 cases of acute coronary syndrome over a 3-year period (2006–2008) from the National Cardiovascular Disease database were analyzed, with focus on women of reproductive age (20–,40 years), looking into association with ethnicity, comorbid illness, and the ACS stratum. Comparison with older women (40–,60 years; Control 1) and men of similar age group (Control 2) was made and analyzed using Fisher's exact test and chi-square test when necessary.

#### Results:

From a total of 9702 cases, 2344 (24.2%) were women. Of these, 45 (1.9%) were women between 20 and ,40 years, which is significantly lower than the two controls (older women 30.8%, and men of same age 6.2%, respectively;  $P < 0.0001$ ). The distribution of ethnicity shows a similar pattern between the study group and the controls, but patients of Indian ethnicity were over-represented when compared with the Malaysian demographics of general population (31.3% versus 7.1%;  $P < 0.0001$ ). ACS in women of reproductive age was associated with diabetes mellitus in 37.8%, hypertension in 40.0%, and dyslipidemia in 24.4% of cases, similar to men of the same age but significantly lower than the older women ( $P < 0.0001$ ). Smoking is not a major risk factor in the study group, where only 6.7% ever smoked, similar to older women (6.8%,  $P = 1.000$ ) and significantly much less compared with men of the same age (84.1%;  $P < 0.0001$ ). Regarding the ACS stratum, a significantly higher percentage of women in the study group had ST-segment elevation myocardial infarction compared with older women ( $P = 0.0085$ ) but less than that of men of similar age ( $P = 0.0187$ ).

Conclusion:

ACS is rare in women of reproductive age. Diabetes, hypertension, and Indian ethnicity were identified as important contributors.

**Key words:** reproductive-aged women, comorbidities, risk factors

Ng Evelyn Hui-Ping, Chu WL, Ambu S. Occurrence of airborne algae within the township of Bukit Jalil in Kuala Lumpur, Malaysia. *Grana (UK)* 2011; 50(3):217-227

## **Occurrence of airborne algae within the township of Bukit Jalil in Kuala Lumpur, Malaysia**

Ng Evelyn Hui-Ping, Wan-Loy Chu, Stephen Ambu

International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

### **Abstract**

There have been relatively few studies on airborne algae although they are known to have health implications. The aim of this study was to conduct a survey on the distribution of airborne algae within Bukit Jalil in Kuala Lumpur, Malaysia. The sampling sites included a quiet residential area, a busy area with high human movement, a highway with heavy traffic, small roads with low traffic, a golf course, two hilly areas, and the man-made lake, Tasik Komanwel. Soils were also collected from these sites when possible. Results based on cultured samples showed that cyanobacteria were the dominant airborne algae, with a total of eight species identified. The dominant species was *Phormidium tenue* while other airborne algae found included *P. retzii*, *Nostoc commune*, and *N. linckia*. The sites with high percentage occurrence of airborne algae were near the animal holding facility of the International Medical University and the Light Railway Transit station. Human movement could be an important factor affecting the occurrence of airborne algae. A very low occurrence of airborne algae was recorded at the sites around the lake area. Some of the airborne algae were also found in the soil samples, suggesting that the algae could originate from the soil.

**Key words:** airborne algae, cyanobacteria, *Phormidium*, *Nostoc*, Bukit Jalil

Ong SL, Ling APK, Poosporagi R, Moosa S. Production of flavonoid compounds in cell cultures of *Ficus deltoidea* as influenced by medium composition. *Int J Med Arom Plant* 2011; 1(2): 62-74

## Production of flavonoid compounds in cell cultures of *Ficus deltoidea* as influenced by medium composition

Ong SL<sup>1</sup>, Ling APK<sup>2</sup>, Poosporagi R<sup>3</sup>, Moosa S<sup>4</sup>

<sup>1</sup>Department of Science, Faculty of Engineering and Science, Tunku Abdul Rahman University (UTAR), Setapak, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Human Biology, International Medical University Malaysia (IMU), Bukit Jalil, Kuala Lumpur, Malaysia

<sup>3</sup>School of Science & Mathematics, INTI College Subang Jaya, Subang Jaya, Selangor, Malaysia.

<sup>4</sup>Agrotechnology and Bioscience Division, Malaysian Nuclear Agency, Bangi, Kajang, Selangor, Malaysia

### Abstract

Manipulation of the nutrient medium is the most fundamental approach in improving the yield of secondary metabolites in plant cell cultures. The main aim of this study was to examine the effects of four different carbon sources (sucrose, glucose, fructose and galactose) and plant growth regulators (2,4-D, NAA, BAP and kinetin) on three types of flavonoid accumulation: rutin, quercetin and naringenin in cell cultures of *Ficus deltoidea*. Analysis using High Performance Liquid Chromatography (HPLC) revealed that the concentration of rutin was enhanced by 2-fold in the culture enriched with either glucose or fructose as compared to the control whilst the concentration of naringenin ( $0.92 \pm 0.35$  mg/g DW) was improved by almost 19 times when glucose served as the sole carbon source. In the study of the effects of plant growth regulators, the maximum production of rutin ( $39.13 \pm 8.38$  mg/g DW) was achieved in the medium supplemented with  $10.74 \mu\text{M}$  of Naphthaleneacetic acid (NAA). The maximum production of quercetin ( $3.92 \pm 0.44$  mg/g DW) and naringenin ( $8.65 \pm 3.03$  mg/g DW) was detected in the cultures with  $4.65 \mu\text{M}$  kinetin, which was 5 and 170 times higher than the control, respectively. Comparatively, auxins gave a higher production in rutin whereas cytokinins showed a moderate production of all the three flavonoids.

**Key words:** Carbon sources; Cell suspension culture; Flavonoids; *Ficus deltoidea*; Plant growth regulators

Ong ST, Keng PS, Lee WN, Ha ST, Hung YT. Dye waste treatment. Water 2011; 3: 157-176

## **Dye waste treatment**

Ong ST<sup>1</sup>, Keng PS<sup>2</sup>, Lee WN<sup>3</sup>, Ha ST<sup>1</sup>, Hung YT<sup>4</sup>

<sup>1</sup>Department of Chemical Science, Faculty of Science, Universiti Tunku Abdul Rahman, Jalan Universiti, Bandar Barat, 31900 Kampar, Perak, Malaysia

<sup>2</sup>Department of Pharmaceutical Chemistry, International Medical University, No.126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>3</sup>Department of Science, Faculty of Engineering and Science, Universiti Tunku Abdul Rahman Jalan Genting Kelang, Setapak 53300 Kuala Lumpur, Malaysia

<sup>4</sup>Department of Civil and Environmental Engineering, Cleveland State University, Cleveland, OH 44115, USA

### **Abstract**

Dye wastes represent one of the most problematic groups of pollutants because they can be easily identified by the human eye and are not easily biodegradable. This literature review paper highlights and provides an overview of dye waste treatments performed over the three years period from 2008–2010. Noteworthy processes for the treatment of dye waste include biological treatment, catalytic oxidation, filtration, sorption process and combination treatments.

**Key words:** dyes waste; textile effluents; treatment methods; modeling

Ong ST, Keng PS, Voon MS, Lee SL. Application of durian peel (*Durio zibethinus* Murray) for removal of methylene blue from aqueous solution. *Asian J Chem* (India) 2011; 23(7): 2898-2902

## **Application of durian peel (*Durio zibethinus* Murray) for removal of methylene blue from aqueous solution**

Ong ST<sup>1</sup>, Keng PS<sup>2</sup>, Voon MS<sup>3</sup>, Lee SL<sup>4</sup>

<sup>1</sup>Department of Chemical Science, Faculty of Science, Universiti Tunku Abdul Rahman, Jalan Universiti, Bandar Barat, 31900 Kampar, Perak, Malaysia

<sup>2</sup>Department of Pharmaceutical Chemistry, International Medical University, No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>3</sup>Department of Science, Faculty of Engineering & Science, Universiti Tunku Abdul Rahman, Jln Genting Kelang, Setapak, 53300 Kuala Lumpur, Malaysia

<sup>4</sup>Ibnu Sina Institute for Fundamental Science Studies, Universiti Teknologi Malaysia, 81310 UTM Skudai, Johor, Malaysia

### **Abstract**

The sorption characteristics of durian (*Durio zibethinus* Murray) peel in the removal of methylene blue from aqueous solutions under batch and continuous flow conditions were studied. The limitation in batch studies can be overcome by carry out flow tests using columns to obtain design models that would be applicable to commercial systems. Two well-known isotherm models, Langmuir and Freundlich were chosen for the fitting of experimental data. The sorption process conformed to Langmuir isotherm with the maximum sorption capacity of 49 mg/g at 25 °C. Mathematical models were employed to analyze and explain experimental data obtained. Increase in the column bed depth yielded longer service time while increase in influent concentration and flow rate resulted in faster breakthrough.

**Key words:** Adsorption, *Durio zibethinus* Murray, Methylene blue, Batch study, Column study

Ong ST, Khoo EC, Keng PS, Hii SL, Lee SL, Hung YT, Ha ST. Plackett-Burman design and response surface methodological approach to optimize basic dyes removal using sugarcane bagasse. *Desalination and Water Treatment (Israel)* 2011; 25(1-3): 310-318

## **Plackett-Burman design and response surface methodological approach to optimize basic dyes removal using sugarcane bagasse**

Ong ST<sup>1</sup>, Khoo EC<sup>2</sup>, Keng PS<sup>3</sup>, Hii SL<sup>2</sup>, Lee SL<sup>4</sup>, Hung YT<sup>5</sup>, Ha ST<sup>1</sup>

<sup>1</sup>Department of Chemical Science, Faculty of Science, Universiti Tunku Abdul Rahman, Jalan Universiti, Bandar Barat, 31900 Kampar, Perak, Malaysia

<sup>2</sup>Department of Science, Faculty of Engineering and Science, Universiti Tunku Abdul Rahman, Jalan Genting Kelang, Setapak 53300 Kuala Lumpur, Malaysia

<sup>3</sup>Department of Pharmaceutical Chemistry, International Medical University, No.126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>4</sup>Ibnu Sina Institute for Fundamental Science Studies, Universiti Teknologi Malaysia, 81310 Skudai, Johor, Malaysia

<sup>5</sup>Department of Civil and Environmental Engineering, Cleveland State University, Cleveland, Ohio, USA

### **Abstract**

Plackett–Burman design was applied to identify the most significant factors in the removal of Basic Blue 3 (BB3), Methylene Blue (MB) and Basic Yellow 11 (BY11) by natural sugarcane bagasse. The effect of operating parameters on dye uptake was studied in a batch system and a mathematical model showing the influence of each variable was obtained. The interaction between the factors and their optimum levels for maximum percentage uptake of BB3 and MB were determined using Response Surface Methodology (RSM). Both models were highly significant with correlation coefficients ( $R^2$ ) of 0.9932 and 0.9944 for BB3 and MB, respectively in binary dye solution. For BB3, the optimum adsorption conditions were determined as initial pH 6.00, contact time 122.50 min, initial dye concentration 50 mg/L and sorbent dosage 0.09 g. Whereas for MB, the model predicted that an uptake greater than 90% could be obtained when the initial dye concentration, contact time and sorbent dosage were set at 80.40 mg/L, 192.37 min and 0.17 g, respectively. The percentage uptake predicted by the model was in good agreement with the experimental values.

**Key words:** Sugarcane bagasse; Basic dyes; Plackett–Burman design; Response surface methodology (RSM); Optimization; Binary

Pabreja K, Dua K, Saurabh Sharma, Satyanarayana S.V. Padi, Shrinivas K. Kulkarni. Minocycline attenuates the development of diabetic neuropathic pain: possible anti-inflammatory and anti-oxidant mechanisms. *European Journal of Pharmacology* 2011; 661:15-21

## **Minocycline attenuates the development of diabetic neuropathic pain: possible anti-inflammatory and anti-oxidant mechanisms**

Kavita Pabreja<sup>a</sup>, Kamal Dua<sup>a</sup>, Saurabh Sharma<sup>b</sup>, Satyanarayana S.V. Padi<sup>b</sup>, Shrinivas K. Kulkarni<sup>c</sup>

<sup>a</sup>School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur-57000, Malaysia

<sup>b</sup>ISF College of Pharmacy, Moga, Punjab-142001, India

<sup>c</sup>Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh-160014, India

### **Abstract**

Painful neuropathy, a common complication of diabetes mellitus is characterized by allodynia and hyperalgesia. Recent studies emphasized on the role of non-neuronal cells, particularly microglia in the development of neuronal hypersensitivity. The purpose of the present study is to evaluate the effect of minocycline, a selective inhibitor of microglial activation to define the role of neuroimmune activation in experimental diabetic neuropathy. Cold allodynia and thermal and chemical hyperalgesia were assessed and the markers of inflammation and oxidative and nitrosative stress were estimated in streptozotocin-induced diabetic rats. Chronic administration of minocycline (40 and 80 mg/kg, i.p.) for 2 weeks started 2 weeks after diabetes induction attenuated the development of diabetic neuropathy as compared to diabetic control animals. In addition, minocycline treatment reduced the levels of interleukin-1 $\beta$  and tumor necrosis factor- $\alpha$ , lipid peroxidation, nitrite and also improved antioxidant defense in spinal cords of diabetic rats as compared to diabetic control animals. In contrast, minocycline (80 mg/kg, per se) had no effect on any of these behavioral and biochemical parameters assessed in age-matched control animals. The results of the present study strongly suggest that activated microglia is involved in the development of experimental diabetic neuropathy and minocycline exerted its effect probably by inhibition of neuroimmune activation of microglia. In addition, the beneficial effects of minocycline are partly mediated by its anti-inflammatory effect by reducing the levels of proinflammatory cytokines and in part by modulating oxidative and nitrosative stress in the spinal cord that might be involved in attenuating the development of behavioral hypersensitivity in diabetic rats.

**Key words:** Allodynia, Diabetic neuropathy, Hyperalgesia, Microglia



Palanisamy UD, Muniswaran Sivanathan, Radhakrishnan AK, Nagaraja HS, Thabamanithevi Subramaniam, Gan Seng Chiew. An effective ostrich oil bleaching technique using peroxide value as an indicator. *Molecules* (Switzerland) 2011; 16: 5709-5719

## **An effective ostrich oil bleaching technique using peroxide value as an indicator**

Palanisamy UD<sup>1</sup>, Muniswaran Sivanathan<sup>2</sup>, Radhakrishnan AK<sup>2</sup>, Haleagrahara N<sup>2</sup>, Thabamanithevi Subramaniam<sup>3</sup>, Gan Seng Chiew<sup>4</sup>

<sup>1</sup>School of Medicine and Health Sciences, Monash University, Sunway Campus, 46150, Malaysia

<sup>2</sup>Faculty of Medicine and Health, International Medical University, 57000, Kuala Lumpur, Malaysia

<sup>3</sup>SIRIM Bhd, 1, Persiaran Dato Menteri, 40911, Shah Alam, Selangor Darul Ehsan, Malaysia

<sup>4</sup>Allergy and Immunology Research Centre, Institute for Medical Research, 50586, Kuala Lumpur, Malaysia

### **Abstract**

Ostrich oil has been used extensively in the cosmetic and pharmaceutical industries. However, rancidity causes undesirable chemical changes in flavour, colour, odour and nutritional value. Bleaching is an important process in refining ostrich oil. Bleaching refers to the removal of certain minor constituents (colour pigments, free fatty acid, peroxides, odour and non-fatty materials) from crude fats and oils to yield purified glycerides. There is a need to optimize the bleaching process of crude ostrich oil prior to its use for therapeutic purposes. The objective of our study was to establish an effective method to bleach ostrich oil using peroxide value as an indicator of refinement. In our study, we showed that natural earth clay was better than bentonite and acid-activated clay to bleach ostrich oil. It was also found that 1 hour incubation at a 150 °C was suitable to lower peroxide value by 90%. In addition, the nitrogen trap technique in the bleaching process was as effective as the continuous nitrogen flow technique and as such would be the recommended technique due to its cost effectiveness.

