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Abdul Hafid SR, Radhakrishnan AK, Nesaretnam K. Tocotrienols are good adjuvants for developing cancer vaccines. *BMC Cancer* 2010; 10:5

Tocotrienols are good adjuvants for developing cancer vaccines

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Abstract

Background:

Dendritic cells (DCs) have the potential for cancer immunotherapy due to their ability to process and present antigens to T-cells and also in stimulating immune responses. However, DC-based vaccines have only exhibited minimal effectiveness against established tumours in mice and humans. The use of appropriate adjuvant enhances the efficacy of DC based cancer vaccines in treating tumours.

Methods:

In this study we have used tocotrienol-rich fraction (TRF), a non-toxic natural compound, as an adjuvant to enhance the effectiveness of DC vaccines in treating mouse mammary cancers. In the mouse model, six-week-old female BALB/c mice were injected subcutaneously with DC and supplemented with oral TRF daily (DC+TRF) and DC pulsed with tumour lysate from 4T1 cells (DC+TL). Experimental mice were also injected with DC pulsed with tumour lysate and supplemented daily with oral TRF (DC+TL+TRF) while two groups of animal which were supplemented daily with carrier oil (control) and with TRF (TRF). After three times vaccination, mice were inoculated with 4T1 cells in the mammary breast pad to induce tumour.

Results:

Our study showed that TRF in combination with DC pulsed with tumour lysate (DC+TL+TRF) injected subcutaneously significantly inhibited the growth of 4T1 mammary tumour cells as compared to control group. Analysis of cytokines production from murine splenocytes showed significant increased productions of IFN-gamma and IL-12 in experimental mice (DC+TL+TRF) compared to control, mice injected with DC without TRF, mice injected with DC pulsed with tumour lysate and mice supplemented with TRF alone. Higher numbers of cytotoxic T cells (CD8) and natural killer cells (NK) were observed in the peripheral blood of TRF adjuvanted DC pulsed tumour lysate mice.

Conclusion:

Our study show that TRF has the potential to be an adjuvant to augment DC based immunotherapy.

Agarwal R, Puneet A. Future target molecules in antiglaucoma therapy: TGF-beta may have a role to play. *Ophthalmic Res* 2010; 43(1):1-10

Future target molecules in antiglaucoma therapy: TGF- β may have a role to play

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Abstract

Glaucoma, a leading cause of irreversible blindness, is often associated with increased resistance to aqueous outflow in trabecular tissue. Increased outflow resistance has been attributed to increased extracellular matrix (ECM) deposition in trabecular tissue. A critical balance between the synthesis and breakdown of the components of extracellular tissue is important in keeping the intraocular pressure within the normal range. Multiple mechanisms have been shown to affect ECM turnover in trabecular tissue. In this review, we examine the related literature to understand the role of TGF- β in ECM turnover, in the development and progression of glaucoma, and in possible therapeutic strategies that can be devised by targeting the TGF- β signaling pathways.

Key words: Glaucoma, Extracellular matrix turnover, Transforming growth factor- β

Ali Anbori, Sirajoon Noor Ghani, Yadav H, Aqil Mohammad Daher, TinTin Su. Patient satisfaction and loyalty to the private hospital in Sana'a, Yemen. *International J Quality in Health Care Advance Access*, 2010; 1-6

Patient satisfaction and loyalty to the private hospitals in Sana'a, Yemen

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Abstract

Objective:

To evaluate patients' satisfaction and loyalty to private hospitals and to identify factors influencing patient loyalty.

Design:

A cross-sectional, population-based study was conducted between May and September of 2005.

Setting:

Sana'a, the capital city of the Republic of Yemen.

Participants:

Eight hundred and nineteen respondents who were admitted for at least 1 day in a private hospital within last 6 months from the date of interview.

Main Outcome Measures:

The scores on the modified SERVQUAL market research instrument including six domains (tangibility, reliability, responsiveness, assurance, empathy and cost) that identify perceptions of service quality. In addition, the respondents were asked whether or not they would return to the same facility when they need future medical care (loyalty).

Results:

Loyalty was higher among females [odds ratio (OR) = 1.44; $P < 0.05$], among those reporting higher reliability scores (OR = 1.24; $P < 0.01$), higher assurance scores (OR = 1.2; $P < 0.01$) and higher empathy scores (OR = 1.13; $P < 0.05$) and also among those reporting higher cost (OR = 1.15; $P < 0.05$). No significant association was found between patient loyalty and, tangibility and responsiveness score.

Conclusions:

Improvements are required to achieve high-quality healthcare services in the private hospitals in Yemen and increase loyalty among patients. Findings from this study could inform private sector healthcare development in low- and middle-income countries.

Key words: user's perception of quality, SERVQUAL, potential patients' Loyalty Private Hospital, Yemen

Amirthalingam SD, Ponnudurai G, Chen YS. Pre and post PBL meetings in ensuring the quality of facilitators in Problem-based learning in the IMU. *IeJSME* 2010; 4(2): 47-53

Pre and post PBL meetings in ensuring the quality of facilitators in Problem-based Learning

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Abstract

Background:

Problem based learning (PBL) is a student - centered curriculum delivery tool believed to promote active student participation. Though the PBL is student - centered, the facilitator plays an important role in maintaining the integrity of this system by providing balance in group interaction and discussion of learning issues. In International Medical University (IMU) one of the strategies to ensure the quality of the facilitators was the pre and post PBL meetings. This study aimed to gauge its usefulness in ensuring the quality of PBL facilitation.

Method:

The questionnaire to study the perceptions of PBL facilitators on the pre and post PBL meetings included close ended questions on pre and post PBL meeting's attendance and their scored opinion in improving PBL facilitation skills, open ended questions inviting suggestions to improve these meetings and PBL facilitation in IMU as a whole and self-evaluation as an effective PBL facilitator using a six point Likert scale to a list of statements.

Results:

84.2% of facilitators agreed the meetings were beneficial. Self-evaluation of their facilitator effectiveness showed on average ratings of seven out of ten indicating strong confidence in facilitating skills. Suggestions ensuring facilitator quality included content expert briefing in pre PBL meetings and student appraisals of facilitators given weightage in staff appraisal.

Conclusion:

Pre and post PBL meetings enhanced facilitator comfort with the triggers, adding to their confidence and provided a venue to obtain feedback on the triggers.

Key words: Problem based learning, PBL facilitator, Pre and post PBL meeting

Boo NY, Chia GJQ, Wong LC, Chew RM, Chong W, Loo RCN. The prevalence of obesity among clinical students in a Malaysian medical school. *Singapore Med J*, 2010; 51: 126-132

The prevalence of obesity among clinical students in a Malaysian medical school

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Abstract

Introduction:

This study aimed to determine the prevalence of obesity among medical students and its relationship with their dietary intake and physical activities.

Methods:

This observational study was carried out on 240 medical students during the clinical phase of their medical course in a private medical school. Their body weight and height were measured, and a standardised questionnaire was used to collect information on their physical activities and dietary intake.

Results:

The median body weight of the participants was 59.0 kg (interquartile range: 51.3-66.8), the mean body height was 166.1 cm (standard deviation [SD] 8.5 cm), and the mean body mass index (BMI) was 21.8 kg/m² (SD 3.4 kg/m²). Based on the World Health Organization BMI cut-offs for the Asian population, 30.1 percent (n is equal to 72) of the students were overweight or obese, with a BMI that was equal to or greater than 23.0 kg/m². Logistic regression analysis showed that, after controlling for various potential confounders, the only significant risk factors associated with overweight/obesity among these students were: male gender (adjusted odds ratio [OR] 2.1; 95 percent confidence intervals [CI] of 1.1 and 4.1; p is equal to 0.03), Malay ethnic group (adjusted OR 2.4; 95 percent CI 1.0 and 5.7; p is equal to 0.04), Indian ethnic group (adjusted OR 3.6; 95 percent CI 1.5 and 8.9; p is equal to 0.005), and the number of soft drinks consumed per week (adjusted OR 1.3; 95 percent CI 1.0 and 1.5; p is equal to 0.02). Skipping breakfast, the frequency of physical exercise per week, the number of hours of sleep per day, and eating noodles or roti canai (a type of Malaysian pancake) for breakfast were not significant risk factors.

Conclusion:

Obesity remains a common problem among medical students in their clinical years.

Key words: medical students, obesity, risk factors, soft drinks

Chravarthi S, Ang Seng Long, Beh Hannien, Thanikachalam PM, Palayan K, Arni Talib. The expression of p53 as a reliable immunohistochemical marker for clinicopathological correlation of gastric adenocarcinomas. Res J Med Sci 2010; 4(1):15-19

The expression of p53 as a reliable immunohistochemical marker for clinicopathological correlation of gastric adenocarcinomas

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Abstract

For evaluation of the prognostic relevance of p53 expression in gastric cancer, the immunohistochemical tissue status of 66 primary gastric cancer patients was investigated for p53 expression and the association between p53 tissue status and clinicopathological parameters was analyzed. p53 immunoreactivity was detected in the nuclei of cancer cells in 42 cases (63.7%). The nuclear p53 immunoreaction was closely associated with tumour location, lymph node metastasis and curability. Tumours with positive p53 stain reactions frequently metastasized to lymph nodes (metastatic rate: 88.3%) in contrast to tumors with negative p53 stain reactivity (59.4%, $p < 0.005$). Immunohistochemical analysis of primary gastric cancer appears to be an accurate and simple method of screening for p53 expression. In combination with common prognostic parameters, determination of p53 tissue status might help to detect prognostically unfavourable subgroups of gastric cancer patients.

Key words: p53, immunohistochemistry, gastric adenocarcinoma, tumours, nuclei, lymph node

Chakravarthi S, Choo Zhen Wei, Nagaraja HS, Wong SF, Mak JW, Thanikachalam PM, Radhakrishnan AK, Tay A. Immunosuppressive effect of disseminated breast carcinoma on severity of hepatic candidiasis. Res J Immunol 2010; 3 (1):1-11

Immunosuppressive effect of disseminated breast carcinoma on severity of hepatic candidiasis

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Abstract

This study aims to demonstrate this relationship by observing the histopathological changes of the livers 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, 5) having co-existence of candidiasis and breast cancer at 2 different doses of candidiasis, respectively. 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, hepatic candidiasis was significantly increased in mice with breast cancer.

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

Chakravarthi S, Nagaraja HS. Implementation of PBL curriculum involving multiple disciplines in undergraduate medical education programme. InternatEduc Studies 2010, 3 (1): 165-169

Implementation of PBL curriculum involving multiple disciplines in undergraduate medical education programme

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Abstract

This article describes how a multidisciplinary problem-based learning (PBL) curriculum was established at the International Medical University in Malaysia for preclinical education in a 5-semester phase 1 programme. Based on positive feedback from a modified PBL program implemented in one discipline, a multidisciplinary PBL curriculum was established. PBL training for facilitators and students, development of resource materials, curriculum design, and case writing were done in a manner that is consistent with the characteristics and learning style preferences of undergraduate medical students. About 80 percent of the lectures were kept in the new PBL program. The multidisciplinary PBL curriculum has been successful in helping undergraduate medical students mentally construct an understanding of the interrelationship between medical knowledge and basic science concepts. The experience at IMU indicates that there are clear benefits for students in the PBL format. A benefit to faculty is that PBL tutorial facilitators were partly liberated from their traditional roles and developed additional skills for facilitating. However, conflict arises when PBL-trained students encounter the traditional exam-centered education system.

Key words: PBL, Multidisciplinary, Undergraduate medical education, Preclinical education

Chakravarthi S, Nagaraja HS, Chong Fu Wen, Nagaraja L, Thanikachalam PM. c-myc regulation and apoptosis in assessing the beneficial effect of Apigenin in cyclosporine induced nephrotoxicity. Res J Pharmacol 2010; 4(1):15-20

c-myc regulation and apoptosis in assessing the beneficial effect of apigenin in cyclosporine induced nephrotoxicity

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Abstract

Cyclosporine-A (CsA) is an immunosuppressant prescribed in organ transplants to prevent rejection. It is a calcineurin inhibitor produced by the fungi *Trichoderma polysporum* and *Cylindrocarpon lucidum*, its adverse effect of renal dysfunction has limited its use in a clinical setting. Apigenin (4', 5', 7'-Trihydroxyflavone), a herbal extract, with anti-inflammatory and anti-tumour properties has shown to reverse this adverse effect. This research was conducted to study the effects of apigenin on reversal of Cyclosporine-A induced damage and this was assessed by immunohistochemical estimation of expression of c-myc and estimation of apoptosis in histopathological sections. Rats were divided into groups and administered with CsA with Apigenin in different doses. The kidneys from the rats were harvested, weighed and observed for gross pathology changes. The renal tissue was processed and stained for haematoxylin and eosin staining, to assess the apoptotic index and stained by immunohistochemistry, for the analysis of the apoptosis regulatory gene c-myc. The apoptotic index was then compared with the c-myc intensity to observe for any correlation. It was found that there was a high apoptotic index and c-myc intensity in the Cyclosporine-A group. Apigenin managed to reduce the values of both parameters. The apoptotic index correlated with the c-myc intensity, especially in the glomeruli. The study proved that Cyclosporine-A enhanced the expression of c-myc in the rat kidney, which signifies accelerated apoptosis. Therefore, c-myc and apoptotic index may be used to assess apigenin and its effect on Cyclosporine-A induced renal damage.

Chakravarthi S, Thanikachalam PM, Low Wee Yang , Linda TjoaHusin , Nadaraja L. Role of immunohistochemistry and apoptosis as investigative tools in assessing prognosis in prostate tumours. *Experimental & Therapeutic Medicine* 2010, 1(2): 391-393

Role of immunohistochemistry and apoptosis as investigative tools in assessing the prognosis of patients with prostate tumours

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Abstract

Apoptosis is a form of programmed cell death necessary for the regulation of the size of organs in adult life. Disruption of apoptotic pathways has been suggested as an important regulatory mechanism in prostatic tumours. The aim of this study was to examine the expression of apoptosis-regulating genes bcl-2 and p53 using immunohistochemistry, and the Gleason score in core needle biopsy specimens of prostate adenocarcinoma. We studied bcl-2 and p53 expression in 30 cases of low-, 30 cases of intermediate- and 20 cases of high-grade prostate adenocarcinoma. Overexpression of bcl-2 and p53 were noted in 54 and 61 of 80 patients (67.5 and 76.25%), respectively. The statistical analysis of the present data suggested that there is significant relation between p53 and bcl-2 expression, and Gleason score in prostate cancer. Thus, immunohistochemistry is a useful investigative parameter in assessing apoptosis to analyse the prognosis of prostatic tumours.

Key words: prostate, adenocarcinoma, apoptosis, immunohistochemistry

Chakravarthi S, Choo Zhen Wei, Nagaraja HS. Susceptibility to renal candidiasis due to immunosuppression induced by breast cancer cell lines. SciWld J 2010, 5 (1): 5-10

Susceptibility to renal candidiasis due to immunosuppression induced by breast cancer cell lines

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Abstract

Candidiasis is a fungal infection which is prone to occur in people with immunosuppression due to debilitating diseases and nosocomial causes. 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 renal candidiasis with breast cancer. This study aims to demonstrate the relationship between renal candidiasis and breast cancer by observing the histopathological changes of the kidneys harvested from female Balb/c mice experimentally induced with breast cancer and inoculated with candida. The mice were randomly assigned to 5 different groups (n=12). Group 1 was injected with phosphate buffer solution (PBS), Group 2 with candida, Group 3 with breast cancer and Groups 4 and 5 having co-existence of candidiasis and breast cancer at 2 different doses of candidiasis respectively. Inoculation of mice with candidiasis spores was done by intravenous injection of *Candida albicans* via the tail vein. Induction of mice with breast cancer was via injection of 4T1 cancer cells at the right axillary mammary fatpad. Stained slides of Haematoxylin and Eosin (H&E), Periodic Acidic Schiff (PAS) and Gomori Methenamine Silver (GMS) were prepared for histopathology analysis. Grading of primary tumour and identification of metastatic deposits were carried out. Scoring of inflammation and congestion in the kidney was also carried out. Results revealed that group 4 exhibited a highly 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. It is concluded that renal candidiasis was significantly increased in mice with breast cancer.

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

Chakravarthi S, Choo Zhen Wei, Nagaraja HS, Wong SF, Mak JW, Shalini Sree Kumar. A histopathological study of severity of cerebral candidiasis as a result of immunosuppression caused by breast carcinoma. *Internat J Mol MedAdvSci* 2010, 6 (1):1-7

A histopathological study of severity of cerebral candidiasis as a result of immunosuppression caused by breast carcinoma

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Abstract

Candidiasis is a fungal infection which is prone to occur in people with immunosuppression due to debilitating diseases and nosocomial causes. 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 cerebral 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 brain 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 brains 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 brains 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), especially in the cerebral areas. The median severity of candidiasis was also increased in group 4 as compared to group 2. In conclusion, based on the above evidences, cerebral candidiasis was significantly increased in mice with breast cancer.

Chakravarthi S, Nagaraja HS. A comprehensive review of the occurrence and management of systemic candidiasis as an opportunistic infection. *Microbiol J* 2010; 1 (2):1-5

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

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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.

Chakravarthi S, Nagaraja HS, Judson JP. An exploration of the strategic challenges of Problem-based Learning (PBL) in medical education environment: a paradigm shift from traditional lectures. Indian J SciTechnol 2010; 3(2): 216-221

An exploration of the strategic challenges of Problem-based Learning (PBL) in medical education environment: a paradigm shift from traditional lectures

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Abstract

This study was done to explore the challenges of problem-based learning (PBL) in medical education and to propose a framework with implications for practice and learning. The paper uses a total of 24 undergraduate medical students divided into 3 groups who participated in the focus group discussions. A quantitative instrument was used as triangulation to gather data on 18 statements through Likert scale ratings. In addition, semi-structured interviews were conducted with 6 medical PBL facilitators. Quotes from the participants are used to support the key themes and issues that have emerged from the data. Quantitative data are used to support certain important issues. The successful development of PBL will depend on re-establishing the strategic direction of PBL within a certain context, evaluating the social and learning structures associated with power distribution, and providing non-routine rigorous educational systems to enhance learning.

Key words: Problem Based Learning (PBL); medical education; focus group discussion; Malaysia.