**Key words:** crude ostrich oil; temperature; time; peroxide value; clay

Palanisamy U, Thamilaani Manaharan, Ling Lai Teng, Radhakrishnan AK, Thavamanithevi Subramaniam, Theanmalar Masilamani. Rambutan rind in the management of hyperglycemia. Food Res International (Netherlands) 2011; doi: 10.1016/J.FOODRES.2011.01.048

## Rambutan rind in the management of hyperglycemia

Palanisamy U<sup>1</sup>, Thamilaani Manaharan<sup>2</sup>, Ling Lai Teng<sup>2</sup>, Ammu KC Radhakrishnan<sup>3</sup>, Thavamanithevi Subramaniam<sup>4</sup>, Theanmalar Masilamani<sup>4</sup>

<sup>1</sup>School of Medicine and Health Sciences, Monash University, Sunway Campus, 46150, Bandar Sunway, Malaysia

<sup>2</sup>Department of Physiology, Faculty of Medicine, University of Malaya, 59100, Kuala Lumpur, Malaysia

<sup>3</sup>Faculty of Medicine, International Medical University, 126, Jalan 19/155B, Sesama Centre, Plaza Komanwel, Bukit Jalil 57000 Kuala Lumpur, Malaysia

<sup>4</sup>SIRIM Bhd, 1, Persiaran Dato Menteri, 40911, Shah Alam, Selangor, Malaysia

### Abstract

Plant extracts have been suggested as a rich as yet unexplored source of potentially useful anti-diabetic drugs. Recent scientific investigations have confirmed the efficacy of many of these preparations, as effective antioxidants; able to regenerate functional pancreatic beta cells and has a hypoglycemic potential. In this study, the exotic rambutan (*Nephelium lappaceum* L.) fruit's rind has been shown to be effective in inhibiting the carbohydrate hydrolyzing enzymes, alpha glucosidase ( $EC_{50}=2.7 \mu\text{g/mL}$ ) and alpha amylase ( $EC_{50}=70.8 \mu\text{g/mL}$ ), at a much more significant level than the drug acarbose ( $EC_{50}=3500 \mu\text{g/mL}$ ; alpha glucosidase;  $EC_{50}=12 \mu\text{g/mL}$ ; alpha amylase). In addition, the geraniin-enriched ethanolic extracts were able to inhibit the key enzyme in the polyol pathway, aldol reductase ( $EC_{50}=0.04 \mu\text{g/mL}$ ) and prevent the formation of advanced glycation end-products (AGE) by 43%. These findings indicate that the geraniin-standardized *N. lappaceum* rind may be a potential source of an anti-hyperglycemic agent.

**Key words:** Type 2 diabetes,  $\alpha$ -glucosidase inhibitor,  $\alpha$ -amylase inhibitor, Advanced glycation end-products inhibitor, Aldose reductase inhibitor

Pan Y, Abd-Rashid BA, Ismail Z, Ismail R, Mak JW, Pook PC, Er HM, Ong CE. In vitro determination of the effect of *Andrographis paniculata* extracts and andrographolide on human hepatic cytochrome P450 activities. *J Nat Medicines* 2011; 65: 440-447

## **In vitro determination of the effect of *Andrographis paniculata* extracts and andrographolide on human hepatic cytochrome P450 activities**

Pan Yan<sup>1</sup>, Abd-Rashid BA<sup>2</sup>, Ismail Z<sup>2</sup>, Ismail R<sup>3</sup>, Mak JW<sup>1</sup>, Pook PC<sup>1</sup>, Er HM<sup>1</sup>, Ong CE<sup>4</sup>

<sup>1</sup>School of Pharmacy and Health Sciences, International Medical University, 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Herbal Medicine Research Centre, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia

<sup>3</sup>Pharmacogenetics Research Group, Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

<sup>4</sup>Jeffrey Cheah School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon Selatan, 46150 Bandar Sunway, Selangor Darul Ehsan, Malaysia

### **Abstract**

We investigated the effects of *Andrographis paniculata* (AP) extracts and andrographolide on the catalytic activity of three human cDNA-expressed cytochrome P450 enzymes: CYP2C9, CYP2D6 and CYP3A4. In vitro probe-based high performance liquid chromatography assays were developed to determine CYP2C9-dependent tolbutamide methylhydroxylation, CYP2D6-dependent dextromethorphan O-demethylation and CYP3A4-dependent testosterone 6 $\beta$ -hydroxylation activities in the presence and absence of AP extracts and andrographolide. Our results indicate that AP ethanol and methanol extracts inhibited CYP activities more potently than aqueous and hexane extracts across the three isoforms. Potent inhibitory effects were observed on CYP3A4 and CYP2C9 activities ( $K_i$  values below 20  $\mu$ g/ml). Andrographolide was found to exclusively but weakly inhibit CYP3A4 activity. In conclusion, data presented in this study suggest that AP extracts have the potential to inhibit CYP isoforms in vitro. There was, however, variation in the potency of inhibition depending on the extracts and the isoforms investigated.

**Key words:** *Andrographis paniculata*, Acanthaceae, Andrographolide, Cytochrome P450, In vitro, Drug–herb interaction

Pan Yan, Abd-Rashid BA, Ismail Z, Ismail R, Mak JW, Pook PC, Er HM, Ong CE. In vitro modulating effects of *Adrographis paniculata*, *Centella asiatica* and *Orthosiphon stamineus* on cytochrome P450 2C19 (CYP2C19). *J Ethnopharmacol* 2011; 133(2): 881-887

## **In vitro modulating effects of *Adrographis paniculata*, *Centella asiatica* and *Orthosiphon stamineus* on cytochrome P450 2C19 (CYP2C19)**

Pan Yan<sup>1</sup>, Abd-Rashid BA<sup>2</sup>, Ismail Z<sup>2</sup>, Ismail R<sup>3</sup>, Mak JW<sup>1</sup>, Pook PC<sup>1</sup>, Er HM<sup>1</sup>, Ong CE<sup>4</sup>

<sup>1</sup>School of Pharmacy and Health Sciences, International Medical University, 126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Herbal Medicine Research Unit, Division of Biochemistry, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia

<sup>3</sup>Pharmacogenetics Research Group, Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

<sup>4</sup>School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon Selatan, 46150 Bandar Sunway, Selangor, Malaysia

### **Abstract**

Ethno pharmacological relevance:

*Adrographis paniculata* (AP), *Centella asiatica* (CA) and *Orthosiphon stamineus* (OS) are three popular herbs traditionally used worldwide. AP is known for the treatment of infections and diabetes and CA is good for wound healing and healthy skin while OS is usually consumed as tea to treat kidney and urinary disorders. Interaction of these herbs with human cytochrome P450 2C19 (CYP2C19), a major hepatic CYP isoform involved in metabolism of many clinical drugs has not been investigated to date.

Aim of the study:

In this study, the modulatory effects of various extracts and major active constituents of AP, CA and OS on CYP2C19 activities were evaluated.

Materials and methods:

S-Mephenytoin, the CYP2C19 substrate probe, was incubated in the presence or absence of AP, CA and OS components. The changes in the rate of metabolite (hydroxymephenytoin) formation were subsequently determined by a high-performance liquid chromatography (HPLC)-based enzyme assay to characterize the modulatory effects.

Results:

Among the herbal extracts studied, AP ethanol extract and CA dichloromethane extract exhibited mixed type inhibition towards CYP2C19 with  $K_i$  values of 67.1 and 16.4  $\mu\text{g/ml}$  respectively; CA ethanol extract and OS petroleum ether extract competitively inhibited CYP2C19 activity ( $K_i = 39.6$  and 41.5  $\mu\text{g/ml}$  respectively). Eupatorin (a major active constituent of OS) was found to significantly inhibit CYP2C19 by mixed type inhibition ( $K_i = 7.11\text{g/ml}$  or 20.6  $\mu\text{M}$ ).

Conclusions:

It was observed that AP, CA and OS inhibited CYP2C19 activity with varying potency. While weak inhibitory effect was observed with AP, moderate to strong inhibition was observed with CA dichloromethane extract and eupatorin, the major OS constituent.

Therefore care should be taken when these CA and OS components are co-administered with CYP2C19 substrates (such as omeprazole, proguanil, barbiturates, citalopram, and diazepam).

**Key words:** Andrographis paniculata, Centella asiatica, Orthosiphon stamineus, CYP2C19, Drug–herb interactions

Pan Y, Badrul Amini Abd-Rashid, Zakiah Ismail, Rusli Ismail, Mak JW, Pook PCK, Er HM, Ong CE. In vitro effects of active constituents and extracts of *Orthosiphon stamineus* on the activities of three major human cDNA-expressed cytochrome P450 enzymes. *Chemico-Biological Interactions (Netherlands)* 2011; 190(1): 1-8

## **In vitro effects of active constituents and extracts of *Orthosiphon stamineus* on the activities of three major human cDNA-expressed cytochrome P450 enzymes**

Pan Yan<sup>1</sup>, Abd-Rashid BA<sup>2</sup>, Ismail Z<sup>2</sup>, Ismail R<sup>3</sup>, Mak JW<sup>1</sup>, Pook PC<sup>1</sup>, Er HM<sup>1</sup>, Ong CE<sup>4</sup>

<sup>1</sup>School of Pharmacy and Health Sciences, International Medical University, 126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Herbal Medicine Research Unit, Division of Biochemistry, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia

<sup>3</sup>Pharmacogenetics Research Group, Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

<sup>4</sup>School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon Selatan, 46150 Bandar Sunway, Selangor, Malaysia

### **Abstract**

*Orthosiphon stamineus* (OS) has been traditionally used to treat diabetes, kidney and urinary disorders, high blood pressure and bone or muscular pain. To assess the possibility of drug–herb interaction via interference of metabolism, effects of four OS extracts of different polarity and three active constituents (sinensetin, eupatorin and rosmarinic acid) on major human cDNA-expressed cytochrome P450 (CYP) enzymes were investigated. Three substrate-probe based high-performance liquid chromatography (HPLC) assays were established to serve as activity markers for CYP2C9, CYP2D6 and CYP3A4. Our results indicate that OS extracts and constituents exhibited differential modulatory effects on different CYPs. While none of the OS components showed significant inhibition on CYP2C9, eupatorin strongly and uncompetitively inhibited CYP2D6 activity with a  $K_i$  value of 10.2  $\mu\text{M}$ . CYP3A4 appeared to be the most susceptible enzyme to OS inhibitory effects. It was moderately inhibited by OS dichloromethane and petroleum ether extract with mixed-type and noncompetitive inhibitions ( $K_i = 93.7$  and 44.9  $\mu\text{g/mL}$ ), respectively. Correlation study indicated that the inhibition was accounted for by the presence of eupatorin in the extracts. When  $\text{IC}_{50}$  values of these extracts were expressed in volume per dose unit to reflect inhibitory effect at recommended human doses from commercially available products, moderate inhibition was also observed. In addition, CYP3A4 was strongly and noncompetitively inhibited by eupatorin alone, with a  $K_i$  value of 9.3  $\mu\text{M}$ . These findings suggest that co-administration of OS products, especially those with high eupatorin content, with conventional drugs may have the potential to cause drug–herb interactions involving inhibition of major CYP enzymes.

**Key words:** *Orthosiphon stamineus*, Lamiaceae, Cytochrome P450, High-performance liquid chromatography, Drug–herb interaction

Pan Y, Badrul Amin AR, Zakiah I, Rusli Ismail, Mak JW, Ong CE. Heterologous expression of human cytochromes P450 2D6 and CYP3A4 in *Escherichia coli* and their functional characterisation. *Protein J* 2011; 30: 581-591

## Heterologous expression of human cytochromes P450 2D6 and CYP3A4 in *Escherichia coli* and their functional characterisation

Pan Yan<sup>1</sup>, Badrul Amin AR<sup>2</sup>, Zakiah I<sup>2</sup>, Rusli Ismail<sup>3</sup>, Mak JW<sup>1</sup>, Ong CE<sup>4</sup>

<sup>1</sup>School of Pharmacy and Health Sciences, International Medical University, 126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Herbal Medicine Research Unit, Division of Biochemistry, Institute for Medical Research, Jalan Pahang, 50588 Kuala Lumpur, Malaysia

<sup>3</sup>Pharmacogenetics Research Group, Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

<sup>4</sup>School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon Selatan, 46150 Bandar Sunway, Selangor, Malaysia

### Abstract

This study aimed to express two major drug-metabolizing human hepatic cytochromes P450 (CYPs), CYP2D6 and CYP3A4, together with NADPH-cytochrome P450 oxidoreductase (OxR) in *Escherichia coli* and to evaluate their catalytic activities. Full length cDNA clones of both isoforms in which the N-terminus was modified to incorporate bovine CYP17 $\alpha$  sequence were inserted into a pCWori<sup>+</sup> vector. The modified CYP cDNAs were subsequently expressed individually, each together with OxR by means of separate, compatible plasmids with different antibiotic selection markers. The expressed proteins were evaluated by immunoblotting and reduced CO difference spectral scanning. Enzyme activities were examined using high performance liquid chromatography (HPLC) assays with probe substrates dextromethorphan and testosterone for CYP2D6 and CYP3A4, respectively. Results from immunoblotting demonstrated the presence of both CYP proteins in bacterial membranes and reduced CO difference spectra of the cell preparations exhibited the characteristic absorbance peak at 450 nm. Co-expressed OxR also demonstrated an activity level comparable to literature values. Kinetic parameters,  $K_m$  and  $V_{max}$  values determined from the HPLC assays also agreed well with literature values. As a conclusion, the procedures described in this study provide a relatively convenient and reliable means of producing catalytically active CYP isoforms suitable for drug metabolism and interaction studies.

**Key words:** Cytochromes P450, Protein expression, Dextromethorphan O-demethylation, Testosterone 6 $\beta$ -hydroxylation, HPLC

Perera J, Tan Joon Heng, Jeevathayaparan S, Chakravarthi S, Nagaraja HS. Neuroprotective effects of alpha lipoic acid on haloperidol-induced oxidative stress in the rat brain. *Cell & Bioscience* 2011; 1: 12-17

## **Neuroprotective effects of alpha lipoic acid on haloperidol-induced oxidative stress in the rat brain**

Perera Joachim<sup>1</sup>, Tan Joon Heng<sup>1</sup>, Jeevathayaparan S<sup>1</sup>, Chakravarthi Srikumar<sup>2</sup>, Haleagrahara Nagarajah<sup>1</sup>

<sup>1</sup>Department of Human Biology, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Pathology, International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

Haloperidol is an antipsychotic drug that exerts its' antipsychotic effects by inhibiting dopaminergic neurons. Although the exact pathophysiology of haloperidol extrapyramidal symptoms are not known, the role of reactive oxygen species in inducing oxidative stress has been proposed as one of the mechanisms of prolonged haloperidol-induced neurotoxicity. In the present study, we evaluate the protective effect of alpha lipoic acid against haloperidol-induced oxidative stress in the rat brain. Sprague Dawley rats were divided into control, alpha lipoic acid alone (100 mg/kg p.o for 21 days), haloperidol alone (2 mg/kg i.p for 21 days), and haloperidol with alpha lipoic acid groups (for 21 days). Haloperidol treatment significantly decreased levels of the brain antioxidant enzymes super oxide dismutase and glutathione peroxidase and concurrent treatment with alpha lipoic acid significantly reversed the oxidative effects of haloperidol. Histopathological changes revealed significant haloperidol-induced damage in the cerebral cortex, internal capsule, and substantia nigra. Alpha lipoic acid significantly reduced this damage and there were very little neuronal atrophy. Areas of angiogenesis were also seen in the alpha lipoic acid-treated group. In conclusion, the study proves that alpha lipoic acid treatment significantly reduces haloperidol-induced neuronal damage.



Pridmore S, Jasmin Ahmadi, Zainab AM. Suicide in old Norse and Finnish folk stories. *Australasian Psychiatry* 2011; 19(4): 321-324

## **Suicide in old Norse and Finnish folk stories**

Pridmore Saxby<sup>1</sup>, Jasmin Ahmadi<sup>2</sup>, Zainab Abd Majeed<sup>3</sup>

<sup>1</sup>University of Tasmania, Hobart, Tasmania, Australia

<sup>2</sup>Shiraz University of Medical Sciences, Shiraz, Iran

<sup>3</sup>International Medical University, Seremban, Malaysia

### **Abstract**

#### **Objective:**

The aim of this study was to examine the folk stories of Norway, Iceland and Finland with a view to discovering accounts of suicide as an escape option from intolerable predicaments, and to compare any such accounts with material from Southern Europe.

#### **Method:**

The Poetic Edda (Norway/Iceland) and The Kalevala (Finland) were examined for accounts of suicide, and evidence regarding the influence of these texts and individual accounts was collected.

#### **Results:**

The Poetic Edda provided one account and The Kalevala three accounts of suicide performed as a means of escaping intolerable situations. Both the Poetic Edda and The Kalevala are in public awareness and have influenced the politics and culture of their respective regions. The individual suicides have been depicted in literature, music and the visual arts, from the distant past to the present time.

#### **Conclusion:**

Suicide as a means of escape from intolerable predicaments has been public knowledge in these regions for a millennium. This is consistent with findings from Southern Europe and substantiates that intolerable predicaments may lead to suicide.

**Key words:** culture, folklore, suicide

Pridmore S, Zainab AM. The suicides of The Metamorphoses. Australasian Psychiatry 2011; 19(1): 22-24

## The suicides of The Metamorphoses

Pridmore S<sup>1</sup>, Zainab AM<sup>2</sup>

<sup>1</sup>University of Tasmania, Hobart, TAS, Australia

<sup>2</sup>International University of Medicine, Seremban, Malaysia

### Abstract

Aim:

The aim of this paper was to explore the attitude toward and motives for suicide recorded in Ovid ' s The Metamorphoses , a document that has influenced Western culture.

Method: The translation by Horace Gregory was examined.

Results:

Twenty-fi ve mentions of suicidal thoughts or actions were identified, mainly by humans but also by a god, a nymph and a centaur. Fifteen suicides by humans were identified. The motives were predicaments including the loss of a loved individual or status and the threat of murder or plague. There was one instance of intolerable physical pain and one of defiance in the face of intimidation. While there are mentions of madness, there is no mention of madness leading to suicide. There was no censure of suicide.

Conclusion:

Suicide in Western culture appears to have roots in ancient times.

**Key words:** *Ovid, suicide, The Metamorphoses*

Quah JX, Ambu S, Lim YAL, Mahidy MAK, Mak JW. Molecular identification of *Cryptosporidium parvum* from avian hosts. *Parasitology (UK)* 2011; 138(5): 573-577

## **Molecular identification of *Cryptosporidium parvum* from avian hosts**

Quah JX<sup>1</sup>, Ambu S<sup>1</sup>, Lim YAL<sup>2</sup>, Mahidy MAK<sup>2</sup>, Mak JW<sup>1</sup>

<sup>1</sup>International Medical University, 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Department of Parasitology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

### **Abstract**

*Cryptosporidium* species are protozoan parasites that infect humans and a wide variety of animals. This study was aimed at identifying *Cryptosporidium* species and genotypes isolated from avian hosts. A total of 90 samples from 37 different species of birds were collected throughout a 3-month period from April 2008 to June 2008 in the National Zoo of Kuala Lumpur, Malaysia. Prior to molecular characterization, all samples were screened for *Cryptosporidium* using a modified Ziehl-Neelsen staining technique. Subsequently samples were analysed with nested-PCR targeting the partial SSU rRNA gene. Amplicons were sequenced in both directions and used for phylogenetic analysis using Neighbour-Joining and Maximum Parsimony methods. Although 9 (10%) samples were positive for *Cryptosporidium* via microscopy, 8 (8.9%) produced amplicons using nested PCR. Phylogenetic trees identified all the isolates as *Cryptosporidium parvum*. Although *C. parvum* has not been reported to cause infection in birds, and the role of birds in this study was postulated mainly as mechanical transporters, these present findings highlight the significant public health risk posed by birds that harbour the zoonotic species of *Cryptosporidium*.

**Key words:** birds, *Cryptosporidium parvum*, zoo, Malaysia

Rajiah K, Elizabeth Mampally Mathew. Clinical manifestation, effects, diagnosis, monitoring of carbon monoxide poisoning and toxicity. Afr J Pharm Pharmacol 2011; 5(2): 259-264

## **Clinical manifestation, effects, diagnosis, monitoring of carbon monoxide poisoning and toxicity**

Kingston Rajiah<sup>1\*</sup> and Elizabeth Mampally Mathew<sup>2</sup>

<sup>1</sup>International Medical University, No. 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Mallige College of Pharmacy, No 71, Silvepura, Bangalore, 560090 Karnataka, India.

### **Abstract**

Carbon monoxide is a product of incomplete combustion of organic matter with insufficient oxygen supply to enable complete oxidation to carbon dioxide (CO<sub>2</sub>) and is often produced in domestic or industrial settings. In this study the clinical manifestation, effects, diagnosis and toxicity of carbon monoxide poisoning were reviewed. Research suggests that the intracellular uptake of carbon monoxide is an important mechanism for neurologic damage. As a result upon the review of many articles and research journals, it is identified that carbon monoxide may be quantitated in blood using spectrophotometric methods or chromatographic techniques in order to confirm the diagnosis of poisoning in hospitalized victims or to assist in the forensic investigation of a case of fatal exposure. A brain computed tomography (CT) scan may be normal in early stages or show signs of cerebral edema. Public education on the safe operation of appliances, heaters, fireplaces and internal combustion engines is required for prevention of CO poisoning. Carbon monoxide detectors with alarms can improve home safety and their use is recommended by various safety organizations.

**Key words:** Carbon monoxide, toxicity, hemoglobin.

Ramdas P, Rajihulzzaman M, Veerasenan SD, Selvaduray KR, Nesaretnam K, Radhakrishnan AK. Tocotrienol-treated MCF-7 human breast cancer cells show down-regulation of AP15 and up-regulation of MIG6 genes. *Cancer Genomics Proteomics (Greece)* 2011; 8(1): 19-31

## **Tocotrienol-treated MCF-7 human breast cancer cells show down-regulation of AP15 and up-regulation of MIG6 genes**

Ramdas P<sup>1,3</sup>, Rajihulzzaman M<sup>1</sup>, Veerasenan SD<sup>3</sup>, Selvaduray KR<sup>3</sup>, Nesaretnam K<sup>3</sup>, Radhakrishnan AK<sup>2</sup>

<sup>1</sup>Department of Human Biology, Faculty of Medicine and Health, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Department of Pathology, Faculty of Medicine and Health, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>3</sup>Department of Nutrition, Malaysian Palm Oil Board, Bandar Baru Bangi, 43000 Kajang, Selangor Darul Ehsan, Malaysia

### **Abstract**

#### **Background:**

Tocotrienols belong to the vitamin E family and have multiple anticancer effects, such as antiproliferative, antioxidant, pro-apoptosis and antimetastatic. This study aimed to identify the genes that are regulated in human breast cancer cells following exposure to various isomers of vitamin E as these may be potential targets for the treatment of breast cancer.

#### **Materials and Methods:**

Gene expression profiling was performed with MCF-7 cells at inhibitory conditions of IC<sub>50</sub> using Illumina's Sentrix Array Human-6 BeadChips. The expression levels of selected differentially expressed genes were verified by quantitative realtime- PCR (qRT-PCR).

#### **Results:**

The treatment with tocotrienolrich palm oil fraction (TRF),  $\alpha$ -tocopherol and isomers of tocotrienols ( $\alpha$ ,  $\gamma$ , and  $\delta$ ) altered the expression of several genes that code for proteins involved in the regulation of immune response, tumour growth and metastatic suppression, apoptotic signalling, transcription, protein biosynthesis regulation and many others.

#### **Conclusion:**

Treatment of human MCF-7 cells with tocotrienol isomers causes the downregulation of the API5 gene and up-regulation of the MIG6 gene and the differential expression of other genes reported to play a key role in breast cancer biology.

Ranade AV, Tripathi Y, Rajalakshmi R, Vinodini N A, Soubhagya RN, Nayanatara AK, Rekha DK, Kumari M. Effect of Vitamin E administration on histopathological changes in rat testes following torsion and detorsion. Singapore Med J 2011; 52(10): 742-746

## Effect of Vitamin E administration on histopathological changes in rat testes following torsion and detorsion

Ranade AV<sup>1</sup>, Tripathi Y<sup>2</sup>, Rajalakshmi R<sup>3</sup>, Vinodini N A<sup>4</sup>, Soubhagya RN<sup>4</sup>, Nayanatara AK<sup>4</sup>, Rekha DK<sup>5</sup>, Kumari M<sup>6</sup>

<sup>1</sup>Department of Anatomy, Gulf Medical College, PO Box 4184, Ajman, United Arab Emirates

<sup>2</sup>Department of Physiology, Santhosh Medical College, Maliwara, Nehru Nagar II, Ghaziabad 201001, Uttar Pradesh, India

<sup>3</sup>Department of Anatomy, Centre for Basic Sciences, Kasturba Medical College (Unit of Manipal University), Mangalore 575004, Karnataka, India

<sup>4</sup>Department of Physiology, Centre for Basic Sciences, Kasturba Medical College (Unit of Manipal University), Mangalore 575004, Karnataka, India

<sup>5</sup>Department of Anatomy, College of Medicine and JNM Hospital, West Bengal University of Health Sciences, Kalyani PO, Nadia 741235, West Bengal, India

<sup>6</sup>Department of Anatomy, International Medical University, 126 Jalan Jalil Perkasa 19, Bukit Jalil, Kuala Lumpur 57000, Malaysia

### Abstract

#### Introduction:

Testicular torsion is a medical emergency, especially in male neonates and adolescents. It is a common clinical outcome and a significant urological issue. From the literature, it is evident that the use of antioxidants in the prevention of testicular reperfusion injury following detorsion is conflicting. This study was conducted to investigate the role of vitamin E in testicular reperfusion injury following detorsion.

#### Methods:

Male Wistar albino rats were divided into Groups I, II, III and IV. Only Group IV rats were pre-treated with vitamin E 100 mg/kg body weight for 30 days. Ischaemia was induced manually by rotating the rat testis to 720 degrees clockwise and counter rotating for reperfusion. The testes were fixed in Bouin's fluid and processed for histopathological examination.

#### Results:

A significant decrease in the standard tubular diameter and epithelial height was observed in Group III rats compared to those in Groups I and II. However, the seminiferous tubules in Group IV rats showed recovery in the standard tubular diameter and epithelial height when compared with the untreated control groups.

Conclusion: The results showed that vitamin E, when administered before torsion of the spermatic cord in rats, provided significant protection against acute testicular torsion and detorsion injury.

**Key words:** ischaemia, reperfusion, testicular torsion, testis

Ravi S, Nurzalina K, Chitneni M, Yusrida D. Formulation and in vivo evaluation of Ondansetron orally disintegrating tablets using different superdisintegrants. Arch Pharm Res (Korea) 2011; 34 (11): 1945-1956

## **Formulation and in vivo evaluation of Ondansetron orally disintegrating tablets using different superdisintegrants**

Ravi S<sup>1,2</sup>, Nurzalina K<sup>1</sup>, Mallikarjun C<sup>1,2</sup>, Yusrida D<sup>1</sup>

<sup>1</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia

<sup>2</sup>School of Pharmacy and Health Sciences, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

The aim of this study was to formulate cost effective taste-masked orally disintegrating tablets of ondansetron, a bitter drug using different superdisintegrants by a wet granulation technique. Microcrystalline cellulose (Avicel) as a diluent and disintegrant in addition to aspartame as a sweetener were used in all formulations. The prepared tablets were evaluated for weight variation, thickness, hardness, friability, drug content, water content, in vitro disintegration time and in vitro drug release. The tablets' hardness was maintained in the range of 2-3 kg and friability was <1% for all batches. All tablet formulations disintegrated rapidly in vitro within 5.83 to 33.0 sec. The optimized formulation containing 15% Polyplasdone XL- 10 released more than 90% of drug within 5 min and the release was comparable to that of a commercial product. In human volunteers, optimized formulation was found to have a pleasant taste and mouth feel and they disintegrated in the oral cavity within 12 sec. The stability results were also satisfactory. A pharmacokinetic study with the optimized formulation was performed in comparison with a reference (Zofer MD 8<sup>®</sup>) and they were found to be bioequivalent. In conclusion, a cost effective ondansetron orally disintegrating tablet was successfully prepared with acceptable hardness, desirable taste and rapid disintegration in the oral cavity.

**Key words:** Ondansetron, Orally disintegrating tablets, Superdisintegrants, Wet granulation, Disintegration time, Pharmacokinetic study

Ravi S, Nurzalina K, Yusrida D. Formulation and optimization of orally disintegrating tablets of Sumatriptan Succinate. *Chem Pharm Bull (Japan)* 2011; 59(8): 920-928

## Formulation and optimization of orally disintegrating tablets of Sumatriptan Succinate

Ravi S<sup>1,2</sup>, Nurzalina K<sup>1</sup>, Yusrida D<sup>1</sup>

<sup>1</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia; 11800 Penang, Malaysia

<sup>2</sup>School of Pharmacy and Health Sciences, International Medical University; Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### Abstract

The aims of the present research were to mask the intensely bitter taste of sumatriptan succinate and to formulate orally disintegrating tablets (ODTs) of the taste masked drug. Taste masking was performed by coating sumatriptan succinate with Eudragit EPO using spray drying technique. The resultant microspheres were evaluated for thermal analysis, yield, particle size, entrapment efficiency and in vitro taste masking. The tablets were formulated by mixing the taste masked microspheres with different types and concentrations of superdisintegrants and compressed using direct compression method followed by sublimation technique. The prepared tablets were evaluated for weight variation, thickness, hardness, friability, drug content, water content, in vitro disintegration time and in vitro drug release. All the tablet formulations disintegrated in vitro within 37—410 s. The optimized formulation containing 5% Kollidon CL-SF released more than 90% of the drug within 15 min and the release was comparable to that of commercial product (Suminat®). In human volunteers, the optimized formulation was found to have a pleasant taste and mouth feel and disintegrated in the oral cavity within 41 s. The optimized formulation was found to be stable and bioequivalent with Suminat®.