Chakravarthi S, Nagaraja HS, Judson JP. Enhancing the efficacy of lecturers in educating student cohorts consisting of culturally diverse groups in a medical university. *InternatEduStudies* 2010; 3(2):161-166

Enhancing the efficacy of lecturers in educating student cohorts consisting of culturally diverse groups in a medical university

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Abstract

Lecturers exert a potent influence over the achievement of all students, low-income culturally diverse students in particular. Although recent research has confirmed that lecturer involvement is critical for promoting academic engagement of low-income and ethnically diverse students in America and other countries, other literature suggests that lecturers have lower expectations for and fewer interactions with these students. These findings have prompted calls for promoting lecturers self-efficacy for working with students from diverse backgrounds, especially in a country like Malaysia, where there is a coexistence of students of various ethnic diverse groups, such as Chinese, Malays and Indians. The purposes of this article are (a) to summarize briefly the literature that examines the effect of lecturers efficacy on academic and behavioral outcomes of students, especially culturally diverse students; (b) to disseminate the findings of a lecturer-training program designed to promote lecturer efficacy in relation to culturally diverse students; and (c) to provide lecturers, administrators, and lecturer trainers with methods to increase lecturer efficacy when working with culturally diverse learners.

Key words: Lecturer efficacy, Lecturer training, Culturally diverse, Ethnic variation

Chakravarthi S, Priya Vijayan. Analysis of the psychological impact of Problem-based Learning (PBL) towards self-directed learning among students in undergraduate medical education. *Internat J Psychol Studies* 2010; 3(1): 38-43

Analysis of the psychological impact of Problem-based Learning (PBL) towards self-directed learning among students in undergraduate medical education

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Abstract

The psychological impact of a learning tool towards self directed learning is an important outcome of medical education. Although problem based learning is believed to facilitate self-directed learning, previous studies have reported conflicting results. This longitudinal survey explored the perceived psychological changes in self directed learning for two and a half years in an undergraduate phase 1 medical education program with an integrated problem-based learning curriculum. 170 of 200 students (response rate, 85%) completed the Self-Directed Learning Readiness Scale at five different time points: at the beginning of each semester year and at program completion. Scores were significantly lower during the first semester compared with other years, and fifth semester scores were significantly higher than in previous years. Scores on the three subscales (i.e., self-management, desire for learning, and self-control) increased significantly during the five semesters years of the programme. These findings support self-directed learning as a maturational process seen psychologically by the students. Implications for medical faculty and curriculum development are discussed.

Key words: Self directed skills, Problem based learning, Medical curriculum

Chee WSS, Chong PN, Chuah KA, Karupaiah T, Mustafa N, Seri Suniza S, Chinna K, Offord-Cavin E. Calcium intake, vitamin D and bone health status of post-menopausal Chinese women in Kuala Lumpur. *Malay J Nutrition* 2010; 16: 233-242

Calcium intake, vitamin D and bone health status of post-menopausal Chinese women in Kuala Lumpur

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Abstract

Bone health status was investigated in 178 free-living Chinese post-menopausal women in Kuala Lumpur. Body mass index (BMI), body composition (using whole body DXA), calcium intake and serum 25-OH vitamin D status were measured along with biochemical markers of bone turnover, that is, pro-collagen Type 1 N-terminal peptide (P1NP), osteocalcin (OC) and C-telopeptide β cross link of Type 1 collagen (CTX- β). Bone mineral density (BMD) was measured using DXA (Hologic, USA) at the lumbar spine, femoral neck and total hip. Results showed that osteopenia was present in 50% of the subjects at the spine and 57.9% at the femoral neck. Osteoporosis was diagnosed in 10% of the subjects at both the femoral neck and spine. A total of 29.3% of the subjects had high levels of CTX- β . Mean serum level of 25-OH vitamin D was 60.4+15.6 nmol/L and 50.6% of the subjects had hypovitaminosis D (defined as <50 nmol/l). Mean total calcium intake of the subjects was 497 + 233 mg, of which only 14% met the RNI for calcium with the additional intake of calcium supplements. Body fat was also significantly correlated ($r=0.181$, $p<0.05$) with BMD at the spine but not BMD at the femoral neck. Lean body mass was positively correlated with BMD at the spine ($r=0.289$, $p<0.001$) and femoral neck ($r=0.295$, $p<0.001$). CTX- β was negatively correlated with BMD at the spine ($r= -0.235$, $p<0.001$), whereas P1NP ($r=-0.215$, $p<0.001$) and osteocalcin ($r=-0.265$, $p<0.001$) were both negatively correlated with BMD at the femoral neck. Generally, the study found that women with osteopenia had higher levels of bone turnover markers, less lean body mass and lower calcium intake than women with normal BMD. In conclusion, this study demonstrated that the majority of free living Chinese post-menopausal women in Kuala Lumpur have low calcium intake, low 25-OH vitamin D status and low bone mass and elevated biochemical markers of bone turnover.

Key words: bone health status, calcium intake, Chinese women, Kuala Lumpur, post-menopausal woman, Vitamin D

Chen SC, Chen CH, Tiong YL, Zhong PY, Lin YS, Chye SM. Para-phenylenediamine induced by DNA damage and apoptosis through oxidative stress and enhanced Caspase-8 and -9 activities in Mardin-Darby canine kidney cells. *Toxicology In Vitro* 2010; 24: 1197–1202

Para-phenylenediamine induced DNA damage and apoptosis through oxidative stress and enhanced caspase-8 and -9 activities in Mardin–Darby canine kidney cells

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Abstract

Para-phenylenediamine (p-PD), a suspected carcinogen, is a component of permanent hair dyes. In this study we examined the mechanism of cytotoxicity and genotoxicity in Mardin–Darby canine kidney cells (MDCK)-treated with p-PD. Our results showed that p-PD decreased cell viability in a dose- and time-dependent manner. In addition, p-PD induced DNA damage was confirmed by the comet and TUNEL assays. Pre-treatment of MDCK cells with antioxidants vitamin C or E significantly inhibited p-PD induced cytotoxicity and reactive oxygen species (ROS) generation. Furthermore, p-PD induced apoptosis through activated initiator caspase-8 and -9, and effector caspase-3/7. Based on these results, we suggested that p-PD induce apoptosis which was mediated with caspase-8, caspase-9 and caspase-3/7 activation via the involvement of ROS.

Key words: para-Phenylenediamine; DNA damage; Reactive oxygen species; Caspase; Mardin–Darby canine kidney cells

Chew MMS, Gan SY, Khoo ASB, Tan EL. Interleukins, laminin and Epstein-Barr virus latent membrane protein 1 (EBV LMP1) promote metastatic phenotype in nasopharyngeal carcinoma. *BMC Cancer* 2010, 10:574-583

Interleukins, laminin and Epstein-Barr virus latent membrane protein 1 (EBV LMP1) promote metastatic phenotype in nasopharyngeal carcinoma

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Abstract

Background:

Nasopharyngeal carcinoma (NPC) is a type of neoplasm that is highly prevalent in East Asia and Africa with Epstein-Barr virus (EBV), genetic, and dietary factors implicated as possible aetiological factors. Previous studies suggested the association of certain cytokines with the invasion and metastatic properties of NPC. The present study examined the roles of EBV latent membrane protein-1 (LMP1), interleukin-6 (IL-6), interleukin-10 (IL-10), transforming growth factor-beta 1 (TGF- β 1) and laminin in the regulation of matrix-metalloproteinases (MMPs) and vascular endothelial growth factor (VEGF) in NPC. The effects of these factors on bmi-1, an oncogene, and ngx6, a tumour suppressor gene, were also investigated.

Methods:

TW01 cells expressing LMP1 (TW01-LMP1) were established via transfection with the B95.8 EBV LMP1 gene. Both TW01 and TW01-LMP1 cells were treated with 100 pg/ml IL-6, 1000 pg/ml IL-10 and 100 pg/ml TGF- β 1, separately and also in combination at their respective concentration for 48 hours. Treated cells were subjected to laminin adherence assay. The cells were also cultured with and without laminin and assayed for MMP-3, MMP-9 and VEGF production using enzyme-linked immunosorbent assay (ELISA). The cellular apoptotic property was analysed using caspase-3 apoptosis assay. The expression of bmi-1 and ngx6 gene was investigated using real time reverse transcriptase polymerase chain reaction.

Results:

LMP1 was found to reduce the adherence of NPC cells towards laminin ($p < 0.05$) as compared to control. Treatment with IL-6 at 100 pg/ml enhanced the production of MMP-9 in both TW01 and TW01-LMP1 cells ($p < 0.05$). When cultured on laminin, the levels of MMP-3 and VEGF were significantly increased ($p < 0.05$) in TW01-LMP1 cells. TW01-LMP1 cells had relatively greater resistance to apoptosis as compared to TW01 cells ($p < 0.05$). Laminin, IL-6 and LMP1 were found to up-regulate the expression of bmi-1 and suppressed the expression of ngx6.

Conclusions:

We conclude that IL-6 reduced cell adherence towards laminin and increased MMP-9 production in NPC cells. Our data suggested that EBV LMP1 was able to confer resistance of apoptosis and increased MMP-9 production in NPC cells. When cultured on laminin, TW01 cells expressing the EBV LMP1 (TW0-LMP1) that were treated with IL-6 at 100 pg/ml displayed increased MMP-9 production, up-regulation of bmi-1 oncogene expression and down-regulation of ngx6 tumour suppressor gene expression. These findings implicate the roles of EBV LMP1, laminin and IL-6 in the promotion of invasion and metastasis in NPC.

Chin SP, Poey AC, Wong CY, Chang SK, Teh W, Mohr TJ, Cheong SK.
Cryopreserved mesenchymal stromal cell treatment is safe and feasible for
severe dilated ischemic cardiomyopathy. *Cytotherapy* 2010; 12: 31-37

Cryopreserved mesenchymal stromal cell treatment is safe and feasible for severe dilated ischemic cardiomyopathy

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Abstract

Background aims:

Bone marrow (BM) mesenchymal stromal cells (MSC) represent a novel therapy for severe heart failure with extensive myocardial scarring, especially when performed concurrently with conventional revascularization. However, stem cells are difficult to transport in culture media without risk of contamination, infection and reduced viability. We tested the feasibility and safety of off-site MSC culture and expansion with freeze-controlled cryopreservation and subsequent rapid thawing of cells immediately prior to implantation to treat severe dilated ischemic cardiomyopathy.

Methods:

We recruited three consecutive patients with end-stage ischemic heart failure with evidence of full-thickness myocardial scarring. MSC was isolated from 20 mL BM aspiration, expanded and cryopreserved using 10% dimethyl sulfoxide (DMSO). Cells were transported in a cryoshipper. Patients underwent concurrent coronary artery bypass graft (CABG) with intramyocardial MSC injection.

Results:

The cell viability after thawing exceeded 90% for all samples. The supernatant was free from bacterial and fungal growth. All patients underwent the procedure safely. There were no arrhythmias noted. There was significant improvement in cardiac function and volume, resolution of scarring and increased wall thickness for all patients on cardiac magnetic resonance imaging at 6 months compared with baseline. The magnitude of improvement was more than was expected with CABG alone. Patients remained well at 1 year.

Conclusions:

Rate-controlled freezing with 10% DMSO is a safe, feasible and practical method of cryopreserving MSC for cell storage and transportation without risk of contamination or cell death. Direct MSC injection may be beneficial as an adjunct to cardiac revascularization.

Key words; cryopreservation, heart failure, ischemic cardiomyopathy, mesenchymal stromal cell

Chiu CK, Chan CYW, Saw LB, Kwan MK. Scarf-related Hangman's fracture: A case report. Eur J Trauma EmergSurg 2010;2:180-182

Scarf-related Hangman's Fracture: a case report

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Abstract

Background:

Injury to the cervical spine due to a scarf-associated accident has not been reported in the literature. We present a case of a hangman's fracture in a 43-year-old woman that resulted from a scarf-related injury as a consequence of a motor vehicle accident.

Purpose:

To identify the mechanism of a scarf-related injury causing Hangman's fracture.

Case Report:

A 43-year-old woman was involved in a motor vehicle accident. She was wearing a scarf, which is a common clothing accessory for women in Malaysia. The scarf was violently torn off her head during the injury, causing a type I hangman's fracture. A halo vest for a total period of 3 months was applied.

Conclusion:

A scarf-related injury can cause an injury that resembles judicial hanging, leading to a traumatic spondylolisthesis of the axis. Careful evaluation of the cervical spine radiographs is crucial as occult fracture of the axis can be missed.

Key words: Axis - Hangman - Spondylolisthesis - Spine - Trauma management and education

How well do the malaria rapid diagnostic tests for detecting the asymptomatic carriers in the endemic countries?

C Naing

Abstract

Background:

Good-quality microscopy remains the standard laboratory method for the diagnosis of malaria. However, access to good-quality microscopic examination in endemic countries is limited, as resources are often lacking. The polymerase chain reaction (PCR) has also been established in the diagnosis of malaria. But, the expertise and the infrastructure required preclude its routine use in many health care settings. Rapid diagnostic tests for malaria (RDTs) detect parasite antigens in lysed blood from a finger-prick blood sample. This test is fast and easy to perform without special equipment or special skills. To date, systematic reviews of the accuracy of various RDTs in well controlled research settings using symptomatic patients in the endemic areas with either microscopy or PCR are available. People living in endemic areas often harbor Plasmodium parasites, but are asymptomatic. This asymptomatic state poses an important source of continuous malaria transmission within in the region. The accuracy of RDTs where people are primarily asymptomatic has not been assessed systematically.

Hence, a research question arises:

Whether RDTs are useful for detection of malaria in primarily asymptomatic people in the endemic countries?

Objectives:

To evaluate the accuracy of RDTs for detection of malaria in primarily asymptomatic people. Method: The method recommended in the Cochrane systematic review of diagnostic test accuracy is applied. The included studies identified for this meta-analysis compared the accuracy of RDTs with reference microscopy and/or PCR. The relevant study population is primarily asymptomatic people residing in endemic areas.

Results: The diagnostic accuracy, and the risk of bias of studies identified for this analysis will be presented. Conclusions: The use of RDTs for rapid mass surveillance in malaria control so as to reduce the transmission and consequently the magnitude of malaria will be justified.

Cho Naing. Do variations in specific aspects of study design produce discrepancies in the benefits of effects in Cochrane intervention review? Cochrane Database Syst Rev Suppl 1 2010 doi: 10.1002/14651858.CD000002.

Do variations in specific aspects of study design produce discrepancies in the benefits of effects in Cochrane intervention review?

C M-Naing

Abstract

Background:

Cochrane reviews address questions about the effects of health care. Certain specific aspects of the study design and its conduct are therefore to be considered when defining the eligibility criteria for the subjects of a Cochrane review. Both restrictive study design criteria and more liberal design criteria are found in the published Cochrane reviews.

The question therefore arises:

Do trials with inadequate randomization exaggerate the intervention effects. Objectives: To explore any discrepancies of intervention effects between Cochrane reviews that include studies with liberal criteria only, and the set of reviews that include studies with restrictive criteria only (after the studies with liberal criteria have been removed from the review).

Methods:

As an illustration, three reviews from the published Cochrane reviews of intervention studies were selected. The included studies in Cochrane review incorporating (i) non-randomized studies, and (ii) randomization without allocation concealment were assessed. Risk of bias and the benefits of intervention effects were comparing with the original results and the results after removal of the included studies with liberal criteria.

Results:

At the time of writing, this work is still ongoing. However, the differences were brought into focus. Full data will be presented at the colloquium.

Conclusion:

Excessively broad criteria can raise a concern about discrepancies in the resulting intervention effects. Ways to eliminate such discrepancies are suggested.

Cho Naing, Daw Khin Win. Do colloids improve mortality in comparison to crystalloids for fluid resuscitation? *Trans R Soc Trop Med Hyg* 2010; 104: 311-312

Do colloids in comparison to crystalloids for fluid resuscitation improve mortality?

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Abstract

Permanent neurological impairment or death arising from hospital-acquired hyponatremia in both children and adults is well documented. The choice of intravenous fluids for fluid resuscitation in critically ill patients is a top priority in evidence-based medicine. The question of whether colloids in comparison to crystalloids can improve mortality in such cases remains to be answered. Well powered, randomized clinical trials addressing the comparative efficacy of different types of intravenous fluids is a high priority as is the ethical justification for such trials. The understanding of the pathophysiological process serves important information on clinical practice.

Key words: Colloids, crystalloids, fluid resuscitation, hyponatremia, critically ill patients, severe acute infections

Cho Naing, Kyan Aung, Daw Khin Win, Mak JW. Efficacy and safety of chloroquine for treatment in patients with uncomplicated Plasmodium vivax infections in endemic countries. Trans Roy Soc Trop Med Hyg 2010; doi:10.1016/j.trstmh.2010.08.009

Efficacy and safety of chloroquine for treatment in patients with uncomplicated Plasmodium vivax infections in endemic countries

Cho Naing, Kyan Aung, Daw-Khin Win, Mak Joon Wah

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Abstract

Chloroquine (CQ) is a relatively inexpensive drug for treatment of malaria. If efficacy of CQ is still assumed, then it should be indicated in malaria treatment policies as the drug of choice for uncomplicated Plasmodium vivax malaria in endemic countries with resource constraints. The objective of this review is to summarize the existing evidence on the relative efficacy and safety of CQ in treating patients with uncomplicated *P. vivax* malaria in endemic countries. We searched online data bases (PUBMED, MEDLINE, EMBASE, The Cochrane Library) and the reference lists of the retrieved articles. Fifteen randomized controlled trials ($n = 6215$) assessing the relative efficacy and safety of CQ for treatment of uncomplicated *P. vivax* malaria were included. CQ monotherapy was compared to CQ plus primaquine (PQ), artemisinin/artemether, artemisinin based combination therapy, quinine, CQ plus tafenoquine, chlorguanil plus dapsone, azithromycin, or placebo. Treatment efficacy was not significantly different between the CQ monotherapy group and that of the CQ with PQ 14 day group at 28 day follow-up (55/711, 7.7% vs 35/712, 4.9%; $P = 0.16$). Evidence from the trials identified for this review draw a fairly clear conclusion about the relative efficacy and safety of CQ for treating uncomplicated *P. vivax* malaria infection. However, further research in this field with well powered, randomized, non-inferiority design, using the standardized protocol is needed.