**Key words:** sumatriptan succinate; orally disintegrating tablet; superdisintegrant; sublimation; disintegration time; in vivo study



Sheikh KA, Kang YB, Rouse JJ, Eccleston GM. Influence of hydration state and homologue composition of magnesium stearate on the physical chemical properties of liquid paraffin lipogels. *Intl J Pharmaceutics* 2011; 411: 121-127

## **Influence of hydration state and homologue composition of magnesium stearate on the physical chemical properties of liquid paraffin lipogels**

Sheikh KA<sup>1,2</sup>, Kang YB<sup>2</sup>, Rouse JJ<sup>1</sup>, Eccleston GM<sup>1</sup>

<sup>1</sup>Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, G1 1XQ, United Kingdom

<sup>2</sup>Department of Chemistry School of Pharmacy, International Medical University, Kuala Lumpur, 57000, Malaysia

### **Abstract**

Lipogels were prepared by dispersing mixed (60:40 C<sub>16</sub>–C<sub>18</sub>) and pure (C<sub>18</sub>) homologue magnesium stearate (MgSt) in liquid paraffin, using three methods of preparation, i.e. addition of water at 95°C during cooling cycle (method 1), homogenisation upon cooling (method 2) or cooling without addition of water or homogenisation (method 3). The systems were characterised by physical inspection, polarised, hot stage and scanning electron microscopy (SEM), differential scanning calorimetry (DSC), rheology, and X-ray diffraction (XRD). Systems formed stable semisolid lipogels (no syneresis), unstable solids showing syneresis or structured fluids, depending on the type of magnesium stearate used and the preparation technique. The stable semisolid lipogels containing mixed homologue MgSt (commercial-as received, anhydrous or dihydrate) prepared by methods 1 (~1–2% water) and 2 contained 1-crystalline lamellar structure. These were not present in the unstable solids formed with method 3 or in systems prepared from pure homologue MgSt which were generally structured fluids rather than semisolids. In addition, semisolid lipogels of pure homologue trihydrate MgSt prepared by method 3 showed plate-like crystals, implying pressure sensitivity. There is significantly more amorphous MgSt in the unstable solids compared to the stable semisolid lipogels, which are mainly crystalline (confirmed by XRD).

**Key words:** Lipogels, Magnesium stearate, Pseudopolymorph, Liquid paraffin, Maltese crosses,  $\alpha$ -Crystalline lamellar structure

Sia FY, Vejayan J, Jamuna A, Ambu S. Efficacy of tannins from *Mimosa pudica* and tannic acid in neutralizing cobra (*Naja kaouthia*) venom. *J Venomous Animals and Toxins including Trop Dis (Brazil)* 2011; 17(1): 42- 48

## **Efficacy of tannins from *Mimosa pudica* and tannic acid in neutralizing cobra (*Naja kaouthia*) venom**

Sia FY<sup>1</sup>, Vejayan J<sup>2</sup>, Jamuna A<sup>3</sup>, Ambu S<sup>1</sup>

<sup>1</sup>International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>School of Medicine and Health Sciences, Monash University, Bandar Sunway, Selangor, Malaysia

<sup>3</sup>Institute of Biological Sciences, University of Malaya, Kuala Lumpur, Malaysia

### **Abstract**

In the present study, the effectiveness of *Mimosa pudica* tannins (MPT) in neutralizing the lethality of *Naja kaouthia* venom was compared with commercially derived tannins. Preincubation of MPT with *N. kaouthia* venom maintained 100% survival of mice after 24 hours. The mouse group in which there was no preincubation, no protection against the effects of the venom was observed. *M. pudica* tannin was found to be more effective in neutralizing the lethality of *N. kaouthia* venom when compared to commercial tannic acid. Two protein spots were missing in the two-dimensional gel electrophoresis (2-DE) of the MPT treated mouse indicating the down-regulation of venom proteins. The results from this study indicated that tannins obtained from *M. pudica* are better than tannic acid in neutralizing the lethality of *N. kaouthia* venom in vitro. However, further investigations are required to establish that *M. pudica* has potential for treating *N. kaouthia* snakebites.

**Key words:** plant extract, snake venom, therapy, tannin, phospholipase A2

Siar CH, Toh CG, Romanos G, Ng KH. Subcutaneous reactions and degradation characteristics of collagenous and noncollagenous membranes in a macaque model. Clin Oral Impl Res 2011; 22: 113-120

## **Subcutaneous reactions and degradation characteristics of collagenous and noncollagenous membranes in a macaque model**

Siar CH<sup>1</sup>, Toh CG<sup>2</sup>, Romanos G<sup>3</sup>, Ng KH<sup>4</sup>

<sup>1</sup>Department of Oral Pathology, Oral Medicine and Periodontology, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia

<sup>2</sup>School of Dentistry, International Medical University, Kuala Lumpur, Malaysia

<sup>3</sup>Department of Clinical Dentistry M&D, School of Medicine and Dentistry, University of Rochester, Rochester, NY, USA

<sup>4</sup>Unit of Stomatology, Institute for Medical Research, Kuala Lumpur, Malaysia

### **Abstract**

#### **Background:**

Collagenous and noncollagenous membranes have been investigated in many animal systems but their effects in the macaque model are unknown.

#### **Objective:**

To determine subcutaneous cellular reactions and degradation characteristics following implantation of collagenous and noncollagenous membranes in a macaque model.

#### **Methods:**

Six adult male *Macaca fascicularis*, aged above 7 years, were used. Six commercially available collagenous (Bio-Gides [BG], Tissue Fleeces [TFL] TissueFoil E fortes [TFO], Lycolls [LC], Surgicolls [SG] and Tutodents [TU]) and two noncollagenous (Tabotamps [TA] and Gelita-Tampons [GT]) membranes (size 2 x 1 x 2 cm each) were implanted in unconnected subcutaneous pouches in the monkey's back and wounds were allowed to heal by primary intention. The total sample size for each membrane was six. Two monkeys were sacrificed for each experimental period of 4, 14 and 28 days. Explanted specimens were prepared for histologic and histomorphometric analysis. Digitized images of implant sites were systematically sampled using an Image Analyzer with a grid containing 35 intersection points. Four parameters were quantified: membrane degradation, foreign body reaction, tissue organization and vascularization.

#### **Results:**

Biodegradation rate and vascularization scored higher in collagenous than in noncollagenous membranes. Except for TFL and TU, the remaining six membranes showed a moderately intense foreign body reaction at week 2. Tissue organization was initiated early in four out of six collagenous (TFL4LC4SG4TFO4BG4TU) compared with one of two noncollagenous (TA4GT) membranes.

#### **Conclusions:**

The results suggest that differences in membrane structure and composition underlie their different cellular reactions and degradation characteristics.

**Key words:** animal studies, collagenous, histomorphometry, macaque model, noncollagenous

Siar CH, Toh CG, Tara Bai Taiyeb Ali, Doris Seiz, Ong ST. Dimensional profile of oral mucosa around combined tooth-implant-supported bridgework in macaque mandible. Clin Oral Implant Res 2011; doi: 10.1111/j.1600-0501.2010.02145.x

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

Siar CH<sup>1</sup>, Toh CG<sup>2</sup>, Tara Bai Taiyeb Ali<sup>1</sup>, Doris Seiz<sup>3</sup>, Ong ST<sup>4</sup>

<sup>1</sup>Department of Oral Pathology, Oral Medicine & Periodontology, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia

<sup>2</sup>School of Dentistry, International Medical University, Jalil, Kuala Lumpur, Malaysia

<sup>3</sup>Department of Oral Surgery, Dental School (Carolinum), Johann Wolfgang Goethe University of Frankfurt, Frankfurt, Germany

<sup>4</sup>Department of Oral & Maxillofacial Surgery, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia

### 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 toothimplant- 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 sacrifice for histomorphometry. Six soft tissue indices were scored: coronal gingival mucosato- 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 ( $BW \frac{1}{4} SD \frac{1}{4} JE \frac{1}{4} CTC$ ); corresponding parameters in the natural tooth abutment were also measured.

#### Results:

Mucosal dimensions in tapered implants ( $nBW \frac{1}{4} 3.33 \pm 0.43$ ;  $SD \frac{1}{4} 1.03 \pm 0.24$ ;  $JE \frac{1}{4} 1.08 \pm 0.13$ ;  $CTC \frac{1}{4} 1.22 \pm 0.23$ mm) were comparable with those of natural tooth abutments ( $BW \frac{1}{4} 3.04 \pm 0.18$ ;  $SD \frac{1}{4} 0.93 \pm 0.1$ ;  $JE \frac{1}{4} 0.78 \pm 0.1$ ; Attachment  $\frac{1}{4} 1.33 \pm 0.09$ mm), but differed from butt-joint implants ( $nBW \frac{1}{4} 4.88 \pm 1.24$ ;  $SD \frac{1}{4} 1.47 \pm 0.38$ ;  $JE \frac{1}{4} 1.49 \pm 0.4$ ;  $CTC \frac{1}{4} 1.92 \pm 0.93$ mm) ( $nPo0.05$ ).

#### 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.

**Key words:** abutments, dental implants, histomorphometry, oral mucosa, soft tissues

Sikarwar AS, Batra HV. Identification of Klebsiella pneumoniae by capsular polysaccharide polyclonal antibodies. Intl J Chem Engineering Applications 2011; 2: 131-134

## Identification of Klebsiella pneumoniae by capsular polysaccharide polyclonal antibodies

A. S. Sikarwar<sup>1</sup> and H. V. Batra<sup>2</sup>

<sup>1</sup>International Medical University, No:126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000, Kuala Lumpur, Malaysia

<sup>2</sup>Defence Research Development organisation, India

### Abstract

The aim of this study is to develop simple and rapid diagnostic method which can be utilized routinely for detection of Klebsiella pneumoniae. This study was done in India at DRDE, Gwalior. We have collected standard K.pneumoniae strain 3296 from Yamaguchi University, Japan and total fifty-nine clinical isolates of Klebsiella species from Armed Force Medical College, Pune, and Patel chest hospital, New Delhi. Bacteria were grown on trypticase soy broth and two Newzealand wistar white rabbit were immunized subcutaneously with purified capsular polysaccharide (CPS) of K.pneumoniae. Specificity of hyper immune sera raised against CPS was tested by counter current immunoelectrophoresis. We have generated four monoclonal antibodies, out of which two IgM producing clones (KP-1 & KP-2) and hyper immune sera against CPS antigen were used for agglutination test. KP-1, KP-2 and CPS hyperimmune sera showed different reactions. Out of the twenty biochemically confirmed K.pneumoniae clinical isolates, hyperimmune sera to CPS detected sixteen as positive whereas KP-1 reacted to eleven and KP-2 to thirteen of these isolates. One clinical Klebsiella species biochemically negative for K.pneumoniae and other Enterobacteriaceae organisms were negative by agglutination test to all the three antibody reagents. K.aerogenes, however, reacted to KP-2 and CPS hyperimmune sera. Standard K.pneumoniae was positive to all the three antibodies. The rapidity and ease of performance merited the hyper immune sera to CPS and IgM monoclonal antibody based agglutination test as the preliminary identification system for K.pneumoniae.

**Key words:** Capsular Polysaccharide, diagnostic method, Klebsiella pneumoniae, polyclonal antibodies.

Sikarwar AS, Harsh Vardhan Batra. Prevalence of antimicrobial drug resistance of *Klebsiella pneumoniae* in India. Intl J Biosci, Biochem Bioinformatics 2011; 1(3): 211-215

## **Prevalence of antimicrobial drug resistance of *Klebsiella pneumoniae* in India**

Archana Singh Sikarwar<sup>1</sup> and Harsh Vardhan Batra<sup>2</sup>

<sup>1</sup>Medicine and Health Sciences, Department at International Medical University, Bukit Jalil, Kuala Lumpur

<sup>2</sup>Defense Research Development Establishment, Gwalior, India.

### **Abstract**

*Klebsiella pneumoniae* has been associated with different types of infections and one of the most important aspects of *Klebsiella* is the emergence of multi-drug resistant strains particularly those involved in nosocomial diseases. Fifty nine clinical isolates were collected from different parts of India. Most of the samples were recovered from respiratory, urinary tract infection and pus cases which were followed by biochemical characterization. Twenty confirmed *K.pneumoniae* isolates were further tested for antimicrobial drug sensitivity and almost fifty percent of them were found to be multidrug resistant. As per our statistical data, all confirmed *K.pneumoniae* isolates were resistant to carbenicillin and one among them recovered from sputum sample of a pneumonic patient was resistant to all the antimicrobial agents tested except exhibiting a partial susceptibility to amikacin. In our studies we found that *K.pneumoniae* strains from clinical cases were highly susceptible to quinolones and the aminoglycoside, amikacin and gentamycin. At the same time over 60 % strains were resistant to chloramphenicol and tetracycline. We also found that 28 to 76 % of them were resistant to cephalosporins (ceftizoxime and cefotaxime). On the basis of statistical binomial test we conclude that piperacillin, carbenicillin, ofloxacin ampicillin, co-trimoxazole and chloramphenicol were significantly resistant, whereas cefotaxime and tetracycline were found to be moderately resistant against *Klebsiella pneumoniae*.

**Key words:** Antibiotic, antimicrobial drug resistance, *Klebsiella pneumoniae*

Sinniah D. Industry and cosmetic uses of talc with their implication on health. *leJSME* 2011; 5(1): 10-16

## **Industry and cosmetic uses of talc with their implication on health**

Sinniah D

International Medical University Clinical School, Seremban, Jalan Rasah, 7030 Seremban, Negeri Sembilan DK, MALAYSIA

### **Abstract**

Talc's softness, whiteness, lamellarity, inertness and affinity for organic chemicals make it valuable for industrial and domestic applications. The largest consumers are the paper and ceramic industry; only 5% is used as cosmetics. It is also used for preserving animal feed, and a carrier for drugs, insecticides, pesticides and chemicals. Talc was introduced as baby powder in 1894 and advertised aggressively worldwide. Widespread and indiscriminate use soon raised concerns about its implications for health. The IARC found that talc containing asbestiform fibres is carcinogenic to humans, but inadequate evidence to implicate talc not-containing asbestiform fibres. Pulmonary manifestations of talc inhalation include talcosis, talcosilicosis, and talcoasbestosis. Drug-users administering talc-adulterated oral medications intravenously develop pulmonary granulomas, fibrosis and irreversible pulmonary hypertension. Worldwide reports reveal talc inhalation is fatal to infants; it coats and dries mucus membranes, causes hemorrhage, edema, desquamation of bronchial epithelium, and clogs and compromises mucociliary clearance; larger quantities completely obstruct airways. Progressive diffuse pulmonary fibrosis is a recognized sequel to massive aspiration of baby powder. IARC has classified perineal use of talcum powder as a possible ovarian carcinogen, while a recent study has found that perineal talcum powder increases the risk of endometrial cancer among postmenopausal women. There is a need to raise public awareness of the serious risks associated with the use of talcum powder and for legislation to protect the health of the uninformed who represent the poorer segment of the community, and infants and young children. The dangers associated with cosmetic use of talc outweigh any possible benefits.

**Key words:** Endometrial, ovarian cancer, pulmonary fibrosis, granuloma, pulmonary hypertension, talc inhalation

Stanislaus Anthony, Sharif Hossain, Chua MJ, Anil PK, Quek Yew Siong, Siong Wei Loong, Lekhsan Othman, Toshihiro Akaike, Chowdhury EH. Fabrication and intracellular delivery of siRNA/carbonate apatite nano-composites for effective knockdown of cyclin B1 gene. *Drugs and Therapy Studies* 2011; 1:e8: 27-30

## **Fabrication and intracellular delivery of siRNA/carbonate apatite nano-composites for effective knockdown of cyclin B1 gene**

Stanislaus Anthony<sup>1</sup>, Sharif Hossain<sup>2</sup>, Chua Ming Jang<sup>1</sup>, Anil Philip Kunnath<sup>1</sup>, Quek Yew Siong<sup>1</sup>, Siong Wei Loong<sup>1</sup>, Lekhsan Othman<sup>3</sup>, Toshihiro Akaike<sup>2</sup>, Ezharul Hoque Chowdhury<sup>3</sup>

<sup>1</sup>Faculty of Medicine and Health Science, International Medical University (IMU), Kuala Lumpur, Malaysia

<sup>2</sup>Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, Yokohama, Japan

<sup>3</sup>Jeffrey Cheah School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon, Selatan, Bandar Sunway, Selangor Darul Ehsan, Malaysia

### **Abstract**

Gene therapy through intracellular delivery of a functional gene or a gene-silencing element is a promising approach to properly treat critical human diseases like cancer. The ability of synthetically designed small interfering RNA (siRNA) to effectively silence genes at post-transcriptional level has made them attractive options in targeted therapeutics. However, naked siRNA being unable to passively diffuse through cellular membranes, poses difficulty in fully exploiting the potential of the technology. pH-sensitive carbonate apatite has been developed as an efficient tool to deliver siRNA into the mammalian cells by virtue of its high affinity interaction with the siRNA and effective cellular endocytosis. Moreover, internalized siRNA has been found to escape from the endosomes in a time-dependent manner and effectively silenced reporter gene expression. Knockdown of cyclin B1 gene with only 10 nM of siRNA delivered by carbonate apatite has resulted in significant death of cervical cancer cells. Moreover, delivery of siRNA against cyclin B1 gene has led to the sensitization of the cancer cells to both cisplatin and doxorubicin at a particular drug concentration. Thus, the new method of siRNA delivery is highly promising for pre-clinical and clinical cancer therapy using siRNA therapeutics.

**Key words:** carbonate apatite, nanoparticles, siRNA, gene knockdown, cancer, cyclin B1, cisplatin, doxorubicin, paclitaxel



Tan MY, Magarey JM, Chee WSS, Lee LF, Tan MH. A brief structured education programme enhances self-care practices and improves glycaemic control in Malaysians with poorly controlled diabetes. *Hlth Educ Res (UK)* 2011; doi: 10.1093/her/cyr047

## **A brief structured education programme enhances self-care practices and improves glycaemic control in Malaysians with poorly controlled diabetes**

Tan MY<sup>1</sup>, Magarey JM<sup>2</sup>, Chee SS<sup>3</sup>, Lee LF<sup>4</sup>, Tan MH<sup>5</sup>

<sup>1</sup>Department of Nursing, Damai Medical and Heart Clinic, Melaka 75300, Malaysia

<sup>2</sup>School of Nursing, University of Adelaide, Adelaide 5005, Australia

<sup>3</sup>Department of Nutrition and Dietetics, International Medical University 126, Jalan 19/ 155B, Bukit Jalil, Kuala Lumpur 57000, Malaysia

<sup>4</sup>Department of Nutrition and Dietetics, University Malaya Medical Centre, Lembah Pantai, Kuala Lumpur 59100, Malaysia

<sup>5</sup>Division of Metabolism, Endocrinology and Diabetes, University of Michigan, Ann Arbor, MI 48104, USA

### **Abstract**

We assessed the effectiveness of a brief structured diabetes education programme based on the concept of self-efficacy on self-care and glycaemic control using single-blind study design. One hundred and sixty-four participants with poorly controlled diabetes from two settings were randomized using computer-generated list into control (n = 82) and intervention (n = 82) groups, of which 151 completed the study. Monthly interventions over 12 weeks addressed the self-care practices of diet, physical activity, medication adherence and self-monitoring of blood glucose (SMBG). These self-care practices were assessed at Weeks 0 and 12 using pre- and post-questionnaires in both groups together with glycosylated haemoglobin A1c (HbA1c) and diabetes knowledge. In the intention-to-treat analysis (n = 164), the intervention group improved their SMBG (P = <0.001), physical activity (P = 0.001), HbA1c (P = 0.03), diabetes knowledge (P = <0.001) and medication adherence. At Week 12, HbA1c difference adjusted for SMBG frequency, medication adherence and weight change remained significant (P = 0.03) compared with control group. For within group comparisons, diabetes knowledge (P = <0.001), HbA1c level (P = <0.001), SMBG (P = <0.001) and medication adherence (P = 0.008) improved from baseline in the intervention group. In the control group, only diabetes knowledge improved (P = <0.001). These findings can contribute to the development of selfmanagement diabetes education in Malaysia.

Tamilvanan S, Kumar BA. Influence of acetazolamide loading on the (in vitro) performances of non-phospholipid-based cationic nanosized emulsion in comparison with phospholipid-based anionic and neutral-charged nanosized emulsions. *Drug Development and Industrial Pharmacy* 2011; 37(9): 1003–1015

## **Influence of acetazolamide loading on the (in vitro) performances of non-phospholipid-based cationic nanosized emulsion in comparison with phospholipid-based anionic and neutral-charged nanosized emulsions**

Shunmugaperumal Tamilvanan<sup>1,2</sup> and Balakrishnan Ajith Kumar<sup>2</sup>

<sup>1</sup>International Medical University (IMU) SDN BHD, Jalan Jalil Perkasa, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup>Arulmigu Kalasalingam College of Pharmacy, Krishnankoil, Tamil Nadu State, India

### **Abstract**

#### Context:

Acetazolamide (ACZM)-loaded anionic, cationic, and neutral-charged oil-in-water nanosized emulsions were prepared and compared with their mean droplet diameter, surface charge, entrapment efficiency, freeze–thaw cycling stability, in vitro drug release, and transcorneal permeation.

#### Objective:

The present study aims to determine the influence of ACZM loading on the performances of non-phospholipid-based cationic nanosized emulsion in comparison with phospholipid-based anionic and neutral-charged nanosized emulsions.

#### Results and discussion:

Regardless of charges, all of these emulsions exhibited a nanometer range mean particle diameter (240–443 nm) following autoclave sterilization. While the anionic and cationic emulsions did show high negative (–36.9 mV) and positive zeta potential (+41.4 mV) values, the neutral-charged emulsion did not. Presence of cryoprotectants (5% w/w sucrose + 5% w/w sorbitol) improved the stability of cationic emulsion to droplet aggregation during freeze–thaw cycling. The in vitro release kinetic behavior of drug exchange with physiological anions present in the simulated tear solution appears to be complex and difficult to characterize using mathematical fitting model equations. Augmentation in drug permeation through goat cornea, in vitro, was noticed for cationic emulsion.

#### Conclusion:

ACZM-loaded cationic nanosized emulsion could be suitable for topical application into eye to elicit better therapeutic effect in comparison with its anionic and neutral-charged emulsions.

**Key words:** Arachis oil, in vitro release, zeta potential, cryoprotectant, cornea, permeation

Tamilvanan S, Venkatesh Babu R, Nappinai A, Sivaramakrishnan G. In vitro and in vivo evaluation of hydrophilic and hydrophobic polymers-based nicorandil-loaded peroral tablet compared with its once-daily commercial sustained-release tablet. *Drug Develop Industrial Pharm* 2011; 37(4): 436-445

## **In vitro and in vivo evaluation of hydrophilic and hydrophobic polymers-based nicorandil-loaded peroral tablet compared with its once-daily commercial sustained-release tablet**

Tamilvanan S<sup>1,2</sup>, Venkatesh Babu R<sup>2,3</sup>, Nappinai A<sup>4</sup>, Sivaramakrishnan G<sup>3</sup>

<sup>1</sup>Department of Pharmaceutical Technology, International Medical University (IMU) SDN BHD, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Pharmaceutics, Arulmigu Kalasalingam College of Pharmacy, Krishnankoil, Tamilnadu, India

<sup>3</sup>SaiMirrah Innopharm (P). Ltd., Chennai, Tamilnadu, India

<sup>4</sup>Department of Pharmaceutics, C. L. Baid Metha College of pharmacy, Chennai, Tamilnadu, India

### **Abstract**

#### **Context:**

Hydrophilic and hydrophobic polymer-based nicorandil (10 mg)-loaded peroral tablets were prepared using the wet granulation technique. The influence of varying amounts of hydroxypropyl methylcellulose (HPMC) (30–50 mg), ethylcellulose (2–4 mg), microcrystalline cellulose (5–20 mg) and Aerosil<sup>®</sup> (5–12 mg) in conjunction with the constant amounts (3 mg) of glidant and lubricant (magnesium stearate and talc) on the in vitro performances of the tablets (hardness, friability, weight variation, thickness uniformity, drug content, and drug release behavior) were investigated.

#### **Objective:**

The objectives of this study were (i) to select a nicorandil-loaded peroral tablet that matched the in vitro dissolution profile of once-daily commercial sustained-release tablet, and (ii) to compare the in vivo sustaining/controlling efficacy of the selected peroral tablet with that of its commercial counterparts.

#### **Results and Discussion:**

Because the nicorandil (10 mg)-loaded tablet prepared based on F-IX composition (50 mg HPMC, 4 mg ethylcellulose, 10 mg MCC and 3 mg glidant and lubricant) showed a release profile comparable to that of the Nikoran<sup>®</sup> OD SR tablet release profile, the tablet with this composition was considered to be the optimized/selected formulation and, therefore, was subjected to stability study and in vivo study in rabbits. Despite of the higher C<sub>max</sub> and AUC values obtained with the optimized tablet, there was no sign of difference between the optimized- and Nikoran<sup>®</sup> OD SR- tablets following a single-dose crossover oral administration into rabbit.

#### **Conclusion:**

The optimized tablet could be used as an alternative to the commercial once-daily tablet.

**Key words:** Ethylcellulose, in vivo bioavailability, nicorandil, peroral tablet

Tan BS, Tiong KH, Aswhin Muruhadas, Nirmal Randhawa, Choo HL, Tracey D Bradshaw, Stevens MFG, Leong CO. CYP2S1 and CYP2W1 mediate 2-(3,4-dimethoxyphenyl)-5-fluorobenzothiazole (GW-610, NSC 721648) sensitivity in breast and colorectal cancer cells. *Molecular Cancer Therapeutics* 2011; 10(10): 1982-1992

## **CYP2S1 and CYP2W1 mediate 2-(3,4-dimethoxyphenyl)-5-fluorobenzothiazole (GW-610, NSC 721648) sensitivity in breast and colorectal cancer cells**

Tan Boon Shing<sup>1</sup>, Tiong KH<sup>1</sup>, Aswhin Muruhadas<sup>2</sup>, Nirmal Randhawa<sup>2</sup>, Choo Heng Lung<sup>1</sup>, Tracey D Bradshaw<sup>3</sup>, Stevens MFG<sup>3</sup>, Leong CO<sup>4</sup>

<sup>1</sup>School of Postgraduate Studies and Research, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup>School of Medicine, International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>3</sup>School of Pharmacy, University of Nottingham, Nottingham, United Kingdom

<sup>4</sup>School of Pharmacy and Health Sciences, International Medical University, Bukit Jalil, Kuala Lumpur,

### **Abstract**

Both 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole (5F-203; NSC 703786) and 2-(3,4-dimethoxyphenyl)-5-fluorobenzothiazole (GW-610; NSC 721648) are antitumor agents with novel mechanism(s). Previous studies have indicated that cytochrome (CYP) P450 1A1 is crucial for 5F-203 activity. In the present study, we investigated the functional role of 2 newly identified CYP P450 enzymes, CYP2S1 and CYP2W1, in mediating antitumor activity of benzothiazole compounds. We generated isogenic breast cancer (MDA-MB-468, MCF-7) and colorectal cancer (KM12 and HCC2998) cell lines depleted for CYP1A1, CYP2S1, or CYP2W1. The sensitivity of these cells to 5F-203 and GW-610 was then compared with vector control cells. 5F-203 exhibited potent activity against breast cancer cells whereas GW-610 was effective against both breast and colorectal cancer (CRC) cells. CYP1A1 was induced in both breast cancer and CRC cells, while CYP2S1 and CYP2W1 were selectively induced in breast cancer cells only, following treatment with 5F-203 or GW-610. Depletion of CYP1A1 abrogated the sensitivity of breast cancer and CRC cells to 5F-203 and GW-610. Although depletion of CYP2S1 sensitized both breast cancer and CRC cells toward 5F-203 and GW-610, CYP2W1 knockdown caused marked resistance to GW-610 in CRC cells. Our results indicate that CYP-P450 isoforms, with the exception of CYP1A1, play an important role in mediating benzothiazole activity. CYP2S1 appears to be involved in deactivation of benzothiazoles, whereas CYP2W1 is important for bioactivation of GW-610 in CRC cells. Because CYP2W1 is highly expressed in colorectal tumors, GW-610 represents a promising agent for CRC therapy.

Tan CH, Leong PK, Fung SY, Sim SM, Ponnudurai G, Ariaratnam C, Khomvilai S, Sitprijia V, Tan Nget Hong. Cross neutralization of *Hypnale hypnale* (hump-nosed pit viper) venom by polyvalent and monovalent Malayan pit viper antivenoms in vitro and in a rodent model. *Acta Tropica* (Netherlands) 2011; 117: 119-124

## **Cross neutralization of *Hypnale hypnale* (hump-nosed pit viper) venom by polyvalent and monovalent Malayan pit viper antivenoms in vitro and in a rodent model**

Tan CH<sup>1</sup>, Leong PK<sup>1</sup>, Fung SY<sup>2</sup>, Sim SM<sup>1</sup>, Ponnudurai G<sup>3</sup>, Ariaratnam C<sup>3</sup>, Khomvilai S<sup>4</sup>, Sitprijia V<sup>4</sup>, Tan Nget Hong<sup>2</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

<sup>2</sup>Department of Molecular Medicine, Faculty of Medicine, CENAR, University of Malaya, 50603 Kuala Lumpur, Malaysia

<sup>3</sup>Department of Human Biology, International Medical University, 126 Jalan 19/155B, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>4</sup>Queen Saovabha Memorial Institute, Rama IV Road, Bangkok, Thailand

### **Abstract**

*Hypnale hypnale* (hump-nosed pit viper) is a medically important venomous snake in Sri Lanka and Southwestern India. Bite of this snake may result in hemostatic dysfunction, acute kidney injury and death. Clinical studies indicated that the locally available polyvalent antivenoms produced in India are not effective against hump-nosed pit viper envenoming. Hence, there is an urgent need to search for effective antivenom. In this paper, we examined the ability of *Calloselasma rhodostoma* (Malayan pit viper) monovalent antivenom and the Hemato polyvalent antivenom (both produced by Thai Red Cross Society, TRCS) to neutralize the lethality and toxic effects of *H. hypnale* venom, as *C. rhodostoma* is considered a sister taxon of *H. hypnale*. In vitro neutralization studies showed that the Hemato polyvalent antivenom effectively neutralized the lethality of *H. hypnale* venom (1.52mgvenom/mL antivenom) as well as the hemorrhagic, procoagulant and necrotic activities of the venom. The monovalent *C. rhodostoma* antivenom could also neutralize the lethality and toxic activities of the venom, but the potency was lower. The Hemato polyvalent antivenom also effectively protected mice from the lethal and local effects of *H. hypnale* venom in an in vivo rodent model of envenoming. Furthermore, the polyvalent antivenom could also effectively neutralize the venom of *Daboia russelii* (2.50mgvenom/mL antivenom), another common cause of snake bites in Sri Lanka and South India. These findings suggested that the Hemato polyvalent antivenom may be beneficial in the antivenom treatment of *H. hypnale* envenoming.