Key words: Plasmodium vivax; treatment; randomized controlled trial; Chloroquine; meta-analysis

Cho Naing, Mohd Hakim, Daniel AngTze Yee et al. HIV/ AIDS related knowledge, attitudes and perceptions: a cross-sectional household survey. Southeast Asian J Trop Med Public Health 2010; 41: 952-960

HIV/ AIDS related knowledge, attitudes and perceptions: a cross-sectional household survey

Cho M Naing, Mohd Hakim, Daniel Ang Tze Yee, Koo Ray Mun, Tan Chang Yung, Kong Keat Jian and Sara Siew Suet Kuan

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Abstract.

This study aimed to assess knowledge of and attitudes toward HIV/AIDS among a community in a semi-urban setting in Malaysia, to determine factors affecting perceptions toward people living with HIV in the community, and to provide baseline information for planning preventive measures against HIV/AIDS. This cross-sectional study was conducted in August 2009. Two hundred sixty-two household members were interviewed with a semi-structured questionnaire. Most respondents (232; 88.5%) had heard of HIV/AIDS. Only a few respondents (6; 2.6%) could correctly answer all the questionnaire items. Misconceptions about disease transmission were seen among surveyed participants, such as the belief HIV/AIDS can be contracted from saliva (104; 44.8%), mosquito bites (95; 40.9%) or casual touch (86; 37.1%). A multivariate linear regression model showed better perceptions towards people living with HIV depend on an improved knowledge of HIV/AIDS transmission. Current data emphasize the need to scale up HIV/AIDS education incorporating the mode of disease transmission.

Key words: HIV/AIDS, knowledge, attitude, perception, Malaysia

Chong Huat Siar, Toh CG, George Romanos, Kok Han Ng. Subcutaneous reactions and degradation characteristics of collagenous and noncollagenous membranes in a macaque model. Clin Oral Implant Research 2010; doi: 10.1111/j.16000501.2010.01970.x.

Subcutaneous reactions and degradation characteristics of collagenous and noncollagenous membranes in a macaque model

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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-Gide[®] [BG], Tissue Fleece[®] [TFL] TissueFoil E forte[®] [TFO], Lycoll[®] [LC], Surgicoll[®] [SG] and Tutodent[®] [TU]) and two noncollagenous (Tabotamp[®] [TA] and Gelita-Tampon[®] [GT]) membranes (size 2 × 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 (TFL>LC>SG>TFO>BG>TU) compared with one of two noncollagenous (TA>GT) 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

Choo Zhen Wei, Chakravarthi S*, Wong SF, Nagaraja HS, Thanikachalam PM, Mak JW, Radhakrishnan AK, Tay A. A comparative histopathological study of systemic candidiasis in association with experimentally induced breast cancer. *Oncology Letters* 2010;1: 215-222

A comparative histopathological study of systemic candidiasis in association with experimentally induced breast cancer

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Abstract

Systemic candidiasis is a fungal infection which coupled with solid malignancies places patients at high risk of succumbing to the disease. Few studies have shown evidence of the relationship between systemic candidiasis and malignancy-induced immunosuppression disease especially in breast cancer. At present, animal studies that exclusively demonstrate this relationship have yet to be conducted. The exact causative mechanism of systemic candidiasis is currently under much speculation. This study therefore aimed to demonstrate this relationship by observing the histopathological changes of organs harvested from female Balb/c mice which were experimentally induced with breast cancer and inoculated with systemic candidiasis. The mice were randomly assigned to five different groups (n=12). The first group (group 1) was injected with phosphate buffer solution, the second (group 2) with systemic candidiasis, the third (group 3) with breast cancer and the final two groups (groups 4 and 5) had both candidiasis and breast cancer at two different doses of candidiasis, respectively. Inoculation of mice with systemic candidiasis was performed by an intravenous injection of *Candida albicans* via the tail vein following successful culture methods. Induction of mice with breast cancer occurred via injection of 4T1 cancer cells at the right axillary mammary fatpad after effective culture methods. The prepared slides with organ tissues were stained with hematoxylin and eosin, periodic acidic schiff and gomori methenamine silver stains for a histopathological analysis. Grading of primary tumour and identification of metastatic deposits, as well as scoring of inflammation and congestion in all the respective organs was conducted. Statistical tests performed to compare groups 2 and 4 showed that group 4 exhibited a highly statistically significant increase in organ inflammation and congestion ($p < 0.01$). The median severity of candidiasis in the kidneys and liver also increased in group 4 as compared to group 2. In conclusion, based on the above evidence, systemic candidiasis significantly increased in mice with breast cancer.

Key words: systemic candidiasis, breast cancer, *Candida albicans*, 4T1 mouse cancer model, metastasis, immunosuppression

Chu WL, Lim YW, Radhakrishnan AK, Lim PE. Protective effect of aqueous extract from *Spirulina platensis* against cell death induced by free radicals. *BMC Complement Altern Med* 2010; 10: 53

Protective effect of aqueous extract from *Spirulina platensis* against cell death induced by free radicals

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Abstract

Background:

Spirulina is a commercial alga well known to contain various antioxidants, especially phycocyanin. Apart from being sold as a nutraceutical, *Spirulina* is incorporated as a functional ingredient in food products and beverages. Most of the previous reports on antioxidant activity of *Spirulina* were based on chemical rather than cell-based assays. The primary objective of this study was to assess the antioxidant activity of aqueous extract from *Spirulina* based on its protective effect against cell death induced by free radicals.

Methods:

The antioxidant activity of the cold water extract from food-grade *Spirulina platensis* was assessed using both chemical and cell-based assays. In the cell-based assay, mouse fibroblast cells (3T3) cells were incubated for 1 h in medium containing aqueous extract of *Spirulina* or vitamin C (positive control) at 25, 125 and 250 µg/mL before the addition of 50 µM 1,1-diphenyl-2-picrylhydrazyl (DPPH) or 3-ethylbenzothiazoline-6-sulfonic acid (ABTS). The cells were incubated for another 24 h before being assessed for cell death due to apoptosis using the Cell Death Detection ELISA Kit. Spectrophotometric assays based on DPPH and ABTS were also used to assess the antioxidant activity of the extract compared to vitamin C and vitamin E (positive controls).

Results:

Spirulina extract did not cause cytotoxic effect on 3T3 cells within the range of concentrations tested (0 - 250 µg/mL). The extract reduced significantly ($p < 0.05$) apoptotic cell death due to DPPH and ABTS by 4 to 5-fold although the activity was less than vitamin C. Based on the DPPH assay, the radical scavenging activity of the extract was higher than phycocyanin and was at least 50% of vitamin C and vitamin E. Based on the ABTS assay, the antioxidant activity of the extract at 50 µg/mL was as good as vitamin C and vitamin E.

Conclusions:

The results showed that aqueous extract of *Spirulina* has a protective effect against apoptotic cell death due to free radicals. The potential application of incorporating *Spirulina* into food products and beverages to enhance their antioxidant capacity is worth exploring.

Cooperstein R, Haneline M, Young M. The interexaminer reliability of thoracic motion palpation using confidence ratings and continuous analysis. J Chiropractic Med 2010; 9(3): 99-106

Interexaminer reliability of thoracic motion palpation using confidence ratings and continuous analysis

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Abstract

Objective:

Motion palpation is integral to most chiropractic techniques and can be found in curricula of most every chiropractic college. Paradoxically, most studies do not show strong reliability for motion palpation. The purpose of this study was to determine if allowing motion palpators to rate their confidence in their findings, as well using a continuous data analytic method, would influence the level of concordance.

Methods:

Subjects were 52 asymptomatic chiropractic student volunteers. Two palpators assessed posterior to anterior glide of T3-10 in the prone position, alternating in their order and blinded as to each other's results. Each examiner identified the location of maximal restriction in this range and also whether they were "very confident" or "not confident" in their finding.

Results:

For all subjects combined, the examiners' calls were "poor": intraclass correlation coefficient [2,1] = .3110 (95% CI, .0458-.5358). In contrast, interexaminer agreement was "good" when both examiners were very confident: intraclass correlation coefficient [2,1] = .8266 (95% CI, 0.6257-0.9253).

Conclusion:

When each examiner was "very confident" as to the most fixated thoracic segment, the levels they identified were very close. This corresponds to "good" agreement, an uncommon result in most interexaminer motion palpation studies. Thus, the confidence level of examiners had an effect on the interexaminer reliability of thoracic spine. Our novel continuous measures, statistical methodology, and subtyping the subjects according to the confidence of the palpators seem more capable than level-by-level discrete analysis of detecting interexaminer agreement.

Key words: Palpation, Reproducibility of results, Spine, Movement, Chiropractic

Dua K, Pabreja K, M.V. Ramana, Preparation, characterization and in vitro evaluation of aceclofenac solid dispersions. *ARS Pharmaceutica* 2010, 51 (1), 57-76

Preparation, characterization and in vitro evaluation of aceclofenac solid dispersions

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Abstract

The objective of the present investigation was to study the effect of various water soluble carriers like urea, mannitol, PVP and PVP/VA-64 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 all four carriers (urea, mannitol, PVP and PVP/VA-64) showed considerable increase in the dissolution rate in comparison with physical mixture and pure drug in 0.1 N HCl, pH1.2 and phosphate buffer, pH, 7.4. Solid dispersions containing PVP showed maximum dissolution rate in comparison to formulation containing urea, mannitol and PVP/VA-64. 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.

FT-IR spectroscopy and differential scanning calorimetry studies indicated no interaction between aceclofenac and carriers 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 various hydrophilic carriers like urea, mannitol, PVP and PVP/VA-64.

Key words: aceclofenac, urea, mannitol, PVP, PVP/VA-64

Dua K, Pabreja P, Malipeddi Venkata Ramana. Aceclofenac topical dosage forms: in vitro and in vivo characterization. *Acta Pharm* 2010; 60: 467-478

Aceclofenac topical dosage forms: in vitro and in vivo characterization

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Abstract

Aceclofenac is a new generation non-steroidal anti-inflammatory drug showing effective anti-inflammatory and analgesic properties. It is available in the form of tablets of 100 mg. Importance of aceclofenac as a NSAID has inspired development of topical dosage forms. This mode of administration may help avoid typical side effects associated with oral administration of NSAIDs, which have led to its withdrawal. Furthermore, aceclofenac topical dosage forms can be used as a supplement to oral therapy for better treatment of conditions such as arthritis. Ointments, creams, and gels containing 1% (m/m) aceclofenac have been prepared. They were tested for physical appearance, pH, spreadability, extrudability, drug content uniformity, in vitro diffusion and in vitro permeation. Gels prepared using Carbopol 940 (AF2, AF3) and macrogol bases (AF7) were selected after the analysis of the results. They were evaluated for acute skin irritancy, anti-inflammatory and analgesic effects using the carrageenan-induced thermal hyperalgesia and paw edema method. AF2 was shown to be significantly ($p < 0.05$) more effective in inhibiting hyperalgesia associated with inflammation, compared to AF3 and AF7. Hence, AF2 may be suggested as an alternative to oral preparations.

Key words: aceclofenac, topical gel, in vitro activity, in vivo activity

Dua K, Ramana MV, Sara UVS, Agrawal DK, Pabreja K, Chakravarthi S. Preparation and evaluation of transdermal plasters containing Norfloxacin: a novel treatment for burn wound healing. *eJ Plastic Surgery* 2010. 10, 364-382

Preparation and evaluation of transdermal plasters containing Norfloxacin: a novel treatment for burn wound healing

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Abstract

Objective:

In an attempt for better treatment of bacterial infections and burn wounds, plaster formulations containing different concentrations of norfloxacin were prepared using polymers like polyvinylpyrrolidone and polyvinyl alcohol and evaluated for physicochemical parameters, in vitro drug release, antimicrobial activity, and burn wound healing properties. The prepared formulations were compared with silver sulfadiazine cream 1%, USP.

Methods:

Plaster formulations containing different concentrations of norfloxacin were prepared by solvent casting method using combination of polymers like polyvinylpyrrolidone and polyvinyl alcohol. These plasters were characterized for drug content, thickness, percentage elongation, tensile strength, in vitro drug release properties, and antimicrobial activity against various strains of aerobic and anaerobic microorganisms. The wound healing property was evaluated by histopathological examination and by measuring the wound contraction.

Results:

The in vitro release and in vitro skin permeation followed the first-order kinetics followed by diffusion as dominant release mechanism. In spite of the significant antimicrobial and wound healing effects produced by plasters, the observed values were less than the values obtained with silver sulfadiazine 1% cream ($P < .05$). Various histopathological changes observed during the study period (days 1, 4, 8, and 12) also supported the wound healing process.

Conclusion:

Based on the observed in vitro performances along with antimicrobial and wound healing effects, the 5% norfloxacin transdermal plasters could be employed as an alternative to commercial silver sulfadiazine 1% cream.

Gorajana A, Ellaiah Poluri, Axel Zeeck. Cytotoxic compounds from a marine actinomycete, *Streptomyces albovinaceus* var. *baredar* AUBN_{10/2}. African J Biotechnol 2010; 9: 7197-7202

Cytotoxic compounds from a marine actinomycete, *Streptomyces albovinaceus* var. *baredar* AUBN_{10/2}

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Abstract

Marine sediment samples from Machilipatnam (Krishna District, A.P) coast off Bay of Bengal, India were investigated as a source of actinomycetes to screen for the production of novel bioactive compounds. More than 10,000 bioactive compounds have been described from marine actinomycetes, with many different properties, ranging from colour pigments to cytotoxic compounds. The search for cytotoxic compounds is continuing due to the demand for new anticancer drugs. In this work, compound I was isolated from the marine derived actinomycete strain AUBN10/2, obtained from marine sediment samples of Bay of Bengal, India. This was obtained by solvent extraction followed by chromatographic purification. The pure compound I was identified from spectroscopic data which was related to the actinomycin D, it showed a potent cytotoxic activity against cell lines HMO2 (gastric adenocarcinoma) and HePG2 (hepatic carcinoma) in vitro. It also exhibited antimicrobial activities against gram positive and negative bacteria.

Key words: Marine actinomycetes, phenoxazinone chromophore, actinomycin D, cytotoxic compounds, antibacterial activity.

Hossain S, Akaike T, Chowdhury EH. Current approaches for drug delivery to central nervous system. *Curr Drug Delivery* 2010; 7(5): 389-397

Current approaches for drug delivery to central nervous system

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Abstract

Brain, the center of the nervous system in all vertebrate, plays the most vital role in every function of human body. However, many neurodegenerative diseases, cancer and infections of the brain become more prevalent as populations become older. In spite of the major advances in neuroscience, many potential therapeutics are still unable to reach the central nervous system (CNS) due to the blood-brain barrier (BBB) which is formed by the tight junctions within the capillary endothelium of the vertebrate brain. This results in the capillary wall behaving as a continuous lipid bilayer and preventing the passage of polar and lipid insoluble substances. Several approaches for delivering drugs to the CNS have been developed to enhance the capacity of therapeutic molecules to cross the BBB by modifying the drug itself, or by coupling it to a vector for receptor-mediated, carrier mediated or adsorption-mediated transcytosis. The current challenge is to develop drug delivery systems that ensure the safe and effective passage of drugs across the BBB. This review focuses on the strategies and approaches developed to enhance drug delivery to the CNS.

Keywords: Central nervous system, blood brain barrier, drug delivery system, drug targeting, nanoparticle

Hossain S, Stanislaus A, Chua MJ, Tada S, Tagawa Y, Chowdhury EH, Akaike T. Carbonate apatite-facilitated intracellularly delivered siRNA for efficient knockdown of functional genes. *J Controlled Release* 2010; 147: 101-108

Carbonate apatite-facilitated intracellularly delivered siRNA for efficient knockdown of functional genes

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Abstract

Gene therapy through intracellular delivery of a functional gene or a gene-silencing element is a promising approach to treat critical diseases. Elucidation of the genetic basis of human diseases with complete sequencing of human genome revealed many vital genes as possible targets in gene therapy programs. RNA interference (RNAi), a powerful tool in functional genomics to selectively silence messenger RNA (mRNA) expression, can be harnessed to rapidly develop novel drugs against any disease target. The ability of synthetic small interfering RNA (siRNA) to effectively silence genes in vitro and in vivo, has made them particularly well suited as a drug therapeutic. However, since naked siRNA is unable to passively diffuse through cellular membranes, delivery of siRNA remains the major hurdle to fully exploit the potential of siRNA technology. Here pH-sensitive carbonate apatite has been developed to efficiently deliver siRNA into the mammalian cells by virtue of its high affinity interactions with the siRNA and the desirable size of the resulting siRNA/apatite complex for effective cellular endocytosis. Moreover, following internalization by cells, siRNA was found to be escaped from the endosomes in a time-dependent manner and finally, more efficiently silenced reporter genes at a low dose than commercially available lipofectamine. Knockdown of cyclin B1 gene with only 10 nM of siRNA delivered by carbonate apatite resulted in the significant death of cancer cells, suggesting that the new method of siRNA delivery is highly promising for pre-clinical and clinical cancer therapy.

Hossain S, Tada S, Akaike T, Chowdhury EH. Influences of electrolytes and glucose on formulation of carbonate apatite nanocrystals for efficient gene delivery to mammalian cells. *Anal Biochem* 2010;397(2):156-161

Influences of electrolytes and glucose on formulation of carbonate apatite nanocrystals for efficient gene delivery to mammalian cells

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Abstract

Generic manipulation of human cells through delivery of a functional gene or a gene-silencing element is an attractive approach to treat critical diseases very precisely and effectively. Extensive research on the generic basis of human diseases with complete sequencing of human genome has revealed many vital genes as possible targets in gene therapy programs. On the other hand, to facilitate cell-or tissue-directed delivery of genes and gene-silencing nucleic acid sequences, both genetic and chemical engineering approaches have led to the generation of various viral and nonviral carriers. However, considering the issues of both safety and efficacy, none of the existing vectors is an ideal candidate for clinical use. We recently established pH-sensitive inorganic nanocrystals of carbonate apatite with capability of efficient intracellular delivery and release of associated DNA molecules for subsequent protein expression. Here we show a new synthetic approach for carbonate apatite crystals with stronger affinity toward DNA, leading to significant increment in both transgene delivery and expression. Moreover, CaCl₂ and NaCl existing as the major electrolytes in the bicarbonate-buffered solution, dose-dependently govern particle size and eventually internalization and expression of particle-associated DNA.