**Key words:** *Hypnale hypnale* venom, Hump-nosed pit viper, Neutralization by commercial antivenoms

Tan Jackie, Nagaraja HS, Chakravarthi S. Antioxidant effects of *Etingera eliator* flower extract against lead acetate-induced perturbations in free radical scavenging enzymes and lipid peroxidation in rats. BMC Research Notes 2011; 4: 67-74

## **Antioxidant effects of *Etingera eliator* flower extract against lead acetate-induced perturbations in free radical scavenging enzymes and lipid peroxidation in rats**

Tan Jackie<sup>1</sup>, Haleagrahara Nagaraja<sup>1</sup>, Chakravarthi Srikumar<sup>2</sup>

<sup>1</sup>Human Biology Division, School of Medicine, International Medical University, Kuala Lumpur, Malaysia <sup>2</sup>Pathology Division, School of Medicine, International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

#### **Background:**

*Etingera eliator* or 'pink torch ginger' (Zingiberaceae) are widely cultivated in tropical countries and used as spices and food flavoring. The purpose of this study was to evaluate the antioxidant effects of *Etingera eliator* against lead - induced changes in serum free radical scavenging enzymes and lipid hydroperoxides in rats.

#### **Findings:**

Rats were exposed to lead acetate in drinking water (500 ppm) for 14 days alone or plus the ethanol extract of *E. eliator* (50, 100 and 200 mg/kg). Blood lead levels, lipid hydroperoxides, protein carbonyl contents and oxidative marker enzymes were estimated. Lead acetate in drinking water elicited a significant increase in lipid hydroperoxides (LPO) and protein-carbonyl-contents (PCC). There was a significant decrease in total antioxidants, superoxide dismutase, glutathione peroxidase and glutathione S-transferase levels with lead acetate treatment. Supplementation of *E. eliator* was associated with reduced serum LPO and PCC and a significant increase in total antioxidants and antioxidant enzyme levels.

#### **Conclusions:**

The results suggest that flower extract of *Etingera eliator* has powerful antioxidant effect against lead - induced oxidative stress and the extract may be useful therapeutic agent against lead toxicity. However, detailed evaluations are required to identify the active antioxidant compounds from this plant extract.

Tan KL. Factors associated with exclusive breastfeeding among infants under six months of age in peninsular Malaysia. *Intl Breastfeeding J* 2011; 6: 2-8

## **Factors associated with exclusive breastfeeding among infants under six months of age in peninsular Malaysia**

Tan Kok Leong

Community Medicine Division, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

#### Background:

Breastfeeding is accepted as the natural form of infant feeding. For mothers to be able to breastfeed exclusively to the recommended six months, it is important to understand the factors that influence exclusive breastfeeding. The aim of the study was to identify factors associated with exclusive breastfeeding in Peninsular Malaysia.

#### Methods:

This was a cross-sectional study involving 682 mother-infant pairs with infants up to six months attending maternal and child health section of the government health clinics in Klang, Malaysia. Data were collected by face-to-face interviews using a pre-tested structured questionnaire over 4 months in 2006. Data on breastfeeding were based on practice in the previous one month period. Logistic regression was used to assess the independent association between the independent variables and exclusive breastfeeding adjusting for infant age.

#### Results:

The prevalence of exclusive breastfeeding among mothers with infants aged between one and six months was 43.1% (95% CI: 39.4, 46.8). In the multivariate model exclusive breastfeeding was positively associated with rural residence, Malay mothers, non-working and non-smoking mothers, multiparous mothers, term infants, mothers with husbands who support breastfeeding and mothers who practice bed-sharing.

#### Conclusions:

Interventions that seek to increase exclusive breastfeeding should focus on women who are at risk of early discontinuation of breastfeeding.

Tan Shin Yee, Kan Elaine, Lim Wei Yin, Chay Grace, Law Jason HK, Soo GW, Bukhari NI, Ignacio S. Metronidazole leads to enhanced uptake of imatinib in brain, liver and kidney without affecting its plasma pharmacokinetics in mice. *J Pharm Pharmacol* 2011; 63: 918-925

## **Metronidazole leads to enhanced uptake of imatinib in brain, liver and kidney without affecting its plasma pharmacokinetics in mice**

Tan Shin Yee, Kan Elaine, Lim Wei Yin, Chay Grace, Law Jason HK, Soo GW, Bukhari Nadeen Irfan, Segarra Ignacio

Department of Pharmaceutical Technology, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

#### **Objectives:**

The pharmacokinetic interaction between metronidazole, an antibiotic–antiparasitic drug used to treat anaerobic bacterial and protozoal infections, and imatinib, a CYP3A4, P-glycoprotein substrate kinase inhibitor anticancer drug, was evaluated.

#### **Methods:**

Male imprinting control region mice were given 50 mg/kg imatinib PO (control group) or 50 mg/kg imatinib PO, 15 min after 40 mg/kg PO metronidazole (study group). Imatinib plasma, brain, kidney and liver concentrations were measured by HPLC and non-compartmental pharmacokinetic parameters estimated.

#### **Key findings:**

Metronidazole coadministration resulted in a double-peak imatinib disposition profile. The maximum concentration ( $C_{max}$ ) decreased by 38%, the area under the curve ( $AUC_{0-\infty}$ ) decreased by 14% and the time to  $C_{max}$  ( $T_{max}$ ) was earlier (50%) in plasma. Apparent volume of distribution ( $V_{ss}/F$ ) and oral clearance ( $Cl/F$ ) increased by 21% and 17%, respectively. Imatinib tissue penetration was higher after metronidazole coadministration, with 1.7 and 2.1-fold  $AUC_{0-\infty}$  increases in liver and kidney, respectively. Metronidazole increased imatinib's tissue-to-plasma  $AUC_{0-\infty}$  ratio in liver from 2.29 to 4.53 and in kidney from 3.04 to 7.57, suggesting higher uptake efficiency. Brain  $C_{max}$  was 3.9-fold higher than control and  $AUC_{0-t_{last}}$  was 2.3-fold greater than plasma (3.5% in control group). No tissueplasma concentration correlation was found.

#### **Conclusions:**

Metronidazole slightly decreased imatinib systemic exposure but enhanced liver, kidney and brain penetration, probably due to metronidazole-mediated inhibition of P-glycoprotein and other efflux transporters. The high brain exposure opens possibilities for treatment of glioma and glioblastoma. Renal and hepatic functions may need to be monitored due to potential renal and hepatic toxicity.

**Key words:** brain drug delivery; drug–drug interaction; imatinib; metronidazole; tissue distribution



Tang JC, Wong SF, Mak JW, Ho TM. Antigenic profile of *Blomia tropicalis*, *Aleuroglyphus ovatus* and *Glycycometus malayensis*. Trop Biomed 2011; 28(2): 223-236

## **Antigenic profile of *Blomia tropicalis*, *Aleuroglyphus ovatus* and *Glycycometus malayensis***

Tang JC<sup>1</sup>, Wong SF<sup>1</sup>, Mak JW<sup>1</sup>, Ho TM<sup>2</sup>

<sup>1</sup>International Medical University, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Acarology Unit, Institute for Medical Research, 50588 Kuala Lumpur

### **Abstract**

House dust mites and storage mites are well-known causes for allergenic diseases. The aim of this study was to investigate the immunogenic sites of *Blomia tropicalis*, *Aleuroglyphus ovatus* and *Glycycometus malaysiensis*. The mites were maintained in a culture medium at 25°C and 75% relative humidity. Mites were harvested either with heat escape or floatation method, purified, homogenized, quantified and used for the production of polyclonal antibody and immunostaining. For each species of mites, five male mice and five male rats were randomly selected and immunized intraperitoneally with respective crude mite extract at two-weekly intervals. *Blomia tropicalis*, *A. ovatus* or *G. malaysiensis* whole mites and paraffin-embedded mite sections were immunostained with the respective polyclonal antibody. The faecal pellets of mites were intensely stained for all the three species in the present study. The legs of sectioned *A. ovatus* were not immunogenic as compared with those of *G. malaysiensis* and *B. tropicalis*. The outer layer (cuticle) of whole mites and the eggs for these species were very immunogenic. Hence, the polyclonal antibodies obtained in this study may serve as potential tools in detecting the eggs and immature mites in environmental samples. Future studies should focus on the antigenic components of eggs since they were relatively abundant in dust and highly antigenic as seen in the present study.

Tang Yee Voon, Phang SM, Chu WL, Ho Anthony, Teo SH, Lee HB. Cyclic tetrapyrrolic photosensitizers from *Cladophora patentiamea* (Cladophoraceae, Chlorophyta) and *Turbinaria conoides* (Sargassaceae, Phaeophyta) for photodynamic therapy. *J Appl Phycol* 2011; doi: 10.1007/s10811-011-9698-8

## **Cyclic tetrapyrrolic photosensitizers from *Cladophora patentiamea* (Cladophoraceae, Chlorophyta) and *Turbinaria conoides* (Sargassaceae, Phaeophyta) for photodynamic therapy**

Tang Yee Voon<sup>1,2</sup>, Phang SM<sup>2,3</sup>, Chu WL<sup>4</sup>, Ho Anthony<sup>1,5</sup>, Teo SH<sup>1</sup>, Lee HB<sup>1</sup>

<sup>1</sup>Cancer Research Initiatives Foundation (CARIF), 2nd floor, Outpatient Centre, Sime Darby Medical Centre, 47500, Subang Jaya, Selangor Darul Ehsan, Malaysia

<sup>2</sup>Institute of Biological Sciences, University of Malaya, 50603, Kuala Lumpur, Malaysia

<sup>3</sup>Institute of Ocean and Earth Sciences, University of Malaya, 50603, Kuala Lumpur, Malaysia

<sup>4</sup>International Medical University, Plaza Komanwel, Bukit Jalil 57000, Kuala Lumpur, Malaysia

<sup>5</sup>Faculty of Engineering and Science, University Tunku Abdul Rahman, 53300 Setapak, Kuala Lumpur, Malaysia

### **Abstract**

In screening for novel photosensitizers for photodynamic therapy, 14 seaweed samples from Port Dickson in Malaysia were collected. Methanolic extracts of these samples were prepared and evaluated for phototoxicity using a short-term cell viability assay, where promyelocytic leukemia cells, HL60 were incubated with the extracts prior to irradiation with a broad spectrum light at  $9.6 \text{ J cm}^{-2}$  (equivalent to  $10.5 \text{ mW cm}^{-2}$  for 10 min). Four of the methanolic extracts demonstrated moderate to strong phototoxicity and bioassay-guided isolation of photosensitizers was carried out on two selected seaweeds to yield a total of eight cyclic tetrapyrrolic compounds which are derivatives of chlorophyll-a and -b. Seven of these compounds showed  $>50\%$  phototoxicity at  $5 \mu\text{g mL}^{-1}$  while exhibiting minimal cytotoxicity in the dark, which is an important characteristic of an ideal photosensitizer.

**Key words:** Photodynamic therapy, Photosensitizer, Seaweeds, Cyclic tetrapyrroles, Chlorophylls

Tee LK, Ling CS, Chua MJ, Abdullah S, Rosli R, Chowdhury EH. Purification of transcriptionally active multimeric plasmid DNA using zwitterionic detergent and carbonate apatite nano-particles. *Plasmid* 2011; 66(1): 38-46

## **Purification of transcriptionally active multimeric plasmid DNA using zwitterionic detergent and carbonate apatite nano-particles**

Tee LK<sup>1</sup>, Ling CS<sup>1</sup>, Chua MJ<sup>1</sup>, Abdullah S<sup>2</sup>, Rosli R<sup>2</sup>, Chowdhury EH<sup>1,3</sup>

<sup>1</sup>Faculty of Medicine and Health Sciences, International Medical University (IMU), No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Faculty of Medicine and Health Sciences, University Putra Malaysia, 43400 UPM Serdang, Selangor Darul Ehsan, Malaysia

<sup>3</sup>Jeffrey Cheah School of Medicine and Health Sciences, Monash University Sunway Campus, Jalan Lagoon Selatan, Bandar Sunway, Selangor Darul Ehsan, Malaysia

### **Abstract**

Plasmid DNA is one of the indispensable components in molecular biology research and a potential biomaterial for gene therapy and DNA vaccination. Both quality and quantity of extracted plasmid DNA are of the great interests in cloning and subsequent expression of genes in vitro and in vivo for basic research and therapeutic interventions. Bacteria with extremely short generation times are the valuable source of plasmid DNA that can be isolated through a number of existing techniques. However, the current methods have some limitations in isolating high quality plasmid DNA since the multimeric plasmid which is believed to be more efficiently transcribed by RNA polymerase than the monomeric form, is almost lost during the extraction process. Recently, we developed a rapid isolation technique for multimeric plasmid based on generation of a 'protein aggregate' using a zwitterionic detergent and alkali. Here we have investigated the roles of different parameters in the whole extraction process to optimise the production of high quality multimeric plasmid DNA. Moreover, we have showed the advantageous effects of nanoparticles to effectively sediment the 'protein aggregate' for smooth elution of multimeric plasmid DNA from it. Finally, quality assessment study has revealed that the isolated multimeric DNA is at least 10 times more transcriptionally active than the monomeric form isolated by the commercially available Qiagen kit.

**Key words:** Carbonate apatite, Nano-crystals, Particle size, NaCl, Glucose, Transfection

Teng CL, Tong SF, Khoo EM, Lee VKM, Zailinawati AH, Mimi O, Chen WS, Salleh Nordin. Antibiotics for URTI and UTI. Prescribing in Malaysian primary care settings. Aust Fam Physician 2011; 40(5): 325-329

## Antibiotics for URTI and UTI. Prescribing in Malaysian primary care settings

Teng CL<sup>1</sup>, Tong SF<sup>2</sup>, Khoo EM<sup>3</sup>, Lee Verna<sup>4</sup>, Zailinawati AH<sup>5</sup>, Mimi O<sup>6</sup>, Chen WS<sup>7</sup>, Salleh Nordin<sup>8</sup>

<sup>1</sup>Department of Family Medicine, International Medical University, Negeri Sembilan, Malaysia

<sup>2</sup>Department of Family Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

<sup>3</sup>Department of Primary Care Medicine, University of Malaya, Kuala Lumpur, Malaysia

<sup>4</sup>Department of Family Medicine, International Medical University, Negeri Sembilan, Malaysia

<sup>5</sup>Klinik Keluarga, Kuala Lumpur, Malaysia

<sup>6</sup>Klinik Kesihatan Kelana Jaya, Selangor, Malaysia

<sup>7</sup>Klinik Alam Medic, Selangor, Malaysia

<sup>8</sup>Institute for Health Systems Research, Kuala Lumpur, Malaysia.

### Abstract

#### Background:

Overprescription of antibiotics is a continuing problem in primary care.

This study aims to assess the antibiotic prescribing rates and antibiotic choices for upper respiratory tract infections (URTI) and urinary tract infections (UTI) in Malaysian primary care.

#### Method:

Antibiotic prescribing data for URTI and UTI was extracted from a morbidity survey of randomly selected primary care clinics in Malaysia.

#### Results:

Analysis was performed of 1163 URTI and 105 UTI encounters. Antibiotic prescribing rates for URTI and UTI were 33.8% and 57.1% respectively. Antibiotic prescribing rates were higher in private clinics compared to public clinics for URTI, but not for UTI. In URTI encounters, the majority of antibiotics prescribed were penicillins and macrolides, but penicillin V was notably underused. In UTI encounters, the antibiotics prescribed were predominantly penicillins or cotrimoxazole.

#### Discussion:

Greater effort is needed to bring about evidence based antibiotic prescribing in Malaysian primary care, especially for URTIs in private clinics.

**Key words:** general practice, prescriptions, drug; upper respiratory tract infection; urinary tract infection; antibiotics, guideline; evidence based medicine

Tong Seng Fah, Khoo EM, Nordin S, Teng CL, Lee VKM, Zailinawati AH, Chen WS, Mimi O. Process of care and prescribing practice for hypertension in public and private primary care clinics in Malaysia. *Asia Pac J Pub Hlth* 2011; doi: 10.1177/1010539511402190

## **Process of care and prescribing practice for hypertension in public and private primary care clinics in Malaysia**

Tong Seng Fah<sup>1</sup>, Khoo EM<sup>2</sup>, Nordin S<sup>3</sup>, Teng CL<sup>4</sup>, Lee VKM<sup>4</sup>, Zailinawati AH<sup>5</sup>, Chen WS<sup>6</sup>, Mimi O<sup>7</sup>

<sup>1</sup>Univerisiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

<sup>2</sup>University of Malaya, Kuala Lumpur, Malaysia

<sup>3</sup>Institute for Health Systems Research, Kuala Lumpur, Malaysia

<sup>4</sup>International Medical University, Seremban, Malaysia

<sup>5</sup>Klinik Keluarga Wangsa Maju, Kuala Lumpur, Malaysia

<sup>6</sup>Klinik Alam Medic, Puchong, Malaysia

<sup>7</sup>Klinik Kesihatan Kelana Jaya, Petaling Jaya, Malaysia

### **Abstract**

This study aimed to compare the process of care and the choice of antihypertensive medications used in both public and private primary care clinics in Malaysia. A cross-sectional survey was completed in 2008 on randomly selected 100 public health clinics and 114 private primary care clinics in Malaysia. A total of 4076 patient records, 3753 (92.1%) from public clinics and 323 (7.9%) from private clinics were analyzed. Less than 80% of the records documented the recommended clinical and laboratory assessments. The rates of documentation for smoking status, family history of premature death, retinal assessment, and urine albumin tests were lower in public clinics. Overall, 21% of the prescription practices were less than optimal. The process of care and the use of antihypertensive medications were not satisfactory in both settings.

**Key words:** family practice, hypertension, Malaysia, health service evaluation, primary health care, process of care, research design

Tudave D, Radhakrishnan AK, Chakravathi S, Nagaraja HS. Modulation of C-reactive protein and tumour necrosis factor-alpha in collagen-induced arthritis in dark Agouti rats: impact of collagen concentration on severity of arthritis. *Inflammation Research* 2011; doi: 10.1007/00011-011-0349-y

## **Modulation of C-reactive protein and tumour necrosis factor-alpha in collagen-induced arthritis in dark Agouti rats: impact of collagen concentration on severity of arthritis**

Tudave D<sup>1</sup>, Radhakrishnan A<sup>2</sup>, Srikumar Chakravathi<sup>2</sup>, Haleagrahara N<sup>3</sup>

<sup>1</sup>Postgraduate and Research Division, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>Division of Pathology, International Medical University, Kuala Lumpur, Malaysia

<sup>3</sup>Division of Human Biology, International Medical University, Kuala Lumpur, Malaysia

### **Abstract**

#### **Objectives:**

The study investigated the effect of collagen-induced arthritis in Dark Agouti (DA) rats on the level of C-reactive protein and inflammatory cytokine tumour necrosis factor-alpha (TNF- $\alpha$ ).

#### **Subjects:**

Female Dark Agouti (DA) rats.

#### **Methods:**

Three different dosages of (2 mg/kg of body weight, 3 mg/kg of body weight and 4 mg/kg of body weight) collagen and complete Freund's adjuvant suspension were tested. After 45 days, serum C-reactive protein, TNF- $\alpha$ , superoxide dismutase and total glutathione assays were done. Radiographic and histopathological changes in the joints were compared.

#### **Results:**

All three groups showed signs of arthritic changes, confirmed by histopathological and radiographic changes. Severe arthritic changes were seen in the rats injected with 4 mg/kg of body weight of collagen. There was a significant increase in C-reactive protein, TNF- $\alpha$ , super oxide dismutase and total glutathione levels in the plasma in arthritis rats and the changes were more significant with 4 mg/kg of collagen.

#### **Conclusion:**

These results demonstrated that the optimal dose to inject to experimental animals in order to get severe arthritic changes was 4 mg/kg of collagen with complete Freund's adjuvant suspension. Severe arthritis changes induced significant elevation in plasma C-reactive protein and TNF- $\alpha$  levels.

**Key words:** Arthritis, Collagen, C-reactive protein, Tumour necrosis factor

Voon KGL, Chua KB, Meng Yu, Cramer G, Barr, JA, Yasmin M, Wang Lin-Fa. Evolutionary relationship of the L-and M-class genome segments of bat-borne fusogenic orthoreoviruses in Malaysia and Australia. J Gen Virol 2011; 92: 2930-2936

## Evolutionary relationship of the L-and M-class genome segments of bat-borne fusogenic orthoreoviruses in Malaysia and Australia

Voon Kenny<sup>1</sup>, Chua KB<sup>1,2</sup>, Meng Yu<sup>3</sup>, Cramer G<sup>3</sup>, Barr, JA<sup>3</sup>, Yasmin M<sup>1</sup>, Wang Lin-Fa<sup>3</sup>

<sup>1</sup>International Medical University, Bukit Jalil, Kuala Lumpur, Malaysia

<sup>2</sup>National Public Health Laboratory, Sg. Buloh, Selangor, Malaysia

<sup>3</sup>CSIRO Livestock Industries, Australian Animal Health Laboratory, Geelong, Australia

### Abstract

We previously described three new Malaysian orthoreoviruses designated Pulau virus, Melaka virus and Kampar virus. Melaka and Kampar viruses were shown to cause respiratory disease in humans. These viruses, together with Nelson Bay virus, isolated from Australian bats, are tentatively classified as different strains within the species *Pteropine orthoreovirus* (PRV), formerly known as *Nelson Bay orthoreovirus*, based on the small (S) genome segments. Here we report the sequences of the large (L) and medium (M) segments, thus completing the whole-genome characterization of the four PRVs. All L and M segments were highly conserved in size and sequence. Conserved functional motifs previously identified in other orthoreovirus gene products were also found in the deduced proteins encoded by the cognate segments of these viruses. Detailed sequence analysis identified two genetic lineages divided into the Australian and Malaysian PRVs, and potential genetic reassortment among the M and S segments of the three Malaysian viruses.

Voon PT, Ng TKW, Lee VKM, Nesaretnam K. Diets rich in palmitic acid (16:0), lauric and myristic acids (12:0 + 14:0), or oleic acid (18:1) do not alter postprandial or fasting plasma homocysteine and inflammatory markers in healthy Malaysian adults. *Am J Clin Nutr* 2011; doi: 103945/ajcn.111.020107

## **Diets rich in palmitic acid (16:0), lauric and myristic acids (12:0 + 14:0), or oleic acid (18:1) do not alter postprandial or fasting plasma homocysteine and inflammatory markers in healthy Malaysian adults**

Voon PT<sup>1</sup>, Ng TKW<sup>1</sup>, Lee VKM,<sup>1</sup> Nesaretnam K<sup>2</sup>

<sup>1</sup>Department of Nutrition and Dietetics, International Medical University, Kuala Lumpur, Malaysia

<sup>2</sup>Malaysian Palm Oil Board, 6, Persiaran Institusi, Bandar Baru Bangi, Kajang, Selangor, Malaysia

### **Abstract**

#### **Background:**

Dietary fat type is known to modulate the plasma lipid profile, but its effects on plasma homocysteine and inflammatory markers are unclear.

#### **Objective:**

We investigated the effects of high-protein Malaysian diets prepared with palm olein, coconut oil (CO), or virgin olive oil on plasma homocysteine and selected markers of inflammation and cardiovascular disease (CVD) in healthy adults.

#### **Design:**

A randomized-crossover intervention with 3 dietary sequences of 5 wk each was conducted in 45 healthy subjects. The 3 test fats, namely palmitic acid (16:0)-rich palm olein (PO), lauric and myristic acids (12:0 + 14:0)-rich CO, and oleic acid (18:1)-rich virgin olive oil (OO), were incorporated at two-thirds of 30% fat calories into high-protein Malaysian diets.

#### **Results:**

No significant differences were observed in the effects of the 3 diets on plasma total homocysteine (tHcy) and the inflammatory markers TNF- $\alpha$ , IL-1 $\beta$ , -6, and -8, high-sensitivity C-reactive protein, and interferon- $\gamma$ . Diets prepared with PO and OO had comparable nonhypercholesterolemic effects; the postprandial total cholesterol for both diets and all fasting lipid indexes for the OO diet were significantly lower ( $P < 0.05$ ) than for the CO diet. Unlike the PO and OO diets, the CO diet was shown to decrease postprandial lipoprotein(a).

#### **Conclusion:**

Diets that were rich in saturated fatty acids prepared with either PO or CO, and an OO diet that was high in oleic acid, did not alter postprandial or fasting plasma concentrations of tHcy and selected inflammatory markers.



Wan Azman Wan Ahmad, Robaayah Zambahari, Omar Ismail, Jeyaindran Sinnadurai, Azhari Rosman, Chin SP, Imran Zainal Abidin, Sim Kui-Hian. Malaysian National Cardiovascular Disease Database (NCVD) - acute coronary syndrome (ACS) registry: how are we different? CVD Prevention Control (Netherlands) 2011; 6(3): 81-89

## **Malaysian National Cardiovascular Disease Database (NCVD) – Acute Coronary Syndrome (ACS) registry: how are we different?**

Wan Azman Wan Ahmad<sup>a</sup>, Robaayah Zambahari<sup>b</sup>, Omar Ismail<sup>c</sup>, Jeyaindran Sinnadurai<sup>d</sup>, Azhari Rosman<sup>b</sup>, Chin Sze Piaw<sup>e</sup>, Imran Zainal Abidin<sup>a</sup>, Sim Kui-Hian<sup>f</sup>

<sup>a</sup>Division of Cardiology, University Malaya Medical Centre, Malaysia

<sup>b</sup>National Heart Institute, Malaysia

<sup>c</sup>Department of Cardiology, Penang Hospital, Malaysia

<sup>d</sup>Medical Department, Kuala Lumpur Hospital, Malaysia

<sup>e</sup>International Medical University, Malaysia

<sup>f</sup>Department of Cardiology, Sarawak General Hospital, Malaysia

### **Abstract:**

#### **Objective:**

The Malaysian NCVD-ACS (National Cardiovascular Disease Database-Acute Coronary Syndrome) registry attempts to determine the incidence and demographic profile of patients with ACS and to identify high risk group among them. It provides a comprehensive view to assess treatment strategies and adherence to existing guidelines for ACS patients; which can help in future development. It also aims to facilitate research using this database.

#### **Methods:**

The study included patients with ST-segment elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA) admitted to 11 participating sites in Malaysia from 1st January 2006 to 31st December 2006. The data were analyzed in terms of characteristics, clinical presentation, treatment, in-hospital outcome and 30-day outcome.

#### **Results:**

A total of 3422 patients were enrolled, with male to female ratio of 3:1, mean age of 59±12years and mean BMI of 25.8±4.4kg/m<sup>2</sup>. Among total study population, 96% had at least one established cardiovascular risk factor. In STEMI population, 70% received fibrinolytic therapy and 8% proceeded for primary percutaneous coronary intervention (PCI). Mean door-to-needle time for fibrinolytic therapy was 103±143min. Medical management was conducted for 86% of NSTEMI and 91% UA patients, with intervention for 14% and 9% respectively. The overall in-hospital mortality and 30-day mortality were 7% and 8% respectively.

**Conclusion:**

In our NCVD-ACS registry, when compared with other registries, the subjects were much younger at presentation and had higher prevalence of established cardiovascular risk factors, indicating the importance of primary prevention programme. Majority of the patients were managed medically, with low rates of cardiac interventions, the factor being driven largely by availability of resources. Mean door-to-needle time was much higher than the recommended guidelines, an issue that needs attention. The results indicate many opportunities for improvement of in-hospital and 30-day mortality.

**Key words:** NCVD, Acute Coronary Syndrome, Malaysian ACS registry

Wazir NN, Kareem BA. New clinical sign of cervical myelopathy: Wazir hand myelopathy sign. Singapore Med J 2011; 52(1): 47-49

## **New clinical sign of cervical myelopathy: Wazir hand myelopathy sign**

Wazir N N, Kareem B A

Department of Orthopaedic Surgery, Clinical School, International Medical University, Jalan Rasah, Seremban 70300, Malaysia

### **Abstract**

#### **Introduction:**

Cervical spondylotic myelopathy (CSM) represents a spectrum of pathologies with progressive compression of the spinal cord. The clinical signs and symptoms play a key role in diagnosis. The characteristic hand myelopathy signs are of significant clinical importance. The aim of this descriptive study was to report a relatively easy to elicit new hand myelopathy sign. The basis for this is finger and wrist flexor disinhibition, which is used for the spinal specificity of cord compression at or above the C5/6 level.

#### **Methods:**

The new clinical test was conducted in 68 patients with a mean age of 62 (range 54–68) years. The patients were divided into two groups according to their level of stenosis. Group 1 (n is 58) patients had stenosis at or above the C5/6 level, while Group 2 (n is 10) patients had stenosis at or below the C6/7 level. All these patients were clinically evaluated and their level of stenosis was confirmed using magnetic resonance imaging.

#### **Results:**

The Wazir sign was observed and well reproducible in 54 (93%) patients (Group 1); the myelopathy signs of three patients were positive (Hoffman's sign, finger escape and tensecond test). In Group 2, the Wazir sign was not reproducible, but the myelopathy signs were also positive in three patients.

#### **Conclusion:**

The Wazir hand myelopathy sign was found to be consistently present in our patients, in addition to the other hand myelopathy signs.