Key words: Carbonate apatite, Nanocrystals, Endocytosis, Particle size, NaCl, Glucose, Gene expression, Transfection

Jeevaratnam K, Nadarajah VD, Judson JP, Nalliah S, Abdullah MF. Periodic assessment of plasma sFlt-1 and PIGF concentrations and its association with placental morphometry in gestational hypertension (GH) - a prospective follow-up study. *BMC Pregnancy Childbirth* 2010;10:58

Periodic assessment of plasma sFlt-1 and PIGF concentrations and its association with placental morphometry in gestational hypertension (GH) - a prospective follow-up study

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Abstract

Background:

Hypertensive disorders in pregnancy contributes to about 12% of maternal deaths in Malaysia and similarly worldwide. Early detection and adequate management are preventable strategies. Biochemical markers of abnormal angiogenesis would be more specific in early detection than routine blood pressure and proteinuria measurements. The aim of this study was to estimate maternal plasma PIGF and sFlt-1 levels in pregnant women with gestational hypertension at three intervals of pregnancy and correlate these biomarker levels with placental morphometry.

Methods:

Venous blood samples (antepartum, intrapartum and post partum periods) were drawn to estimate for sFlt-1 and PIGF levels while placental tissue samples were examined for placental morphometry.

Results:

PIGF levels were lower in gestational hypertension (GH) compared to normotensive during antepartum and intrapartum period, whereas sFlt-1 levels were elevated in GH at antepartum, intrapartum and postpartum intervals during pregnancy. An inverse relationship between these two biomarkers was observed through correlation analysis. PIGF levels were inversely correlated with total villous surface area of the placental periphery (TCsa-C) and villous capillarization (VC-C) of the placental periphery.

Conclusion:

We established periodic values of for sFlt-1 and PIGF levels for the first time in an ethnically diverse Malaysian setting. We suggest the development of GH in women is related to defective capillarization. In demonstrating periodic changes, this study suggest the possibility of developing GH and other long term health complications as a result of prolonged exposure to sFlt-1. The correlation between PIGF levels and morphometric findings also support possible capillarization defect.

Judson JP, Chakravarthi S, Lee Soo Han, Salman R, Nalliah S. The role of extracellular matrix (ECM) in the aetiology of gestational hypertension and preeclampsia – a preliminary study. Trends in MolSci 2010, 1 (2):1-11

The role of extracellular matrix in the aetiology of gestational hypertension and preeclampsia: a preliminary study

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Abstract

The aim of this study is to determine the alteration of extracellular matrix (ECM), namely fibronectin and collagen type IV, in the aetiology of hypertensive disorders of pregnancy. Gestational hypertension and preeclampsia account for 5-7% of the maternal mortality and morbidity worldwide. Gestational hypertension and preeclampsia is characterised by blood pressure of 140/90 mmHg or greater after the 20th week of gestation. The aetiology of gestational hypertension and preeclampsia is closely related to the disorder of placenta implantation. It is thought that shallow trophoblast invasion into maternal decidua causes malfunction of the utero-placental arteries, thus leading to both the diseases. The exact cause of shallow trophoblast invasion remains controversial. Placenta implantation involves activation and migration of trophoblast into the decidua and myometrium. These processes are dependent on extracellular matrix, where activation of appropriate adhesion molecules and integrins are essential for appropriate trophoblast activity. In this study, collagen type IV and fibronectin were investigated in a total of 30 placentas by immunohistochemistry and H&E stains. Observation on the staining intensity of the antibodies were done in both villous (foetal) and decidual (maternal) areas. Statistical analysis was performed using Mann-Whitney test. The analysis showed a significant increase of number of villi in gestational hypertensive and preeclamptic placentas compared to normotensive placentas. Staining intensity of collagen type IV and fibronectin suggested an alteration of level of these components in gestational hypertension and preeclampsia group compared to normotensive group and this alteration may play a role in the aetiology of the two hypertensive diseases.

Key words: Placenta, preeclampsia, collagen type IV, Fibronectin, immunohistochemistry

Judson JP, Lee Pui Fun, Nadarajah VD, Nalliah S, Chakravarthi S, Thanikacalam PM, Santhanaraj L. Ultrastructural and immunofluorescence studies of placental tissue in hypertensive diseases of pregnancy. *Res J BiolSci* 2010; 5(2): 155-163

Ultrastructural and immunofluorescence studies of placental tissue in hypertensive diseases of pregnancy

John Paul Judson , Lee Pui Fun , Vishna Devi Nadarajah , Sivalingam Nalliah , Srikumar Chakravarthi , P. Thanikacalam and L. Santhanaraj

Abstract

Gestational hypertension and preeclampsia account for 5-7% of the maternal mortality and morbidity worldwide. Gestational hypertension and preeclampsia is characterised by blood pressure of 140/90 mm Hg or greater after the 20th week of gestation. The aetiology of gestational hypertension and preeclampsia is closely related to the disorder of placenta implantation. It is thought that shallow trophoblast invasion into maternal decidua causes malfunction of the utero-placental arteries, thus leading to both the diseases. The exact cause of shallow trophoblast invasion remains controversial. Placenta implantation involves activation and migration of trophoblast into the decidua and myometrium. These processes are dependent on keratin expression where activation of appropriate adhesion molecules and integrins are essential for appropriate trophoblast activity. This integrated study aimed to detect and analyse the trophoblastic keratin expression, as well as to examine the placenta ultrastructure for presence of degenerative changes in normal, gestational hypertensive and preeclamptic placenta. Immunofluorescence double staining method was performed on placental sections and trophoblastic expression of keratin 19 (K19) and keratin 18 (K18) were analysed qualitatively and quantitatively in normal (n = 10), gestational hypertensive (n = 10) and preeclamptic (n = 10) placenta. Statistical analysis of means was performed using one-way ANOVA. Representative placental samples from each of three groups were analysed via electron microscopy. Immunofluorescence results showed that both K19 and 18 expression in gestational hypertension and preeclampsia were reduced compared to normal but significant reduction was observed only for K19 expression in gestational hypertensive placenta. Gestational hypertensive placenta showed more reduction than preeclampsia for both keratins. Electron microscopic results demonstrated obvious degeneration and significant changes in the placental ultrastructure in all representative samples of gestational hypertension and preeclampsia when compared to normal. The researchers conclude that the fundamental link exists between keratin expression and placental ultrastructural changes. The present keratin findings, especially in gestational hypertension, need to be confirmed by larger studies in future.

Kajal Ghosal, Rajabalaya R, SubrataChakraborty, Arunabha Nanda. Formulation and characterization of both hydrophilic and hydrophobic HPMC based hydrogels containing Diclofenac Potassium. Latin Am J Pharm, 2010; 29(7): 1137-1143

Formulation and characterization of both hydrophilic and hydrophobic HPMC based hydrogels containing diclofenac potassium

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²Dr B. C. Roy College of Pharmacy and Allied Health Sciences, Meghnad Saha Sarani, Bidhannagar, Durgapur, India

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Abstract

The aim of this study was to develop topical hydrogels containing diclofenac potassium (DP) at 1 % w/v concentration using conventional hydrophilic hydroxypropyl methyl cellulose (HPMC, 50cPs) and modified hydrophobic hydroxypropyl methyl cellulose (HPMC, 90L grade). The differences between in vitro release profiles of both types of polymer based hydrogels were studied using model dependent equations. Three formulations were prepared from hydrophobic HPMC at 1 %, 1.5 % and 2 % (w/v) concentration. Other two formulations were prepared from hydrophilic HPMC at 12 % and 15 % (w/v) concentration. Hydrophobic formulations of higher viscosity with small quantity of polymer show higher release compared to hydrophilic formulations of lower viscosity with higher polymer concentration. Combined effect of swelling and erosion leads to anomalous diffusion in case of hydrophobic HPMC based hydrogels whereas only swelling leads to Fickian diffusion in case of hydrophilic HPMC based hydrogels. The formulations follow Higuchi release pattern as well as Weibull model.

Key words: Diclofenac potassium, Hydrophobic, Hydrophilic, Release kinetics, Release models.

Kew ST. "Text messaging: an innovative method of data collection in medical research" BMC Research Note 2010, 3:342, published 20 Dec 2010

Text messaging: an innovative method of data collection in medical research

ST Kew

Department of Internal Medicine, International Medical University, Kuala Lumpur, Malaysia

Abstract

Background:

The ubiquitous use of mobile phones in sending and receiving text messages has become a norm for young people. Undeniably, text messaging has become a new and important communication medium not only in the social realm but in education as well. The aim of this study is to evaluate the effectiveness of using text messaging as a means to collect data for a medical research project. A cross sectional study was carried out during a double blind, randomized controlled trial to assess the efficacy and safety of a probiotic in the management of Irritable Bowel Syndrome (IBS). The study aim was to assess the response rate of weekly symptom reports via Short Message Service (SMS). The subjects were undergraduates in a private medical university in Malaysia. They were identified through a previous university wide study as suffering from IBS based on Rome III criteria. The subjects were randomly assigned to either the treatment arm receiving a daily probiotic, or the placebo arm. They were required to score their symptoms using eight-item-questionnaires at baseline, and thereafter weekly, for a total of 8 weeks. All subjects were given the choice to communicate their symptom scores by text messaging via mobile phones or by email. SMS text messages were sent to remind trial subjects to attend face-to-face visits and to complete a paper based 34-item-questionnaires on IBS quality of life assessment at baseline and at end of 8 weeks.

Findings:

The response rate of weekly symptom scores via Short Message Service (SMS) from a total of 38 subjects was 100%. Through the study, 342 reports were submitted: 33.3% of these were received on the due date without reminder, 60.0% one day after the deadline, after a single reminder, 6.1% 2-3 days after the deadline, after 2-3 reminders and 0.6% 5 days after the deadline, after SMS, phone reminder and face-to-face encounter. All SMS symptom reports, whether on time or late, were complete. With the help of SMS reminder, all trial subjects completed the paper based IBS quality of life assessment at baseline and at end of study.

Conclusions:

This study found using text messaging via mobile phone an excellent instrument for collecting weekly symptom reports in response to trial medication, reminding trial subjects to attend face to face visits and completing more complex paper based evaluation. The 100% response rate of weekly symptom reports was facilitated by using simple number codes for SMS submission.

Krishnan K, Jeremy Er An Ker, Shar Mariam M, Nadarajah VD. Identification of Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as a binding protein for a 68-kDa *Bacillus thuringiensis* parasporal protein cytotoxic against leukaemic cells. *J Biomed Sci* 2010; 17: 86

Identification of Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as a binding protein for a 68-kDa *Bacillus thuringiensis* parasporal protein cytotoxic against leukaemic cells

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³Department of Human Biology, Faculty of Medicine and Health Sciences, International Medical University, No 126 Jalan 19/155B Bukit Jalil, Kuala Lumpur, 57000 Malaysia

Abstract

Background:

Bacillus thuringiensis (Bt), an ubiquitous gram-positive spore-forming bacterium forms parasporal proteins during the stationary phase of its growth. Recent findings of selective human cancer cell-killing activity in non-insecticidal Bt isolates resulted in a new category of Bt parasporal protein called parasporin. However, little is known about the receptor molecules that bind parasporins and the mechanism of anti-cancer activity. A Malaysian Bt isolate, designated Bt18 produces parasporal protein that exhibit preferential cytotoxic activity for human leukaemic T cells (CEM-SS) but is non-cytotoxic to normal T cells or other cancer cell lines such as human cervical cancer (HeLa), human breast cancer (MCF-7) and colon cancer (HT-29) suggesting properties similar to parasporin. In this study we aim to identify the binding protein for Bt18 in human leukaemic T cells.

Methods:

Bt18 parasporal protein was separated using Mono Q anion exchange column attached to a HPLC system and antibody was raised against the purified 68-kDa parasporal protein. Receptor binding assay was used to detect the binding protein for Bt18 parasporal protein in CEM-SS cells and the identified protein was sent for N-terminal sequencing. NCBI protein BLAST was used to analyse the protein sequence. Double immunofluorescence staining techniques was applied to localise Bt18 and binding protein on CEM-SS cell.

Results:

Anion exchange separation of Bt18 parasporal protein yielded a 68-kDa parasporal protein with specific cytotoxic activity. Polyclonal IgG (anti-Bt18) for the 68-kDa parasporal protein was successfully raised and purified. Receptor binding assay showed that Bt18 parasporal protein bound to a 36-kDa protein from the CEM-SS cells lysate. N-terminal amino acid sequence of the 36-kDa protein was GKVKVGVNGFGRIGG. NCBI protein BLAST revealed that the binding protein was Glyceraldehyde-3-phosphate dehydrogenase (GAPDH). Double immunofluorescence staining showed co-localisation of Bt18 and GAPDH on the plasma membrane of the CEM-SS cells.

Conclusions:

GAPDH has been well known as a glycolytic enzyme, but recently GAPDH was discovered to have roles in apoptosis and carcinogenesis. Pre-incubation of anti-GAPDH antibody with CEM-SS cells decreases binding of Bt18 to the susceptible cells. Based on a qualitative analysis of the immunoblot and immunofluorescence results, GAPDH was identified as a binding protein on the plasma membrane of CEM-SS cells for Bt18 parasporal protein.

Lai NM, Nalliah S. Information- seeking practices of senior medical students: the impact of an evidence-based medicine training programme. *Educ Health (Abingdon)* 2010; 23: 151

Information-seeking practices of senior medical students: the impact of an evidence-based medicine training programme

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²International Medical University, Seremban, Negeri Sembilan, Malaysia

Abstract

Context:

The practice of Evidence-based Medicine (EBM) involves physicians regularly accessing and appraising clinical information. Few prior studies have assessed the information-seeking behaviours of medical undergraduates. At the International Medical University (IMU), Malaysia, senior medical students receive clinically-integrated EBM training to facilitate their future practice of EBM.

Objectives:

We assessed whether EBM training in the final six months of medical training changes our students' information-seeking practices and their confidence in understanding and appraising clinical evidence.

Methods:

Between September 2005 and February 2006, self-administered questionnaires were distributed to 65 senior medical students at the beginning and again at the end of their clerkship training during which there was a clinically-integrated EBM curriculum. The questionnaires covered the topics of their preferred sources of clinical information, online search frequencies, estimated time to retrieve an abstract, and their understanding and confidence in their critical appraisal skills.

Findings:

Sixty-four (98%) students completed the initial survey and 63 (97%) completed the follow-up survey. The majority indicated that they preferred to first consult another individual (colleagues, lecturers, hospital staff) for their clinical queries (60.9% in the initial survey and 61.9% in the follow-up survey), with no change in their overall preference following the EBM curriculum six months later ($p=0.144$). There were significant increases in search activities following the curriculum, for example, students who searched PubMed or Medline for more than three times per week increased from 9.7% to 31.7% ($p < 0.001$). Students reported that they more often accessed single journals than databases. Despite significant improvements in students' reported understanding of journals and their confidence in critical appraisal ($p < 0.001$), there was no improvement in reported search speed, with 48.4% in the initial survey and 49.2% in the follow-up survey reporting to take 30 minutes or less to trace an abstract of interest ($p=0.979$).

Conclusions:

Our EBM training, offered within a supportive curriculum, increased our students' confidence and activity related to EBM, but failed to change students' reported information-seeking behaviours. Other factors influencing medical students' information-seeking practice need to be explored.

Key words: Evidence-based medicine, medical students, clerkship, information-seeking behaviour

Lai NM, Teng CL, Lee ML. The place and barriers of evidence based practice: knowledge and perceptions of medical, nursing and allied health practitioners in Malaysia. *BMC Res Notes* 2010; 3(1):279

The place and barriers of evidence based practice: knowledge and perceptions of medical, nursing and allied health practitioners in Malaysia

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Abstract

Background:

Despite a recent increase in activities to promote evidence-based practice (EBP), it was unclear how Malaysian hospital practitioners received this new approach in medicine. This study examines their confidence and perceptions on EBP.

Findings:

We conducted cross-sectional surveys using a self-administered questionnaire during two EBP training courses in two Malaysian hospitals in January and June 2007. Our subjects (n = 144) were doctors and nursing and allied health staff (NAH) participating in the EBP courses. Our questionnaire covered three domains: confidence and understanding (six items), attitude (five items) and barriers to practice (four items). We presented simple descriptive statistics, including the sum ratings and the proportions with different responses for each item, and compared different groups using Mann-Whitney U test for scaled ratings and Chi-square test for dichotomous responses. Ninety-two doctors and 52 NAH staff completed the surveys. Overall, doctors expressed slightly higher confidence on EBP compared to NAH staff. Out of a maximum sum rating of 27 over six items, doctors reported an average of 18.3 (SD 3.2) and NAH staff reported an average of 16.0 (SD 3.4), $p = 0.002$. Doctors were also more positive in their views on EBP. For example, 67.4% of doctors disagreed, but 61% of NAH staff agreed that "the importance of EBP in patient care is exaggerated", and 79.3% of doctors disagreed, but 46.2% of NAH staff agreed that "EBP is too tedious and impractical". Similar responses were observed for other items in the domain. Doctors and NAH staff shared similar concerns on barriers to evidence-based practice. The highest proportions considered poor facilities to access evidence a barrier (76% of doctors and 90% of NAH), followed by poor awareness of evidence (62% of doctors and 70% of NAH) and time constraints (63% of doctors and 68% of NAH), $p = 0.09$ for the combined rating of four items in the domain.

Conclusions:

The findings of our survey suggest a need for greater efforts in promoting EBP among Malaysian hospital practitioners especially for NAH staff. From the responses based on the barriers to EBP, improving facilities for accessing evidence and promoting more user-friendly resources to address time constraints appear to be the priorities.