**Key words:** cervical myelopathy, hand myelopathy signs

Wong SF, Chong Ai Ling, Mak JW, Tan Jessie, Ling Suk Jiun, Ho Tze Ming.  
Molecular identification of house dust mites and storage mites. *Exp Appl Acarol*  
(Netherlands) 2011; doi: 10.1007/s10493-011-9460-6

## **Molecular identification of house dust mites and storage mites**

Wong SF<sup>1</sup>, Chong Ai Ling<sup>1</sup>, Mak JW<sup>1</sup>, Tan Jessie<sup>1</sup>, Ling Suk Jiun<sup>1</sup>, Ho Tze Ming<sup>2</sup>

<sup>1</sup>International Medical University, No. 126, Jalan Jalil Perkasa 19, Bukit Jalil,  
57000 Kuala Lumpur, Malaysia

<sup>2</sup>Acarology Unit, Institute for Medical Research, 50588 Kuala Lumpur, Malaysia

### **Abstract**

Mites are known causes of allergic diseases. Currently, identification of mites based on morphology is difficult if only one mite is isolated from a (dust) sample, or when only one gender is found, or when the specimen is not intact especially with the loss of the legs. The purpose of this study was to use polymerase chain reaction–restriction fragment length polymorphism (PCR–RFLP) of the ITS2 gene, to complement the morphological data for the identification of mites to the species level. For this, six species were cultured: *Dermatophagoides pteronyssinus*, *D. farinae*, *Blomia tropicalis*, *Tyrophagus putrescentiae*, *Aleuroglyphus ovatus* and *Glycycometus malaysiensis*. Genomic DNA of the mites was extracted, quantified, amplified and digested individually with restriction enzymes. *Hinf* I and *Ple* I differentiated the restriction patterns of *D. pteronyssinus* and *D. farinae*. *Bfa* I and *Alu* I enzymes differentiated *B. tropicalis* and *G. malaysiensis*. *Ple* I enzyme was useful for the differentiation between *T. putrescentiae* and *A. ovatus*. *Bfa* I was useful for the differentiation of *G. malaysiensis* from the rest of the species. In conclusion, different species of mites can be differentiated using PCR–RFLP of ITS2 region. With the established PCR–RFLP method in this study, identification of these mites to the species level is possible even if complete and intact adult specimens of both sexes are not available. As no study to date has reported PCR–RFLP method for the identification of domestic mites, the established method should be validated for the identification of other species of mites that were not included in this study.

**Key words:** House dust mites, PCR–RFLP, Restriction enzymes, Species identification, Storage mites

Wong SW, Tiong KH, Kong WY, Yue YC, Chua CH, Lim JY, Lee CY, Quah SI, Fow C, Chung C, So I, Tan BS, Choo HL, Rosli R, Cheong SK, Leong CO. Rapamycin synergizes cisplatin sensitivity in basal-like breast cancer cells through up-regulation of p73. *Breast Cancer Res Treat* 2011, 128(2): 301-313

## **Rapamycin synergizes cisplatin sensitivity in basal-like breast cancer cells through up-regulation of p73**

Su Wei Wong<sup>1</sup>, Kai Hung Tiong<sup>1</sup>, Weng Yip Kong<sup>1</sup>, Yuen Chee Yue<sup>1</sup>, Choon Hooi Chua<sup>1</sup>, Jae Ying Lim<sup>1</sup>, Chai Yui Lee<sup>1</sup>, Sean I. Quah<sup>1</sup>, Cindy Fow<sup>1</sup>, Cyril Chung<sup>1</sup>, Irene So<sup>1</sup>, Boon Shing Tan<sup>1</sup>, Heng Lungh Choo<sup>1</sup>, Rozita Rosli<sup>2</sup>, Soon-Keng Cheong<sup>3</sup> and Chee-Onn Leong<sup>1</sup>

<sup>1</sup>School of Postgraduate Studies and Research, School of Pharmacy and Health Sciences, International Medical University, 126 Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>2</sup>Medical Genetics Laboratory, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

<sup>3</sup>Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Bandar Sungai Long, Selangor, Malaysia

### **Abstract**

Recent gene expression profiling studies have identified five breast cancer subtypes, of which the basal-like subtype is the most aggressive. Basal-like breast cancer poses serious clinical challenges as there are currently no targeted therapies available to treat it. Although there is increasing evidence that these tumors possess specific sensitivity to cisplatin, its success is often compromised due to its dose-limiting nephrotoxicity and the development of drug resistance. To overcome this limitation, our goal was to maximize the benefits associated with cisplatin therapy through drug combination strategies. Using a validated kinase inhibitor library, we showed that inhibition of the mTOR, TGF $\beta$ RI, NF $\kappa$ B, PI3K/AKT, and MAPK pathways sensitized basal-like MDA-MB-468 cells to cisplatin treatment. Further analysis demonstrated that the combination of the mTOR inhibitor rapamycin and cisplatin generated significant drug synergism in basal-like MDA-MB-468, MDA-MB-231, and HCC1937 cells but not in luminal-like T47D or MCF-7 cells. We further showed that the synergistic effect of rapamycin plus cisplatin on basal-like breast cancer cells was mediated through the induction of p73. Depletion of endogenous p73 in basal-like cells abolished these synergistic effects. In conclusion, combination therapy with mTOR inhibitors and cisplatin may be a useful therapeutic strategy in the treatment of basal-like breast cancers.

**Key words:** Rapamycin – p73 – Cisplatin – Basal-like breast cancer – Synergism

Wong RSY. Extrinsic factors involved in the differentiation of stem cells into insulin-producing cells: an overview. *Exp Diabetes Res (US)* 2011; doi:10.1155/2011/406182.

## **Extrinsic factors involved in the differentiation of stem cells into insulin-producing cells: an overview**

Rebecca S. Y. Wong

Division of Human Biology, School of Medical and Health Sciences, International Medical University, No. 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Diabetes mellitus is a chronic disease with many debilitating complications. Treatment of diabetes mellitus mainly revolves around conventional oral hypoglycaemic agents and insulin replacement therapy. Recently, scientists have turned their attention to the generation of insulin-producing cells (IPCs) from stem cells of various sources. To date, many types of stem cells of human and animal origins have been successfully turned into IPCs *in vitro* and have been shown to exert glucose-lowering effect *in vivo*. However, scientists are still faced with the challenge of producing a sufficient number of IPCs that can in turn produce sufficient insulin for clinical use. A careful choice of stem cells, methods, and extrinsic factors for induction may all be contributing factors to successful production of functional beta-islet like IPCs. It is also important that the mechanism of differentiation and mechanism by which IPCs correct hyperglycaemia are carefully studied before they are used in human subjects.

Wong RSY. Mesenchymal stem cells: angels or demons? J of Biomed and Biotech (US) 2011; doi:10.1155/2011/459510.

## **Mesenchymal stem cells: angels or demons?**

Rebecca S. Y.Wong

Division of Human Biology, School of Medical and Health Sciences, International Medical University, No. 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

### **Abstract**

Mesenchymal stem cells (MSCs) have been used in cell-based therapy in various disease conditions such as graft-versus-host and heart diseases, osteogenesis imperfecta, and spinal cord injuries, and the results have been encouraging. However, as MSC therapy gains popularity among practitioners and researchers, there have been reports on the adverse effects of MSCs especially in the context of tumour modulation and malignant transformation. These cells have been found to enhance tumour growth and metastasis in some studies and have been related to anticancer-drug resistance in other instances. In addition, various studies have also reported spontaneous malignant transformation of MSCs. The mechanism of the modulatory behaviour and the tumorigenic potential of MSCs, warrant urgent exploration, and the use of MSCs in patients with cancer awaits further evaluation. However, if MSCs truly play a role in tumour modulation, they can also be potential targets of cancer treatment.

## **Apoptosis in cancer: from pathogenesis to treatment**

Rebecca SY Wong

Division of Human Biology, School of Medical and Health Sciences, International Medical University. No. 126, Jalan Jalil Perkasa 19, Bukit Jalil 57000 Kuala Lumpur, Malaysia

### **Abstract**

Apoptosis is an ordered and orchestrated cellular process that occurs in physiological and pathological conditions. It is also one of the most studied topics among cell biologists. An understanding of the underlying mechanism of apoptosis is important as it plays a pivotal role in the pathogenesis of many diseases. In some, the problem is due to too much apoptosis, such as in the case of degenerative diseases while in others, too little apoptosis is the culprit. Cancer is one of the scenarios where too little apoptosis occurs, resulting in malignant cells that will not die. The mechanism of apoptosis is complex and involves many pathways. Defects can occur at any point along these pathways, leading to malignant transformation of the affected cells, tumour metastasis and resistance to anticancer drugs. Despite being the cause of problem, apoptosis plays an important role in the treatment of cancer as it is a popular target of many treatment strategies. The abundance of literature suggests that targeting apoptosis in cancer is feasible. However, many troubling questions arise with the use of new drugs or treatment strategies that are designed to enhance apoptosis and critical tests must be passed before they can be used safely in human subjects.

**Key words:** Apoptosis, defective apoptotic pathways, carcinogenesis, treatment target



Wu JC, Hseu YC, Tsai JS, Chen LC, Chye SM, Chen CH, Ching Chen S. Fenthion and terbufos induce DNA damage, the expression of tumor-related genes, and apoptosis in HEPG2 cells. *Environmental Mol Mutagenesis* 2011; 52: 529-537

## **Fenthion and terbufos induce DNA damage, the expression of tumor-related genes, and apoptosis in HEPG2 cells**

Wu JC<sup>1</sup>, Hseu YC<sup>2</sup>, Tsai JS<sup>3</sup>, Chen LC<sup>4</sup>, Chye SM<sup>5</sup>, Chen CH<sup>6,7</sup>, Ching Chen S<sup>8</sup>

<sup>1</sup>Department of Applied Chemistry, Fooyin University, Kaohsiung, Taiwan, Republic of China

<sup>2</sup>Department of Cosmeceutics, China Medical University, Taichung, Taiwan, Republic of China

<sup>3</sup>Department of Biotechnology, National Kaohsiung Normal University, Kaohsiung, Taiwan, Republic of China

<sup>4</sup>Department of Medical Nutrition, I-Shou University, Kaohsiung, Taiwan, Republic of China

<sup>5</sup>Department of Human Biology, School of Medicine, International Medical University, Bukit Jalil, Kuala Lumpur 57000, Malaysia

<sup>6</sup>School of Pharmacy, Taipei Medical University, Taipei 110-31, Taiwan

<sup>7</sup>Department of Medical Technology, Yuanpei Institute of Science and Technology, Hsin-Chu County, Taiwan, Republic of China

<sup>8</sup>Department of Life Science, National Central University, Chung-Li City, Taoyan County, Taiwan, Republic of China

### **Abstract**

This study investigates the effects of fenthion and terbufos, two organophosphorous pesticides, on DNA damage, tumor-related gene expression, and apoptosis in HepG2 cells. We found that exposure to concentrations ranging from 50 to 200  $\mu$ M of fenthion and terbufos for 2 hr caused significant death in HepG2 cells. Both compounds induced DNA damage in a concentration-dependent manner as measured using the alkaline comet assay. Tumor-related genes (*jun*, *myc*, and *fos*) and apoptosis-related genes (*socs3*, *tnfaip3*, *ppp1r15a*, and *nr4a1*) were up-regulated by both compounds. Finally, both compounds induced apoptosis. The results demonstrate that both terbufos and fenthion induce DNA damage and should be considered potentially hazardous to humans.

**Key words:** fenthion; terbufos; comet assay; apoptosis; tumor-related genes

Yoshinobu Shoji. Cluster headache following dental treatment: a case report.  
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## **Cluster headache following dental treatment: a case report**

Yoshinobu Shoji

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

### **Abstract**

Cluster headache is a neurovascular disorder characterized by attacks of severe and strictly unilateral pain presenting in and around the orbit and temporal area. Attacks occur in series lasting for weeks or months separated by remission periods. An individual attack lasts 15-180 min with a frequency of once every other day to as often as 8 times per day. Ipsilateral radiation of the headache to orofacial regions, including the teeth, is not unusual. The area of involvement may obscure the diagnosis and lead to irreversible and unnecessary dental treatment. A case in which cluster attacks occurred immediately after a dental procedure is described.

**Key words:** cluster headache; orofacial pain; sphenopalatine ganglion

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## Acute atrial arrhythmogenicity and altered Ca<sup>2+</sup> homeostasis in murine *RyR2-P2328S* hearts

Yanmin Zhang<sup>1,2</sup>, James A. Fraser<sup>1</sup>, Kamalan Jeevaratnam<sup>1,3</sup>, Xiaojin Hao<sup>4</sup>, Sandeep S. Hothi<sup>1</sup>, Andrew A. Grace<sup>5</sup>, Ming Lei<sup>4</sup>, and Christopher L.-H. Huang<sup>1</sup>

<sup>1</sup>Physiological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 3EG, UK

<sup>2</sup>Department of Paediatrics, First Affiliated Hospital, Xi'an Jiaotong University, Xi'an 710061, Peoples' Republic of China

<sup>3</sup>Department of Human Biology, Faculty of Medicine, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

<sup>4</sup>Cardiovascular Group, School of Clinical and Laboratory Sciences, University of Manchester, Grafton Street, Manchester M13 9NT, UK

<sup>5</sup>Cardiovascular Biology Group, Department of Biochemistry, University of Cambridge, Tennis Court Road, Cambridge CB2 1QW, UK

### Abstract

Aim:

The experiments explored for atrial arrhythmogenesis and its possible physiological background in recently developed hetero- (*RyR2<sup>+S</sup>*) and homozygotic (*RyR2<sup>S/S</sup>*) *RyR2-P2328S* murine models for catecholaminergic polymorphic ventricular tachycardia for the first time. They complement previous clinical and experimental reports describing increased ventricular arrhythmic tendencies associated with physical activity, stress, or catecholamine infusion, potentially leading to ventricular tachycardia and fibrillation.

Methods and Results:

Atrial arrhythmogenic properties were compared at the whole animal, Langendorff-perfused heart and single isolated atrial myocyte levels using electrophysiological and confocal fluorescence microscopy methods. This demonstrated that: (1) ECG parameters in *intact anaesthetised* wild-type (WT), *RyR2<sup>+S</sup>* and *RyR2<sup>S/S</sup>* hearts were statistically indistinguishable both before and following addition of isoproterenol apart from increases in heart rates. (2) Bipolar electrogram and monophasic action potential recordings showed significantly higher incidences of arrhythmogenesis in isolated perfused *RyR2<sup>S/S</sup>*, but not *RyR2<sup>+S</sup>*, relative to WT hearts during either regular pacing and programmed electrical stimulation. Addition of isoproterenol increased such incidences in all three groups. (3) However, there were no accompanying differences in cardiac anatomy, action potential durations at 90% repolarization and refractory periods. (4) In contrast, episodes of diastolic Ca<sup>2+</sup> release were observed under confocal microscopy in isolated fluo-3-loaded *RyR2<sup>S/S</sup>*, but not *RyR2<sup>+S</sup>* or WT, atrial myocytes. Introduction of isoproterenol resulted in significant diastolic Ca<sup>2+</sup> release in all three groups.

Conclusions:

These findings establish acute atrial arrhythmogenic properties in *RyR2-P2328S* hearts, and correlated these with altered Ca<sup>2+</sup> homeostasis in an absence of repolarization abnormalities for the first time.

**Key words:** RyR2, Atrial arrhythmia, Calcium, Electrocardiography, Monophasic action potentials