Lai Teng Ling, Radhakrishnan AK, Thavamanithevi Subramaniam, Hwee Ming Cheng, Uma D. Palanisamy. Assessment of antioxidant capacity and cytotoxicity of selected Malaysian plants. *Molecules* 2010; 15(4):2139-2151

Assessment of antioxidant capacity and cytotoxicity of selected Malaysian plants

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Abstract

Thirteen Malaysian plants; *Artocarpus champedon*, *Azadirachta indica*, *Fragaria x ananassa*, *Garcinia mangostana*, *Lawsonia inermis*, *Mangifera indica*, *Nephelium lappaceum*, *Nephelium mutabile*, *Peltophorum pterocarpum*, *Psidium guajava* and *Syzygium aqueum*, selected for their use in traditional medicine, were subjected to a variety of assays. Antioxidant capability, total phenolic content, elemental composition, as well as its cytotoxicity to several cell lines of the aqueous and ethanolic extracts from different parts of these selected Malaysian plants were determined. In general, the ethanolic extracts were better free radical scavengers than the aqueous extracts and some of the tested extracts were even more potent than a commercial grape seed preparation. Similar results were seen in the lipid peroxidation inhibition studies. Our findings also showed a strong correlation of antioxidant activity with the total phenolic content. These extracts when tested for its heavy metals content, were found to be below permissible value for nutraceutical application. In addition, most of the extracts were found not cytotoxic to 3T3 and 4T1 cells at concentrations as high as 100 µg/mL. We conclude that although traditionally these plants are used in the aqueous form, its commercial preparation could be achieved using ethanol since a high total phenolic content and antioxidant activity is associated with this method of preparation.

Key words: free radical scavenging; lipid peroxidation, cytotoxicity; total phenolic content; elemental analysis; Malaysian plants

Lee CL, Norimah AK, Ismail MN. Association of energy intake and micronutrient composition with overweight and obesity in Malay women from Klang Valley. *Mal J Nutrition* 2010; 16: 250-260

Association of energy intake and macronutrient composition with overweight and obesity in Malay women from Klang Valley

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Abstract

This cross-sectional study investigates the association between energy intake and macronutrient composition of the diet with overweight and obesity among Malaysian women. One hundred and fifteen adult Malay women aged 20 to 59 years (mean age 37.2 ±7.6 years) were interviewed. Dietary intake was assessed using the food history method. Body weight status was assessed using weight, height, waist circumference and fat percentage measurements. When energy intake was assessed for accuracy, only 41% of the subjects (n=47) were normal energy reporters. Among the normal energy reporters, 55% were of normal weight whereas 32% and 13% were overweight and obese. Mean energy intake for normal weight, overweight and obese subjects was 1685 ±199 kcal/day, 1810 ±166 kcal/day and 2119 ±222 kcal/day, respectively. Energy intake increased with body mass index (BMI) category. Among the overweight and obese, energy intake was respectively higher by 125 kcal/day and 434 kcal/day as compared to their normal weight counterparts (p<0.001). There was also a significant, moderate and positive correlation between energy intake and BMI (r=0.635), waist circumference (r=0.545), and body fat percentage (r=0.534). When macronutrient composition of diet was analysed (% energy and g/1000 kcal), there was no significant difference in carbohydrate, protein or fat intake between the obese, overweight and normal weight subjects. There was also no significant correlation between macronutrient composition of the diet and body weight status. Based on these findings, we conclude that the subjects' body weight status is likely to be influenced by energy intake rather than the macronutrient composition of the diet.

Key words: Energy intake, Klang Valley, macronutrient composition, obese Malay women, overweight Malay women

Lim Adeline YL, Ignacio Segarra, Srikumar Chakravarthi, SufyanAkram, John Paul Judson. Histopathology and biochemistry analysis of the interaction between sunitinib and paracetamol in mice. BMC Pharmacology 2010; 10:14; 1-17

Histopathology and biochemistry analysis of the interaction between sunitinib and paracetamol in mice

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Abstract

Background:

Sunitinib, a tyrosine kinase inhibitor to treat GIST and mRCC may interact with paracetamol as both undergo P450 mediated biotransformation and P-glycoprotein transport. This study evaluates the effects of sunitinib-paracetamol coadministration on liver and renal function biomarkers and liver, kidney, brain, heart and spleen histopathology. ICR male mice (n = 6 per group/dose) were administered saline (group-A) or paracetamol 500 mg/kg IP (group-B), or sunitinib at 25, 50, 80, 100, 140 mg/kg PO (group-C) or coadministered sunitinib at 25, 50, 80, 100, 140 mg/kg PO and paracetamol IP at fixed dose 500 mg/kg (group-D). Paracetamol was administered 15 min before sunitinib. Mice were sacrificed 4 h post sunitinib administration.

Results:

Group-A serum ALT and AST levels were 14.29 ± 2.31 U/L and 160.37 ± 24.74 U/L respectively and increased to 249.6 ± 222.7 U/L and 377.1 ± 173.6 U/L respectively in group-B; group-C ALT and AST ranged 36.75-75.02 U/L and 204.4-290.3 U/L respectively. After paracetamol coadministration with low sunitinib doses (group-D), ALT and AST concentrations ranged 182.79-221.03 U/L and 259.7-264.4 U/L respectively, lower than group-B. Paracetamol coadministration with high sunitinib doses showed higher ALT and AST values (range 269.6-349.2 U/L and 430.2-540.3 U/L respectively), $p < 0.05$. Hepatic histopathology showed vascular congestion in group-B; mild congestion in group-C (but lesser than in group-B and D). In group-D, at low doses of sunitinib, lesser damage than in group-B occurred but larger changes including congestion were observed at high sunitinib doses. BUN levels were higher ($p < 0.05$) for group-B (33.81 ± 5.68 mg/dL) and group-D (range 35.01 ± 6.95 U/L to 52.85 ± 12.53 U/L) compared to group-A (15.60 ± 2.17 mg/dL) and group-C (range 17.50 ± 1.25 U/L to 26.68 ± 6.05 U/L). Creatinine remained unchanged. Renal congestion and necrosis was lower in group-C than group-B but was higher in group-D ($p > 0.05$). Mild cardiotoxicity occurred in groups B, C and D. Brain vascular congestion occurred at high doses of sunitinib administered alone or with paracetamol. Hepatic and renal biomarkers correlated with histopathology signs.

Conclusions:

Paracetamol and sunitinib coadministration may lead to dose dependent outcomes exhibiting mild hepatoprotective effect or increased hepatotoxicity. Sunitinib at high doses show renal, cardiac and brain toxicity. Liver and renal function monitoring is recommended.

Lim SL, Chu WL, Phang SM. Use of *Chlorella vulgaris* for bioremediation of textile wastewater. *BioresourTechnol* 2010; 101(9): 7314-7322

Use of *Chlorella vulgaris* for bioremediation of textile wastewater

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Abstract

The potential application of *Chlorella vulgaris* UMACC 001 for bioremediation of textile wastewater (TW) was investigated using four batches of cultures in high rate algae ponds (HRAP) containing textile dye (Supranol Red 3BW) or TW. The biomass attained ranged from 0.17 to 2.26 mg chlorophyll a/L while colour removal ranged from 41.8% to 50.0%. There was also reduction of NH₄-N (44.4–45.1%), PO₄-P (33.1– 33.3%) and COD (38.3–62.3%) in the TW. Supplementation of the TW with nutrients of Bold's Basal Medium (BBM) increased biomass production but did not improve colour removal or reduction of pollutants.

The mechanism of colour removal by *C. vulgaris* is biosorption, in accordance with both the Langmuir and Freundlich models. The HRAP using *C. vulgaris* offers a good system for the polishing of TW before final discharge.

Key words: *Chlorella vulgaris*, Textile wastewater, Colour removal, Bioremediation, Microalgae

Lim TO, Adrian Goh, Lim Yam-Ngo, Zaki Mohamad Zaher, Abu Bakar S. How public and private reforms dramatically improved access to dialysis therapy in Malaysia. *Health Affairs*, 2010; 29(12): 1-10

How public and private reforms dramatically improved access to dialysis therapy in Malaysia

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Abstract

Between 1990 and 2005, dialysis treatment rates in Malaysia increased more than eightfold. Dialysis treatment reached a level comparable to rates in developed countries. This remarkable transformation was brought about in large part by the Malaysian government's large-scale purchase of dialysis services from the highly competitive private sector. This paper traces a series of public- and private-sector reforms that dramatically increased access to dialysis for patients with kidney failure from 13 per million people in the population in 1990 to 119 per million in 2005. Not all developing countries have had uniformly positive experiences with private-sector participation in health care. However, our data suggest that strong participation by the private sector in Malaysia has helped make for a stronger health care system as well as healthier patients. Yet the policy decisions that enabled the private sector to participate fully in providing dialysis have not been repeated with other medical services.

Ling APK, Jullian XC Ong, Sobri H, Abdul Rahim H. Morphological and physiological responses of *Orthosiphon stamineus* callus to gamma irradiation at different doses. *World J Agricult Sci*, 2010; 6 (1): 58-66

Morphological and physiological responses of *Orthosiphon stamineus* callus to gamma irradiation at different doses

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Abstract

In this mutagenic study, different doses of gamma rays (10,20, 30, 40 and 50 Grays) have been used to induce mutations by physical means to *Orthosiphon stamineus* callus. No obvious changes were observed in terms of colour and morphology of the callus. After three weeks of irradiation, various biochemical studies such as the chlorophyll content, total soluble protein and rosmarinic acid content as well as the specific peroxidase activity of the callus were conducted. Results showed a steady decrement of total soluble protein content with the increment of irradiation strength, with the non-irradiated sample demonstrated the highest total soluble protein content (6.31 ± 1.64 mg/g FW). Similar trend was observed for specific peroxidase activity where the non-irradiated samples recorded the highest value of 1652.68 ± 1160.78 units/mg soluble protein. Total chlorophyll content of gamma irradiated callus was also found to be lower compared to the non-irradiated callus. Nevertheless, there was an exception for callus irradiated at 30Gy which was found to be 15.62% higher in the total chlorophyll content compared to the non-irradiated callus. With higher irradiation doses, the production of rosmarinic acid was found to be higher where samples irradiated at 50Gy demonstrated the highest rosmarinic acid concentration (132.64 ± 27.03 mg/g/FW).

Loganathan R, Selvaduray KR, Nesaretnam K, Radhakrishnan AK. Health promoting effects of phytonutrients found in palm oil. *Mal J Nutrition*, 2010; 16: 309-322

Health promoting effects of phytonutrients found in palm oil

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²Product Development and Advisory Services Division, Malaysian Palm Oil Board Bandar Baru Bangi, 43000 Kajang, Selangor, Malaysia

Abstract

The oil palm tree, *Elaeis guineensis*, is the source of palm oil, otherwise known as the 'tropical golden oil'. To date, Malaysia and Indonesia are the leading producers of palm oil. Palm oil is widely used for domestic cooking in Malaysia. Palm oil is a rich source of phytonutrients such as tocotrienols, tocopherol, carotene, phytosterols, squalene, coenzyme Q10, polyphenols, and phospholipids. Although the phytonutrients constitute only about 1% of its weight in crude palm oil, these are the main constituents through which palm oil exhibits its nutritional properties. Among the major health promoting properties shown to be associated with the various types of phytonutrients present in palm oil are anti-cancer, cardio-protection and anti-angiogenesis, cholesterol inhibition, brain development and neuro protective properties, antioxidative defence mechanisms, provitamin A activity and anti-diabetes.

Key words: *Elaeis guineensis*, health promoting effects, phytonutrients

Loh KY, Lee XE. Hypereosinophilia responding to empirical antihelminthic treatment. Southeast Asian J Trop Med Pub Hlth 2010; 41(6): 1322-1323

Hypereosinophilia responding to empirical antihelminthic treatment

Loh KY, Lee XE.

International Medical University Malaysia, Seremban, Malaysia

Abstract

We report a 20-year-old college student presents with bilateral ankle edema associated with hypereosinophilia following a history of traveling in a rural area. Physical examinations and investigations failed to diagnose any underlying cause. She was treated with antihelminth medication and the edema subsided within a week and the eosinophil counts normalized within two weeks.

Mahadeva S, Yadav H, Rampal S, Everett SM, Goh KL. Ethnic variation, epidemiological factors and quality of life impairment associated with dyspepsia in urban Malaysia. *Aliment Pharmacol Ther* 2010;31(10): 1141-1151

Ethnic variation, epidemiological factors and quality of life impairment associated with dyspepsia in urban Malaysia

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⁴Department of Gastroenterology, Leeds General Infirmary, Leeds, UK

Abstract

Background:

The role of ethnicity in the development of dyspepsia remains uncertain.

Aims:

To examine the epidemiology of dyspepsia in a multi-ethnic Asian population and its impact on health-related quality of life (HRQOL).

Methods:

A cross-sectional survey was conducted in a representative urban population in Kuala Lumpur, Malaysia.

Results:

A total of 2039 adults (mean \pm s.d. age: 40.5 \pm 11.8 years, males 44.2%, ethnicity: Malays 45.3%, Chinese 38.0% and Indians 13.1%, tertiary education level 62%, professional employment 47.7% and median monthly income USD 850.00) were interviewed. Dyspepsia was prevalent in 496 (24.3%) adults. Independent predictors for dyspepsia, explored by logistic regression, were identified as: Malay (OR 2.17, 95% CI = 1.57–2.99) and Indian (OR 1.59, 95% CI = 1.03–2.45) ethnicity, heavy chilli intake (OR 2.35, 95% CI = 1.15–4.80), use of regular analgesia (OR 3.51, 95% CI = 2.54–4.87) and chronic illness (OR 1.67, 95% CI = 1.22–2.28). HRQOL was assessed with the EQ-5D and significantly lower scores were noted in dyspeptics compared with healthy controls (0.85 \pm 0.17 vs. 0.95 \pm 0.12, $P < 0.0001$).

Conclusion:

Ethnicity, in addition to recognized epidemiological factors, is a risk factor for dyspepsia in an urban multi-racial Asian population.

Mitra NK, Lee MS, Nadarajah VD. Evaluation of difference in the neurotoxicity produced by dermal application of chlorpyrifos on the neonatal and adult mice. Trop Biomed 2010; 27(1): 19-29

Evaluation of difference in the neurotoxicity produced by dermal application of chlorpyrifos on the neonatal and adult mice

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²Research and Postgraduate Studies Department, International Medical University, No. 126, Jalan 19/155B, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Abstract.

Dermal exposure to organophosphate pesticide is important because of its popular use. This study planned to compare the changes in serum acetylcholinesterase, paraoxonase and neuronal density of hippocampus and iso-cortex between two age groups of Swiss albino mice (18-day-old and 150-day-old) after dermal application of ½ LD50 of chlorpyrifos for 14 days. Statistically significant reduction was observed in serum acetylcholinesterase (Mann-Whitney test, $p < 0.05$) and neuronal density (Independent samples t-test, $p < 0.05$) in exposed groups compared to the control. The reduction in serum AChE and neuronal density was more pronounced in exposed adult mice than in exposed neonatal mice. The paraoxonase level was insignificant in control neonatal mice, whereas it was 890-fold more in exposed neonatal mice. Upregulated paraoxonase levels may be extrapolated to produce relatively lower reduction of cholinesterase and neuronal density in neonatal mice.

Moo KS, Radhakrishnan S, Teoh M, Narayanan P, Bukhari NI, Segarra I. Disposition and tissue distribution of imatinib in a liposome formulation after intravenous bolus dose to mice. Yao XueXueBao 2010; 45: 901-908

Disposition and tissue distribution of imatinib in a liposome formulation after intravenous bolus dose to mice

Moo KS, Radhakrishnan S, Teoh M, Narayanan P, Bukhari NI, Segarra I.

Department of Pharmaceutical Technology, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur 57000, Malaysia

Abstract

Imatinib is an efficacious anticancer drug with a spectrum of potential antitumour applications limited by poor biodistribution at therapeutic concentrations to the tissues of interest. We assess the pharmacokinetic and tissue distribution profile of imatinib in a liposome formulation. Its single dose (6.25 mg x kg⁻¹) in a liposome formulation was administered iv to male mice. Imatinib concentration was measured in plasma, spleen, liver, kidney and brain using a HPLC assay. Non-compartmental pharmacokinetic approach was used to assess the disposition parameters. The plasma disposition profile was biphasic with a plateau-like second phase. The AUC(0-->infinity) was 11.24 microg x h x mL⁻¹, the elimination rate constant (k_{el}) was 0.348 h⁻¹ and the elimination half life (t_{1/2}) was 2.0 h. The mean residence time (MRT) was 2.59 h, V(SS) was 1.44 L x kg⁻¹ and clearance was 0.56 L x h x kg⁻¹. Liver achieved the highest tissue exposure: C_{MAX} = 18.72 microg x mL⁻¹; AUC(0-->infinity)= 58.18 microg x h x mL⁻¹ and longest t_{1/2} (4.29 h) and MRT (5.31 h). Kidney and spleen AUC(0-->infinity) were 47.98 microg x h x mL⁻¹ and 23.46 microg x h x mL⁻¹, respectively. Half-life was 1.83 h for the kidney and 3.37 h for the spleen. Imatinib penetrated into the brain reaching approximately 1 microg x g⁻¹. Upon correction by organ blood flow the spleen showed the largest uptake efficiency. Liposomal imatinib presented extensive biodistribution. The drug uptake kinetics showed mechanism differences amongst the tissues. These findings encourage the development of novel imatinib formulations to treat other cancers.

Mrudula G, Pichika MR, Jayaveera KN, Arshad MD, Rehman SA. Antistress and antioxidant effects of *Prunella vulgaris* leaves. *Pharmacologyonline*, 2010; 2: 952-962

Antistress and antioxidant effects of *Prunella vulgaris* leaves

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²International Medical University, Kuala Lumpur, Malaysia

³Oil Technology Research Institute, Jawaharlal Technological University, Anantapur, Andhra Pradesh, India

Abstract

The ethanolic extract of *Prunella vulgaris* (PV) (10, 25, 50 mg/kg, p.o) was tested for its adaptogenic activity by using forced swimming test and invitro antioxidant activity by using 1,1- Diphenyl, 2-Picryl – hydrazyl free radical, Nitric oxide scavenging activity and reducing power method. In antistress activity, pretreatment with PV extract significantly reduced the immobility time at 50 mg/kg was comparable to that of imipramine (20 mg/kg, i.p) treated group. Under invitro 1,1- Diphenyl, 2-Picryl – hydrazyl free radical and nitric oxide free radicals are considerably inhibited in a dose dependent manner and there is increase in absorbing power indicates increase in reducing power. The results suggest that it could be used for the treatment of oxidative stress induced disorder.

Key words: *Prunella vulgaris*, Adaptogenic, Antistress, Antioxidant

Mrudula G, Pichika MR, Jayaveera KN, Pasah SY, Basha KM, Fatima H, Swaditha E, et al. Evaluation of hepatoprotective activity of *Prunella vulgaris* by carbontetrachloride induced hepatotoxicity. *Pharmacologyonline* 2010; 2: 1045-1053

Evaluation of hepatoprotective activity of *Prunella vulgaris* by carbontetrachloride induced hepatotoxicity

G. Mrudula¹, P. Mallikarjuna Rao², K.N. Jayaveera³, S.Y. Pasha¹, K.M. Basha¹, H. Fatima¹, E. Swaditha¹, MD. Zaheeruddin¹, S.A.H. Zubair¹

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²International Medical University, Kuala Lumpur, Malaysia

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Abstract

The hepatoprotective effect of ethanolic extract of leaves of *Prunella Vulgaris* against carbon tetrachloride (CCL₄) induced hepatic damage was investigated. The degree of protection was determined measuring levels of serum marker enzymes like Serum glutamate oxaloacetate transaminase (SGOT), Serum glutamate pyruvate transaminase (SGPT), Alkaline phosphatase (ALP), Total and direct bilirubin and liver weight of rat. The histopathological studies were also carried out. Silymarin was used as standard drug for comparisons. Administration of ethanolic extract of *Prunella Vulgaris* (50,100 mg/kg p.o) markedly decrease CCL₄ induced elevation levels of Serum marker enzymes and liver weight in dose dependent manner. The effects of extract were compared with standard, Silymarin at 100 mg/kg dose. In ethanolic extract treated animals, the toxic effect of CCl₄ was controlled significantly by restoration of the levels of enzymes as compared to the normal and standard drug silymarin treated groups. Histology of the liver sections of the animals treated with extract showed the presence of liver cells, absence of necrosis and fatty infiltration, which further evidenced the hepato protective activity. It was concluded that Ethanolic extract of leaves of *Prunella vulgaris* possesses significant hepatoprotective activity.

Key words: *Prunella vulgaris*, Carbon tetrachloride, Hepato protective activity, Serum marker enzymes

Mudassir A, Sulaiman SA, Keivan A, Khan TM. Awareness of school students on sexually transmitted infections (STIs) and their sexual behaviour: a cross-sectional study conducted in Pulau Pinang, Malaysia. BMC Pub Hlth 2010; 10: 47-52

Awareness of school students on sexually transmitted infections (STIs) and their sexual behavior: a cross-sectional study conducted in Pulau Pinang, Malaysia

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²School of Pharmaceutical Sciences, Universiti Sains Malaysia, Pulau Pinang, Malaysia

³School of Pharmacy, Island College of Technology, Sungai Rusa, 11000 Balik Pulau, Pulau Pinang, Malaysia

Abstract

Background:

Sexually transmitted Infections (STIs) rank among the most important health issues for the people especially the young adults worldwide. Young people tend to engage in sexual activity at younger ages in the past decade than in the 1970s, and 1980s. Knowledge is an essential precursor of sexual risk reduction. A cross-sectional study was conducted in Pulau Pinang, Malaysia, to produce the baseline information about school students' awareness and perception about sexually transmitted Infections (STIs) and their sexual activity to help establish control and education programmes.

Methods:

Students from form 4 (aged between 15 to 16 years), form 5 (aged between 16 to 17 years) and form 6 (aged between 18 to 20 years) in their class rooms were approached and asked to complete self-administered and anonymous pre-validated questionnaires. SPSS for windows version 13 was used to analyze the results statistically and results were presented in tabular form.

Results:

Data was collected from 1139 students aged between 15 to 20 years, 10.6% of which claimed that they never heard about STIs. Sexual experience related significantly with gender, race, and education level. Approximately 12.6% claimed to have sexual experience of which 75.7% had their sexual debut at 15-19 years and 38.2% were having more than 3 partners. Sexual experience was found to be significantly associated with gender ($p = 0.003$), ethnicity ($p = 0.001$) and education level ($p = 0.030$). However, multiple partner behaviour was significantly associated only with gender ($p = 0.010$). Mean knowledge score was 11.60 +/- 8.781 and knowledge level was significantly associated with religion ($p = 0.005$) education level ($p = 0.000$), course stream ($p = 0.000$), socioeconomic class ($p = 0.000$) and sexual experience ($p = 0.022$).

Conclusions:

It was concluded that school students have moderate level of knowledge about STIs although they are sexually active. Interventions such as reinforcing the link between STIs and HIV/AIDS, assessing the current status of sexuality education in schools and arranging public talks and seminars focusing on STIs prevention education are needed to improve their awareness.

Mudassir A, Sulaiman SA, Khan TM. A survey of knowledge of sexually transmitted infections among patients at a public hospital in Pulau Pinang, Malaysia. *Med Princ Pract* 2010; 19: 312-318

A survey of knowledge of sexually transmitted infections among patients at a public hospital in Pulau Pinang, Malaysia

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Abstract

Objective:

The aim of this study was to assess the patients' knowledge and awareness of sexually transmitted infections (STIs).

Subjects and methods:

A face-to-face interview was conducted among the patients visiting the Venereal Diseases Outpatient Department of the General Hospital of Pulau Pinang (Malaysia). A 19-item questionnaire was used. A total of 116 patients participated in the study and 107 patients had valid responses. The reliability and internal consistency of the questionnaire tool was estimated on the basis of Cronbach's alpha (= 0.81). The Statistical Package for Social Sciences (SPSS 13.0(R)) was used for data analysis. Student's t test and analysis of variance were used to analyse the knowledge differences among the groups.

Results:

Of the 107 patients, 82 (76.6%) were diagnosed with syphilis; AIDS was the most commonly known STI among the patients. Of the 107 patients, 35 were sexually active and of these 23 (65.7%) had more than 1 sexual partner. The most popular source of knowledge was newspapers (51 patients, 47.7%), with hospitals (3 patients, 2.8%) being the least popular one. Overall mean score on knowledge questions was 12.21 out of the maximum of 33 points. Knowledge about causative organisms, risk groups, transmission, symptoms, prevention and treatment of STIs was inadequate. The knowledge level was significantly related to gender ($p = 0.03$), religion ($p = 0.005$), educational level ($p = 0.000$), marital status ($p = 0.000$) and income level ($p = 0.036$).

Conclusion:

This study demonstrated evidence of poor knowledge of STIs amongst the patients attending an STI service in the General Hospital of Pulau Pinang (Malaysia). Hence there is an immediate need for efforts towards improving patient knowledge of STIs.

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Key words: Knowledge, sexually transmitted infections, Patients

Nagaraja HS, Jackie Tan, Chakravarthi S, Pichika MR, Anupama Kulur.
Protective effects of *Etingera elatior* extract on lead acetate - induced
hepatotoxicity in rats. *J ToxicolSci* 2010; 35 (5): 663-671

Protective effect of *Etingera elatior* (torch ginger) extract on lead acetate--induced hepatotoxicity in rats

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Abstract

Lead is known to disrupt the biological systems by altering the molecular interactions, cell signaling, and cellular function. Exposure to even low levels of lead may have potential hazardous effects on brain, liver, kidneys and testes. The efficacy of *Etingera elatior* (torch ginger) to protect hepatotoxicity induced by lead acetate was evaluated experimentally in male Sprague - Dawley rats. Rats were exposed to lead acetate in drinking water (500 ppm) for 21 days and the effects of concurrent treatment with extract of *E. elatior* on hepatic lipid hydroperoxides (LPO), protein carbonyl content (PCC), total antioxidants (TA), superoxide dismutase (SOD), glutathione peroxidase (GPX) and glutathione S- Transferase (GST) levels and histopathological changes in liver were evaluated. There was a significant decrease in TA and other antioxidant enzymes ($p < 0.05$) and increase in LPO and PCC ($p < 0.05$) with lead acetate ingestion. Concurrent treatment with *E. elatior* extract significantly reduced the LPO and PCC ($p < 0.05$) in serum and increased the antioxidant enzyme levels ($p < 0.05$) in the liver. Significant histopathological changes were seen in hepatic tissue with chronic lead ingestion. Treatment with *E. elatior* significantly reduced these lead-induced changes in hepatic architecture. *E. elatior* has also reduced the blood lead levels (BLL). Thus, there has been extensive biochemical and structural alterations indicative of liver toxicity with exposure to lead and *E. elatior* treatment significantly reduced these oxidative damage. Our results suggest that *E. elatior* has a powerful antioxidant effect against lead-induced hepatotoxicity.

Key words: Lead acetate, Hepatotoxicity, *Etingera elatior*, Lipid peroxidation, Antioxidants

Nagaraja HS, Jackie Tan, Chakravarthi S, Pichika MR, Thanikachalam PM. Protective effects of *Etlingera elatior* extract on lead acetate - induced, changes in oxidative biomarkers in bone marrow of rats. *Food Chem Toxicol*, 2010; 48: 2688–2694

Protective effects of *Etlingera elatior* extract on lead acetate-induced changes in oxidative biomarkers in bone marrow of rats

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Abstract

Several environmental toxins with toxic effects to the bone marrow have been identified. Pathology associated with lead intoxication is due to the cellular damage mediated by free radicals. In the current study, we examined the effect of *Etlingera elatior* extract on lead-induced changes in the oxidative biomarkers and histology of bone marrow of rats. Sprague–Dawley rats were exposed to 500 ppm lead acetate in their drinking water for 14 days. *E. elatior* extract was treated orally (100 mg/kg body weight) in combination with, or after lead acetate treatment. The results showed that there was a significant increase in lipid hydroperoxide, protein carbonyl content and a significant decrease in total antioxidants, super oxide dismutase, glutathione peroxidase and glutathione – S-transferase in bone marrow after lead acetate exposure. Treatment with *E. elatior* decreased lipid hydroperoxides and protein carbonyl contents and significantly increased total antioxidants and antioxidant enzymes. Treatments with *E. elatior* extract also reduced, lead-induced histopathological damage in bone marrow. In conclusion, these data suggest that *E. elatior* has a powerful antioxidant effect, and it protects the lead acetate-induced bone marrow oxidative damage in rats.

Key words: *Etlingera elatior*; Lead acetate; Oxidative stress; Bone marrow

Nagarajah HS, Ponnusamy Kumar. Neuroprotective effect of *Centella asiatica* extract (CAE) on experimentally induced parkinsonism in aged Sprague-Dawley rats. J ToxicolSci 2010; 35: 41- 47

Neuroprotective effect of *Centella asiatica* extract (CAE) on experimentally induced parkinsonism in aged Sprague-Dawley rats

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Abstract

Reactive oxygen species (ROS) play an important role in ageing and age-related neurodegenerative changes including Parkinson's disease (PD). PD is characterized by signs of major oxidative stress and mitochondrial damage in the pars compacta of the substantia nigra. Present study was designed to investigate whether the *Centella asiatica* extract (CAE) would prevent 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced neurotoxicity in aged Sprague-Dawley rats. Adult, male Sprague-dawley rats of 300-350 g were divided into control, *C. asiatica* alone, MPTP alone (20 mg/kg, for 21 days) and MPTP with *C. asiatica* (300 mg/kg for 21 days) groups. Effect of aqueous extract of *C. asiatica* on oxidative biomarker levels in corpus striatum and hippocampus homogenate was examined. MPTP-challenged rats elicited a significant increase in lipid hydroperoxides (LPO) ($p < 0.01$), protein-carbonyl-content (PCC) ($p < 0.01$) and xanthine oxidase (XO) ($p < 0.01$) when compared with control rats. There was a significant decrease in total antioxidants (TA) ($p < 0.001$), superoxide dismutase (SOD) ($p < 0.001$), glutathione peroxidase (GPx) ($p < 0.01$) and catalase (CAT) ($p < 0.001$) levels with MPTP treatment. Supplementation of CAE reduced LPO and PCC and significantly increased ($p < 0.01$) TA and antioxidant enzyme levels ($p < 0.01$) in corpus striatum and hippocampus. These results show that administration of *C. asiatica* was effective in protecting the brain against neurodegenerative disorders such as Parkinsonism.

Key words: Parkinsonism, *Centella asiatica*, Neurotoxicity, Oxidative stress, Antioxidants

Nalliah S, Chan S L J, Ong C L S, Suthan T H, Tan K C, She V N J, Das Gupta E. Effectiveness of the use of internet search by third year medical students to establish a clinical diagnosis. Singapore Med J 2010;51(4): 332-338

Effectiveness of the use of internet search by third year medical students to establish a clinical diagnosis

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Abstract

Introduction:

Internet search has been the main source for information and data mining in medical research. Its use by medical students has immensely contributed to learning activities. The main aim of the study was to determine the effectiveness of internet use by medical students during their initial years of clinical instruction in order to establish a diagnosis after being provided with the history and physical findings of a clinical problem.

Methods:

A total of 47 cases derived from the New England Journal of Medicine (NEJM) were utilised. The Google search engine was utilised to establish a reasonable diagnosis.

Results:

A congruency rate of 44.7% was obtained. This was considered commendable in view of the complexities of the cases published in the NEJM and the fact that the medical students were only in the third year of their Bachelor of Medicine and Bachelor of Surgery program.

Conclusion:

The study illustrates that common search engines could complement the traditionally used medical education methods.

Key words: congruency, Google search, medical diagnosis

Nazimah I, Noor Sham YL, Khairun Niza CN, MohdIkhsan S, Nadzratulaiman N, Juliana Y. Evaluating the deciding factors for termination of pregnancy with fetal anomaly – experience from 2 centers in Malaysia. *IeJSME* 2010; 4 (2): 41-46

Evaluating the deciding factors for termination of pregnancy with fetal anomaly – experience from two centers in Malaysia

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Abstract

Objective:

To evaluate the factors that contributes to the decision for termination of pregnancy in prenatally diagnosed fetal anomaly cases.

Methods:

A retrospective analysis of all cases of prenatally diagnosed fetal anomaly who delivered between 1 January 2007 and 30 June 2009 in two tertiary hospitals in Malaysia.

Results:

A total of seventy-two (72) prenatally diagnosed pregnancies with fetal anomalies were identified. Mean maternal age was 29.8 ± 5.5 years and mean parity 1.47 ± 1.8 . 70.8% of patients were ethnic Malay, 15.3% Chinese and 12.5% ethnic Indian. 22 (30.6%) fetuses were lethally abnormal. The overall pregnancy termination rate was 29.2%. 50% of pregnancies with lethally abnormal fetuses were terminated compared to 20% of pregnancies with non-lethal abnormality ($p < 0.05$). There were no significant differences seen in the decision for pregnancy termination with regards to mean maternal age, parity and between mothers of different ethnic backgrounds.

Conclusion:

Severity of fetal anomaly is the main determinant in the decision for pregnancy termination. Maternal age, parity and ethnic background did not significantly influence the decision.

Key words: Prenatal diagnosis, Fetal anomaly, Termination of pregnancy, Determining factors

Nesaretnam K, Mahalingam D, Radhakrishnan AK, Premier R. Supplementation of tocotrienol-rich fraction increases interferon-gamma production in ovalbumin-immunized mice. *Eur J Lipid Sci Technol* 2010; 112(5): 531-536

Supplementation of tocotrienol-rich fraction increases interferon-gamma production in ovalbumin-immunized mice

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Abstract

Palm oil is a rich source of vitamin E. The tocotrienol-rich fraction (TRF) extracted from palm oil contain 70% tocotrienols and 30% tocopherols. The effect of TRF supplementation on the immune modulation was evaluated in 6-wk-old female BALB/c mice immunized with ovalbumin (OVA) adjuvanted with alum. Mice in control and experimental groups were immunized subcutaneously (s.c.) on days 14 and 28 with a single dose of 50 µg OVA. The mice in the experimental group were orally gavaged daily with 1 mg of TRF from palm oil while those in the control group received carrier oil. The results show that mice in the experimental group produced significantly ($p < 0.05$) higher levels of interferon-gamma (IFN- γ) compared to the control group. There was no significant ($p > 0.05$) difference in the levels of interleukin-4 (IL-4) produced between the control and experimental animals. Lymphocyte proliferation in response to mitogen or OVA stimulation was significantly ($p < 0.05$) higher in splenocytes derived from the TRF supplemented mice compared to control mice. These findings show that daily supplementation of palm TRF can induce a strong cell-mediated immune response, *i.e.*, T-helper-1 (Th1) response, which would be beneficial to fight viral infections and cancer.

Key words: Interferon-gamma;Ovalbumin;Tocotrienol-rich fraction;Vitamin E

Ng CH, Lee KT, Taib NA, Yip CH. Experience with hookwire localisation excision biopsy at a medical centre in Malaysia. Singapore Med J 2010; 51: 306-310

Experience with hookwire localisation excision biopsy at a medical centre in Malaysia

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Abstract

Introduction:

With an increasing number of women undergoing breast screening, an effective method of removing non-palpable lumps detected by mammography or sonography is by hookwire localisation excision biopsy (HWLB). The aim of this paper was to audit the practice of HWLB at the University Malaya Medical Centre.

Methods:

Patients with benign or suspicious preoperative diagnoses of a non-palpable lump and who underwent HWLB were included in this study. Pathological examination of the surgical specimens was conducted and a correlation with preoperative assessment modalities was reported.

Results:

A total of 59 HWLBs were carried out in 57 female patients. The mean age of the patients was 51.5 years. The overall malignancy rate was 32.3 percent (19 out of 59 cases) with a benign to malignant ratio of 3.1 to 1. Ten of these cases were ductal carcinoma-in-situ. Out of 25 patients who were suspicious on preoperative assessment, 16 malignancies were found, while in the 33 patients thought to be benign on preoperative assessment, there were three malignancies, giving a sensitivity of 84.2 percent and a specificity of 76.9 percent (p is less than 0.05). The mean tissue volume excised in 53 available records was 50.0 cm³, with pathological tissue comprising only 15.4 percent of the total excised volume. Clear margins were obtained in 42.1 percent of the patients. The overall operative complication rate was 10.2 percent.

Conclusion:

Malignancy was reported in one third of women undergoing HWLB, of which 16 had suspicious features on radiological assessment and/or fine needle aspiration cytology/core needle biopsy preoperatively. Non-palpable lumps should be excised by HWLB for a definitive diagnosis in case of any suspicion on preoperative assessment, as the prognosis is excellent.

Key words: breast cancer, excision biopsy, hookwire localisation, non-palpable breast lesion

Ng TKW, Chow SSF, Chan LPY, Lee CYM, Lim SQ. Recommended nutrient intake for dietary fibre: bar set too high for Malaysians? *Mal J Nutrition* 2010; 16: 271-280

Recommended nutrient intake for dietary fibre: bar set too high for Malaysians?

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Abstract

This article presents findings from three separate data sets on food consumption in apparently healthy Malaysian adult males and females aged 22-60 years, and secondary data extracted from the Malaysian Adult Nutrition Survey (MANS) 2003. Assessment of food intake by 24-hour recall or the food diary method and use of the nutrient calculator-DietPLUS- to quantify intake of macronutrients and dietary fibre (DF) in the primary data, revealed low mean DF intakes of 10.7 ± 1.0 g/day (Course participants, n=52), 15.6 ± 1.2 (University sample, n=103), and 16.1 ± 6.1 (Research Institute staff, n=25). An alarmingly high proportion of subjects (75 to 95%) in these three data sets did not meet the national population intake goal of 20-30 g DF/day. A list of 39 food items which contain fibre, extracted from the MANS 2003 report as being average amounts consumed daily by each Malaysian adult, provided 19.2 g DF which meant that >50% of Malaysian adults consumed less than the recommended DF intake of 20-30 g/day. This large deficit of actual intake versus recommended intakes is not new and is also observed in developed western nations. What is of great concern is that the preliminary findings presented in this article indicate that the national population goal of 20-30 g DF/day may be beyond the habitual diets of the majority of Malaysians. Appropriately, the authors propose the inclusion of a daily minimum requirement for DF intake in the Malaysian Dietary Guidelines, which would somewhat mimic the Malaysian Dietary Guidelines 1999 for dietary fat, as well as the stand taken by the Scientific Advisory Committee on Nutrition (SACN) of the United Kingdom. This minimum requirement, if agreed to, should not be higher than the 16 g DF or so provided by the hypothetical 'high-fibre' healthy diet exemplified in this article.

Key words: Dietary fibre, minimum requirement, Recommended Nutrient In

Omar H, Atta O, El-Mowafy O, Khan SA. Efficacy of CAD-CAM porcelain veneers thickness on their cemented color. J Dent 2010; 38(suppl 2): e95-e99

Effect of CAD–CAM porcelain veneers thickness on their cemented color

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Abstract

Objective:

To determine the effect of thickness of porcelain veneers constructed from CAD–CAM on their final color when two resin cements were used.

Methods:

Buccal surfaces of extracted sound human molars with shade 3M2 [verified using digital spectrophotometer (Vita Easyshade-Vident)] were reduced to expose flat enamel surfaces. CAD–CAM blocks (Vitablocks Mark II) of the same shade were sectioned into three groups of 0.3, 0.5 and 0.7 mm thickness. Each group was subdivided into two subgroups; one subgroup was cemented to enamel using an etch-and-rinse resin cement (Calibra/Prime and bond-NT, Dentsply) and the other was cemented to enamel using a self-etching resin cement (Panavia-F, Kuraray). The shade of the two resin cements was “light”. Change in color (ΔE) between the selected shade (3M2) and the resulted shade was measured for each specimen using a digital spectrophotometer (Vita Easyshade-Vident). Means and SDs were calculated and data was statistically analyzed using ANOVA and post hoc tukey's.

Results:

Change in color (ΔE) between the selected and the produced shade for the Calibra subgroups was 2.8 (0.3) for the 0.3 mm, 1.67 (0.2) for the 0.5 mm thick specimens and 1.26 (0.3) for the 0.7 mm. Panavia F subgroups showed ΔE of 2 (0.4) for the 0.3 mm, 1.13 (0.23) for the 0.5 mm thick specimens and 1.21 (0.31) for the 0.7 mm. The 0.7 mm subgroups showed no significant difference in color change among the two cements ($P > .05$), however, Calibra resulted in significantly higher change in color values for the 0.5 mm thick specimens ($P < .05$). In spite of the presence of significant difference for the Calibra 0.5 mm thick subgroup, the color change was considered to be within the clinically acceptable range. The 0.3 mm showed high significant difference for the two tested cements with the Panavia showing less change in color and Calibra showing clinically detectable change in color.

Conclusion:

Increasing porcelain veneer thickness from 0.5 to 0.7 mm did not significantly affect the final color of cemented veneers. Whilst the color was significantly affected at the thickness of 0.3 mm.

Key words: CAD/CAM; Veneer shade; Veneer thickness

Ong ST, Keng PS, Lee SL, Leong MH, Hung YT. Equilibrium studies for the removal of basic dye by sunflower seed husk (*Helianthus annuus*). Int J Physical Sci 2010; 5: 1270-1276

Equilibrium studies for the removal of basic dye by sunflower seed husk (*Helianthus annuus*)

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Abstract

The sorption characteristics of sunflower (*Helianthus annuus*) seed husk (SSH) to remove Methylene Blue (MB) from aqueous solution under batch conditions have been investigated. Sorption of MB was found to be pH, concentration and agitation dependent. The kinetics of sorption was rapid with 80% sorption taking place within the first 60 min regardless of its initial concentration. The fast attainment of equilibrium implying the biosorbent could be suitable for continuous flow system. Using the pseudosecond order kinetics model, the predictive model for MB sorbed at time t (q_t) with the initial concentration of (C_0) is given by $q_t = C_0 t / [0.0607 C_0 + 2.0762 + (0.0012 C_0 + 5.1949) t]$. Results indicated that the predicted uptakes of MB agreed closely with experimental values obtained. The experimental data fitted well to Langmuir isotherm model with the correlation coefficient of 0.9860 and maximum monolayer sorption capacity of 45.25 mg/g.

Key words: Sunflower seed husk, sorption, basic dye, methylene blue, kinetics, modelling.

Pabreja K, Dua K, Satyanaryana S.V. Padi. Evaluation of extemporaneously manufactured topical gels containing Aceclofenac on inflammation and hyperalgesia in rats, *Curr Drug Delivery*, 2010; 7(4): 324-328

Evaluation of extemporaneously manufactured topical gels containing Aceclofenac on inflammation and hyperalgesia in rats

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Abstract

The systemic use of non-steroidal anti-inflammatory drugs (NSAIDs) which act by inhibiting cyclooxygenase (COX) is severely hampered by gastric and peptic ulcers. The topical delivery of NSAIDs has the advantages of avoiding gastric and peptic ulcers and delivering the drug to the inflammation site. Importance of aceclofenac as a new generational NSAID has inspired the development of topical dosage forms. This mode of administration may help to avoid typical side effects of NSAIDs associated with oral and systemic administration such as gastric irritation, particularly diarrhoea, nausea, abdominal pain and flatulence. The aim of this study was to formulate topical gel containing 1% of aceclofenac in carbopol and PEG base and to evaluate it for analgesic and anti inflammatory activity using carrageenan-induced thermal hyperalgesia and paw oedema in rats. Carrageenan administration into the hind paw produced a significant inflammation associated with hyperalgesia as shown by decreased rat paw withdrawal latency in response to a thermal stimulus ($47\pm 0.5^{\circ}\text{C}$) 4 h after carrageenan injection. Topical application of AF1 significantly attenuated the development of hypersensitivity to thermal stimulus as compared to control ($P < 0.05$) and other formulation treated groups ($P < 0.05$). All the AF semisolid formulations, when applied topically 2 h before carrageenan administration, inhibited paw edema in a time dependent manner with maximum percent edema inhibition of 80.33 ± 2.52 achieved with AF1 after 5 h of carrageenan administration. However, topical application of AF2 markedly prevented the development of edema as compared to other formulation (AF2 and AF3) treated groups ($P < 0.05$). Among all the semisolid formulations, Carbopol gel base was found to be most suitable dermatological base for aceclofenac.

Key words: NSAID, hyperalgesia, topical, inflammation

Pan Y, Abd-Rashid BA, Ismail Z, Ismail R, Mak JW, Pook PC, Er HM, Ong CE. In vitro modulatory effects on three major human cytochrome P450 enzymes by multiple active constituents and extracts of *Centella asiatica*. J Ethnopharmacol 2010; 130: 275-283

In vitro modulatory effects on three major human cytochrome P450 enzymes by multiple active constituents and extracts of *Centella asiatica*

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Abstract

Ethnopharmacological relevance:

Centella asiatica (CA) has been widely cultivated as a vegetable or spice in China, Southeast Asia, India, Sri Lanka, Africa, and Oceanic countries and traditionally used for wound healing and maintaining normal blood pressure.

Aim of the study:

The present study was carried out to examine the potential modulatory effects of three commercially available active components (asiaticoside, asiatic acid and madecassic acid) and four extracts (aqueous, ethanol, dichloromethane and hexane) of CA on three major cDNA-expressed human cytochrome P450 (CYP) isoforms.

Materials and methods:

High-performance liquid chromatography (HPLC)-based enzyme assays, namely tolbutamide 4-methylhydroxylase, dextromethorphan O-demethylase and testosterone 6 β -hydroxylase assays were developed to probe activities of CYP2C9, CYP2D6 and CYP3A4, respectively. Probe substrates were incubated with or without each active component and extract for each isoform, followed by examination of the kinetics parameters, IC₅₀ and K_i, to characterize modulatory effects.

Results:

CYP2C9 was more susceptible to inhibitory effects by CA extracts compared to CYP2D6 and CYP3A4. Moderate degree of inhibition was observed in ethanol (K_i = 39.1 μ g/ml) and dichloromethane (K_i = 26.6 μ g/ml) extracts implying potential risk of interaction when CYP2C9 substrates are consumed with CA products. The two extracts however showed negligible inhibition towards CYP2D6 and CYP3A4 (IC₅₀'s of 123.3 μ g/ml and above). Similarly CA aqueous and hexane extracts did not significantly inhibit all three isoforms investigated (IC₅₀'s of 117.9 μ g/ml and above). Among the active constituents investigated, asiatic acid and madecassic acid appeared to selectively inhibit CYP2C9 and CYP2D6 more than CYP3A4. Of particular interest is the potent inhibitory effect of asiatic acid on CYP2C9 (K_i = 9.1 μ g/ml). This signifies potential risk of interaction when

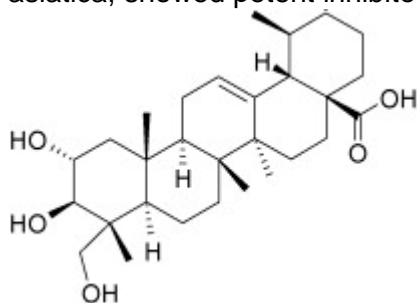
substrates for this isoform are taken together with CA products with high asiatic acid content. Inhibitions of asiatic acid with the other isoforms and that of madecassic acid with all isoforms were only moderate (K_i 's ranged from 17.2 to 84.4 $\mu\text{g/ml}$). On the other hand, the IC_{50} values for asiaticoside were high (1070.2 $\mu\text{g/ml}$ or above) for all three isoforms, indicating negligible or low potential of this compound to modulate CYP enzymatic activity.

Conclusion:

Centella asiatica extracts and active constituents inhibited CYP2C9, CYP2D6 and CYP3A4 activities with varying potency with CYP2C9 being the most susceptible isoform to inhibition. Significant inhibition was observed for asiatic acid and CA ethanol and dichloromethane extracts, implying involvement of semipolar constituents from CA in the effect. This study suggested that CA could cause drug–herb interactions through CYP2C9 inhibition.

Graphical abstract:

Asiatic acid, (1S,2R,4aS,6aR,6aS,6bR,8aR,9S,10S,11R,12aS,14bR)-10,11-dihydroxy-9-(hydro-xymethyl)-1,2,6a,6b,9,12a-hexamethyl-2,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydro-1H-picene-4a-carboxylic acid, a triterpenoid isolated from Centella asiatica, showed potent inhibitory effect on catalytic activity of human CYP2C9.



Key words: Centella asiatica; Apiaceae; Cytochrome P450; Drug–herb interaction; Enzyme inhibition

Perera J, Galy M, Satpal Kaur. The use of objective structured self-assessment and peer-feedback (OSSP) for learning communication skills: evaluation using a controlled trial. *Adv in Health Sci Educ* 2010; 15: 185-193

The use of objective structured self-assessment and peer-feedback (OSSP) for learning communication skills: evaluation using a controlled trial

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Abstract

Feedback is essential to guide students towards expected performance goals. The usefulness of teacher feedback on improving communication skills (CS) has been well documented. It has been proposed that self-assessment and peer-feedback has an equally important role to play in enhancing learning. This is the focus of this study. Objectively structured self-assessment and peer feedback (OSSP) was incorporated into small group CS teaching sessions of a group of semester one medical students who were learning CS for the first time, to minimise the influence of previous educational interventions. A control group matched for academic performance, gender and age was used to enable parallel evaluation of the innovation. A reflective log containing closed and open ended questions was used for OSSP. Facilitators and simulated patients provided feedback to students in both groups during CS learning as per routine practice. Student perceptions on OSSP and acceptability as a learning method were explored using a questionnaire. CS were assessed in both groups using objective structured clinical examination (OSCE) as per routine practice and assessors were blinded as to which group the student belonged. Mean total score and scores for specific areas of interview skills were significantly higher in the experimental group. Analysis of the questionnaire data showed that students gained fresh insights into specific areas such as empathy, addressing patients' concerns and interview style during OSSP which clearly corroborated the specific differences in scores. The free text comments were highly encouraging as to acceptability of OSSP, in spite of 67% being never exposed to formal self- and peer-assessment during pre-university studies. OSSP promotes effective CS learning and learner acceptability is high.

Key words: Communication skills learning, objectively structured self-assessment, Peer-feedback

Rajabalaya R, Sheba R David, Jasmina Khanam, Arunabha Nanda. Studies on effect of plasticizer on invitro release and exvivo permeation from Eudragit E100 based Chlorpheniramine maleate matrix type transdermal delivery system. J Excipients Food Chem 2010; 1(2): 3- 12

Studies on the effect of plasticizer on in vitro release and ex vivo permeation from Eudragit E 100 based chlorpheniramine maleate matrix type transdermal delivery system

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Abstract

The release and permeation studies were carried out for developing transdermal therapeutic systems with chlorpheniramine maleate (CPM). The patches were prepared with Eudragit E100 with/without polyvinyl pyrrolidone (PVP) and dibutyl phthalate (DBP) as well as dibutyl sebacate (DBS) as the plasticizer in different compositions. Thickness, tensile strength, modulus of elasticity, drug content, moisture content and water absorption studies of the patches were measured. In vitro release/permeation of CPM was studied in modified Keshary-Chien diffusion cell. Chemical enhancers like l-menthol, oleic acid and phospholipon80 were added to compare the release pattern of the drug. The percent release of the drug from matrix patch increased with the increase of PVP & plasticizers but the tensile strength decreased. Experimental release/permeation data of different formulations of the matrix systems are reported. Also the drug-polymer interaction was investigated by ATR-FTIR studies. This study reports that the suitable plasticizer & chemical enhancers for Eudragit E 100 polymer for controlled release/permeation of CPM; hence this drug could be a potential candidate for transdermal antihistamine & wound healing applications in film device industry.

Key words: Chlorpheniramine maleate, Eudragit polymer, Polyvinyl pyrrolidone, Dibutyl phthalate, Dibutyl sebacate, Chemical enhancers

S Sulaiha SA, Nazimah I, Zainur Rashid Z. I am hot, irritable and feeling low; what alternatives do I have besides hormone replacement therapy? *Malaysian Fam Physician* 2010; 5(3): 126-129

I am hot, irritable and feeling low; what alternatives do I have besides hormone replacement therapy?

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Abstract

Women at the end of their reproductive age often complain of climacteric symptoms which can be quite debilitating at times. Physiological changes due to deficient oestrogen have received global attention in the search for an acceptable and safe measure to improve quality of life for women with these complaints. Hormone replacement therapy (HRT) used to be the main treatment for menopausal symptoms. Lately there are concerns about its possible adverse effects of increasing risks of breast malignancy, heart diseases, etc. Complementary Alternative Medicine (CAM) plays a significant role in relieving these climacteric symptoms especially in women with contraindications to hormonal therapy and in those who are worried of its adverse effects. It is important for women to be aware of these CAM to provide them with options to improve their quality of life. This paper explores other pharmacological and non-pharmacological measures as alternatives to hormone replacement therapy (HRT), to assess how useful and reliable they are according to available scientific evidence.

Key words: Menopausal symptoms, hormone replacement therapy, lifestyle changes, pharmacological therapy, complementary therapy

S Sulaiha SA, Wee Yun Ling, Lie Joo Chin, Wei-Liang Eow, Muhamad Faiz S, Noris Chien Fook Tan. The lack of effective hand washing practice despite high level of knowledge and awareness in medical students of clinical years. *leJSME* 2010; 4(2): 18-26

The lack of effective hand washing practice despite high level of knowledge and awareness in medical students of clinical years

S Sulaiha S A, Wee Yun Ling, Lie Joo Chin, Wei-Liang Eow, Muhamad Faiz S, Noris Chien Fook Tan

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Abstract

Background:

Nosocomial infection is among the leading problem in many major hospitals resulting in soaring cost expenditure in managing its affect. Hand washing practice is a crucial preventive way to contain such mischief but many ignored its importance. This is perhaps due to lack of appropriate role modeling from senior practitioners.

Subjects and methods:

Our study examined the prevalence of hand washing practice among medical students from year 3 to 5 and compared it to their knowledge and level of awareness on its importance in clinical practice. 142 students were randomly observed during their clinical work in the wards on this practice and questionnaires were later distributed to 268 students from all semesters on their knowledge on the technique and awareness on its importance.

Results:

Out of 142, almost 80% washed their hands but only 41.6% performed effective hand washing. In contrary, 80 to 90% showed good level of knowledge and awareness as well as perception about its importance in clinical practice.

Conclusions:

The contradictory findings between the actual practice of hand washing and knowledge as well as awareness suggest that enforcement on the practice is necessary. This requires motivation and cooperation from all health alliances and higher authority in the health system. Remedial measures are much needed in order to contain high incidence of nosocomial infection in our local practice.

Key words: Effective hand washing, Nosocomial infection, Practice of hand washing

Seak CK, Lin CC, Seak CJ, Hsu TY, Chang CC. A case of black urine and dark skin – cresol poisoning. *Clin Toxicol (Phila)* 2010; 48(9):959-960

A case of black urine and dark skin — cresol poisoning

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Abstract

Cresol is a phenol derivative used as a disinfectant worldwide. Acute cresol poisoning is potentially fatal as it may cause multiple organ failure. We present a case of acute cresol intoxication in a male patient to illustrate the effects of cresol poisoning. **Case.** A 42-year-old male presented with black urine, painless brownish dermal burns, and a strong carbolic acid odor. The patient was immediately resuscitated with adequate oxygenation and aggressive fluid resuscitation. He was subsequently admitted to the intensive care unit, where his treatment course was complicated by pneumonia, gastrointestinal bleeding, hepatic dysfunction, and acute renal failure. After receiving supportive intensive care, the patient recovered and was discharged with no sequelae. **Conclusion.** The distinctive clinical features of this case may be useful in diagnosis, because laboratory analytical methods for cresols are not routinely available at most hospitals.

Key words: Cresol, Poisoning, Carbolic acid, Dermal burn, Black urine

Selvaduray KR, Radhakrishnan AK, Kutty Methil Kannan, Nesaretnam K. Palm tocotrienols inhibit proliferation of murine mammary cancer cells and induce expression of IL-24 mRNA. *J Interferon Cytokine Res* 2010; 30(12): 909-916

Palm tocotrienols inhibit proliferation of murine mammary cancer cells and induce expression of interleukin-24 mRNA

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Abstract

Several mechanisms have been postulated for the anticancer effects of tocotrienols. In this study, for the first time, the anticancer effect of tocotrienols is linked to increased expression of interleukin-24 (IL-24) mRNA, a cytokine reported to have antitumor effects in many cancer models. Tocotrienol isomers (α -T3, γ -T3, and δ -T3) and tocotrienol-rich fraction (TRF) inhibited the growth of the 4T1 murine mammary cancer cells ($P < 0.05$), with IC_{50} values 8.99, 4.79, 3.73, and 8.63 $\mu\text{g/mL}$, respectively. Tumor incidence and tumor load in TRF-supplemented BALB/c mice was decreased by 57.1% and 93.6% ($P < 0.05$), respectively. The induction of the IL-24 mRNA in the 4T1 cells by vitamin E decreased in the following order: δ -T3 > γ -T3 > TRF > α -T3 > α -T, which was similar to their antiproliferative effects. The IL-24 mRNA levels in tumor tissues of BALB/c mice supplemented with TRF increased 2-fold when compared with control mice. Increased levels of IL-24 have been associated with inhibition of tumor growth and angiogenesis. Treatment of 4T1 cells with TRF and δ -T3 significantly decreased IL-8 and vascular endothelial growth factor mRNA levels. Hence, we report that tocotrienols have potent antiangiogenic and antitumor effects that is associated with increased levels of IL-24 mRNA.

Shabnam M, Nalliah S, Radhakrishnan AK. Is there a genetic variation association in the IL-10 and TNF α promoter gene with gestational diabetes mellitus? *Hereditas* 2010; 147: 94-102

Is there a genetic variation association in the IL-10 and TNF α promoter gene with gestational diabetes mellitus?

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Abstract

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance diagnosed for the first time during pregnancy, affects both maternal and fetal health. Possession of a specific genetic polymorphism can be a predisposing factor for susceptibility to some diseases. The aim of this study was to investigate the association between single nucleotide polymorphisms (SNP) in the promoter gene of interleukin-10 (IL-10) as well as tumor necrosis factor- α (TNF α) with the development of GDM. Two hundred and twelve consecutive series of eligible normal pregnant women (controls) and gestational diabetes mellitus women were selected based on the study's inclusion and exclusion criteria. DNA was extracted from blood and genotyped for IL-10 at three positions and TNF α for gene polymorphism using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. Plasma levels of IL-10 and TNF α at different gestational periods as well as postpartum were quantified using enzyme linked immunosorbent assay (ELISA). The results of the study showed that the difference in the frequency of SNP at position -597 in the promoter of the human IL-10 gene between the control and GDM groups was statistically significant ($p < 0.05$). In contrast, there was no significant difference in the frequency of SNP at the other two sites in the promoter region of the human IL-10 gene (-824 and -1082) as well as position -308 in the promoter of the human TNF- α ($p < 0.05$). In addition, there was no significant difference between the two groups in terms of plasma levels of IL-10 as well as TNF α in different stages of pregnancy. SNP at position -597 was significantly associated with the development of GDM and shows potential for use as a predictive marker for GDM.

Shabnam M, Nalliah S, Radhakrishnan AK. Association between polymorphisms in human tumor necrosis factor-alpha (-308) and -beta (252) genes and development of gestational diabetes mellitus. *Diabetes Res Clin Pract* 2010; 88: 139-145

Association between polymorphisms in human tumor necrosis factor-alpha (-308) and -beta (252) genes and development of gestational diabetes mellitus

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Abstract

Objective:

The aim of this study is to investigate if an association exists between single nucleotide polymorphism (SNP) in the tumor necrosis factor-alpha (TNF- α) and TNF- β genes.

Methods:

The DNA was extracted and SNP in the human TNF- α and TNF- β genes at positions -308 (G/A) and 252 (A/G), respectively, was analyzed using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. Plasma levels of TNF- α in different stages of pregnancy were quantified using enzyme linked immunosorbent assay (ELISA).

Results:

There was no significant difference in genotype and allele frequency of SNP at position -308 (G/A) in the promoter region of the human TNF- α gene as well as the SNP at position 252 (A/G) in the human TNF- β gene between the GDM and control subjects. Using the logistic regression model, it was found that the SNP in the TNF- α as well as TNF- β were not associated with development of GDM. In addition, the TNF- α levels in the plasma of GDM and control mothers were not significantly different.

Conclusions:

In the population studied, the SNP in position -308 (G/A) of the human TNF- α or in position 252 (A/G) of the human TNF- β gene is not an independent risk factor or a predictor for GDM.

Abbreviations:

DM, diabetes mellitus; ELISA, enzyme linked immunosorbent assay; GDM, gestational diabetes mellitus; PBL, peripheral blood leukocytes; PCR, polymerase chain reaction; RFLP, restriction fragment length polymorphism; SNP, single nucleotide polymorphism; TNF- α , tumor necrosis factor-alpha; TNF- β , tumor necrosis factor-beta

Key words: Gestational diabetes mellitus (GDM); TNF- α ; TNF- β ; Single nucleotide polymorphism; Cytokine

Shalini Sree Kumar, Radhakrishnan AK, SK Cheong. Rapid metastasis of breast cancer cells from primary tumour to liver. Pak J BiolSci 2010; 13: 303-315

Rapid metastasis of breast cancer cells from primary tumour to liver

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Abstract

The aim of this study was to establish an animal model of mammary carcinoma metastasis to discern the in vivo effects of growth and spread of breast cancer. Six-week-old female BALB/c mice were inoculated with 4T1 murine breast cancer cells. Mice weight and primary tumour mass volume were regularly recorded to study the physical effects of a vigorously growing and spreading of cancer cell line. Gross and histological studies were carried out to determine the approximate day of metastatic onset. Production of IFN-gamma was assessed by ELISA to understand its role in tumour growth and metastasis. Lymphocyte markers such as CD8+, CD25 and CD49b were analysed to elucidate its role in tumour growth and progression. Present study showed that the metastatic onset occurs approximately 11 days after the mice were inoculated with the 4T1 murine breast cancer cells. Gross studies showed hepatosplenomegaly. The breast cancer cells from primary tumour were found to spread rapidly to the liver on day 11. IFN-gamma production was higher in inoculated mice serum compared to control mice serum. Higher numbers of CD8+, CD25 and CD49b cells were observed in the peripheral blood of inoculated mice, compared to control mice. In conclusion, the 4T1 murine breast cancer cells can migrate and metastasise rapidly to the liver, eliciting various immune responses.

Key words: 4T1, breast cancer metastasis, BALB/c mice, IFN-gamma, lymphocyte markers

Shalini Sree Kumar, Radhakrishnan AK, Cheong SK. Immune Responses in the Microenvironment of a Metastatic 4T1 Mouse Model. Egypt Academic Journal of Biological Sciences 2010;2(2):19-26

Immune response in the microenvironment of a metastatic 4T1 mouse model

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²Dept of Medicine, Faculty of Medicine and Health, International Medical University, Kuala Lumpur, Malaysia

Abstract

The 4T1 murine mammary carcinoma cells have the ability to spread to target organs in BALB/c mice breast cancer model. The spread of 4T1 cells mimics human stage IV breast cancer and elicits immune responses. The aim of this study is to establish an animal model of mammary carcinoma metastasis to discern the in vivo effects of growth and spread of breast cancer. Six weeks old female BALB/c mice were inoculated with 4T1 murine breast cancer cells. Gross and histological studies were carried out to determine the approximate day of metastatic onset. Production of IFN-gamma was assessed by ELISA to understand its role in tumor growth and metastasis. Lymphocyte markers such as CD8+, CD25 and CD49b were analysed to elucidate its role in tumour growth and progression. The metastatic onset occurs approximately 11 days after inoculation and accompanied with hepatosplenomegaly. The breast cancer cells from primary tumour were found to spread rapidly to the liver on day 11. IFN-gamma production was higher in inoculated mice serum compared to control. Higher numbers of CD8+, CD25 and CD49b cells were observed in the peripheral blood of inoculated mice, compared to control. In conclusion, the 4T1 murine breast cancer cells can migrate and metastasize rapidly to the liver, eliciting various immune responses.

Key words: 4T1, Breast cancer metastasis, BALB/c mice, IFN-gamma, Lymphocyte markers

Soo GW, Law HK Jason, Elaine Kan, Tan SY, Lim WY, Grace Chay, Bukhari NI, Segarra I. Differential effects of ketoconazole and primaquine on the pharmacokinetics and tissue distribution of imatinib in mice. *Anti-Cancer Drugs* 2010; 21(7): 695-703

Differential effects of ketoconazole and primaquine on the pharmacokinetics and tissue distribution of imatinib in mice

Gian Wan Soo, Jason H.K. Law, Elaine Kan, Shin Yee Tan, Wei Yin Lim, Grace Chay, Nadeem I. Bukhari and Ignacio Segarra

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Abstract

Imatinib, a selective inhibitor of c-KIT and Bcr-Abl tyrosine kinases, approved for the treatment of chronic myelogenous leukemia and gastrointestinal stromal tumors, shows further therapeutic potential for gliomas, glioblastoma, renal cell carcinoma, autoimmune nephritis and other neoplasms. It is metabolized by CYP3A4, is highly bound to alpha-1-acid glycoprotein and is a P-glycoprotein substrate limiting its brain distribution. We assess imatinib's protein binding interaction with primaquine, which also binds to alpha-1-acid glycoprotein, and its metabolic interaction with ketoconazole, which is a CYP3A4 inhibitor, on its pharmacokinetics and biodistribution. Male ICR mice, 9-12 weeks old were given imatinib PO (50 mg/kg) alone or co-administered with primaquine (12.5 mg/kg), ketoconazole (50 mg/kg) or both, and imatinib concentration in the plasma, kidney, liver and brain was measured at prescheduled time points by HPLC. Noncompartmental pharmacokinetic parameters were estimated. Primaquine increased 1.6-fold plasma AUC(0)→infinity, C(Max) decreased 24%, T(Max) halved and t(1/2) and mean residence time were longer. Ketoconazole increased plasma AUC(0)→infinity 64% and doubled the C(Max), but this dose did not affect t(1/2) or mean residence time. When ketoconazole and primaquine were co-administered, imatinib AUC(0)→infinity and C(Max) increased 32 and 35%, respectively. Ketoconazole did not change imatinib's distribution efficiency in the liver and kidney, primaquine increased it two-fold and it was larger when both the drugs were co-administered with imatinib. Ketoconazole did not change brain penetration but primaquine increased it approximately three-fold. Ketoconazole and primaquine affect imatinib clearance, bioavailability and distribution pattern, which could improve the treatment of renal and brain tumors, but also increase toxicity. This would warrant hepatic and renal functions monitoring.

Key words: bioavailability, drug–drug interaction, imatinib, ketoconazole, primaquine, tissue distribution

Syed Shahzad H, Alen YK, Wayne WG, Keivan A, Mudassir A, Goh GK.
Understanding of and attitudes toward epilepsy among the urban Chinese
population in Malaysia. Singapore Med J 2010; 51: 290-299

Understanding of and attitudes toward epilepsy among the urban Chinese population in Malaysia

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Abstract

Introduction:

People with epilepsy are socially discriminated against on the grounds of widespread negative public attitudes, misunderstandings and defensive behaviour. The primary purpose of this study was to evaluate the public understanding of and attitudes toward epilepsy among the Chinese population in Malaysia.

Methods:

A validated, self-administered questionnaire comprising 23 questions was utilised to evaluate the understanding of and attitudes toward epilepsy among randomly approached respondents from the Chinese population living in the urban areas of Penang, Klang Valley, Kuala Lumpur and Sibu in Malaysia.

Results:

Out of 1,000 people approached, 697 (69.7 percent) respondents agreed to participate in the study. When asked whether people with epilepsy are slow learners and have intellectual functioning below normal, 448 (64.3 percent) respondents answered 'no'. This positive answer was mainly provided by female (35.6 percent) as compared to male (28.6 percent) respondents. Moreover, more than half responded positively to the following statements: people with epilepsy should not be isolated from the normal population; epileptics can perform daily activities; epileptics can receive academic education; and epileptics can become useful members of society. In addition, significant associations were discovered between the education level of the respondents and several statements, including whether epileptics are as intelligent as everyone else (p-value is 0.009), whether epilepsy can be treated with drugs (p-value is 0.037) and whether epileptics can be as successful as other people in their chosen career (p-value is 0.009). Positive responses were mainly acquired from those with secondary education and above. A large number of the respondents felt that people with epilepsy should not be employed as lorry drivers, firefighters, doctors and army personnel.

Conclusions:

The general Chinese population in the urban areas of Malaysia had, at the time of the investigation, a relatively high level of understanding and positive attitudes toward certain aspects of epilepsy, although a minority of the study population demonstrated prejudice and discriminatory behaviours toward people with epilepsy.

Key words: attitudes, Chinese, epilepsy, understanding, urban areas

Syed Shahzad H, Choon Keong See, Christopher Lee Kwok Choong, Syed Imran A, Keivan A, Mudassir A. Reasons, perceived efficacy, and factors associated with complementary and alternative medicine use among Malaysian patients with HIV/AIDS. *The J Alternat Complementary Med* 2010; 16(11): 1171-1176

Reasons, perceived efficacy, and factors associated with complementary and alternative medicine use among Malaysian patients with HIV/AIDS

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²Department of Medicine, Hospital Sungai Buloh, Selangor, Malaysia

Abstract

Objectives:

The primary objective of this study was to evaluate the pattern of use, reasons for use, and perceived effect of complementary and alternative medicine (CAM), accompanied by identification and comparison of the factors that are potentially associated with CAM use.

Design:

This cross-sectional study was carried out in 325 randomly sampled patients with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), at HIV/AIDS referral clinics in the Hospital Sungai Buloh, Malaysia. Simple random sampling was used, where randomization was done using patients' medical record numbers.

Subjects and methods: Semistructured face-to-face interviews were conducted using 38 questions pertaining to type, pattern, perceived efficacy, adverse effects, and influential factors associated with CAM use. In addition, CD4 count and viral load readings were recorded.

Results:

Of 325 randomly sampled patients with HIV/AIDS, 254 of them were using some forms of CAM, resulting in a utilization rate of 78.2%. Vitamins and supplements (52.6%), herbal products (33.8%), and massage (16.6%) were the top three most frequently used CAM modalities. Sociodemographic factors including education level ($p = 0.021$, $r_s = 0.148$), monthly income ($p = 0.001$, $r_s = 0.260$), and family history of CAM use ($p = 0.001$, $r_s = 0.231$) were significantly associated and positively correlated with CAM use. However, the majority of these patients (68%) did not disclose CAM use to health care professionals. About half of those who rated their health as good or very good perceived it as a result of CAM use.

Conclusions:

This study confirmed the range of 30%–100% CAM use among individuals infected with HIV/AIDS. Although, on the one hand some types of CAM reduced viral load and enhanced the immune system, on the other hand some forms of CAM produced a detrimental effect on the virological suppression, opening this platform to more research and investigation in order to optimize the use of CAM among patients with HIV/AIDS.

Syed Shahzad H, David CWK, Keivan A, Wong PS, Ahmed SI, Sathvik BS, Hassali AH, Ernieda MH, Hadi MA, Low BY, Benny E. Influences on Malaysian pharmacy students' career preferences. *Am J Pharm Educ* 2010; 74(9): 1- 6

Influences on Malaysian pharmacy students' career preferences

Hasan SS^a, Kwai Chong DW^a, Ahmadi K^a, Se WP^a, Hassali MA^b, Hata EM^c, Hadi MA^d, Sridhar SB^a, Ahmed SI^a, Yean LB^a, Efendie B^a

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Abstract

Objectives:

To identify and evaluate factors affecting the career preferences of fourth-year bachelor of pharmacy (BPharm) students in Malaysia in the presence of a 4-year period of mandatory government service.

Methods:

A validated self-administered questionnaire was used in this cross-sectional study to collect data from final-year BPharm students enrolled at 3 government-funded universities and 1 private university in Malaysia. Both descriptive and inferential statistics were used for data analysis.

Results:

Three hundred fourteen students responded (213 from public universities and 101 from the private university). Approximately 32% of public university students and 37% of private university students ranked their own interest in pharmacy as the reason for undertaking pharmacy degree studies; 40.4% of public and 19.8% of private university respondents stated that they would enter a nonpharmacy-related career upon graduation if given the choice. Public university students ranked hospital pharmacy as their choice of first career setting (4.39, $p = 0.001$), while private students ranked community pharmacy first (4.1, $p = 0.002$). On a scale of 1 to 5, salary received the highest mean score (3.9 and 4.0, $p = 0.854$) as the extrinsic factor most influencing their career choice.

Conclusions:

Final-year students at Malaysian public universities were most interested in hospital pharmacy practice as their first career step upon graduation, while private university students were most interested in community pharmacy. The top 3 extrinsic factors rated as significant in selecting a career destination were salary, benefits, and geographical location.

Key words: career, graduate, Malaysia, pharmacy students

Tamilvanan S. Microbial colonization of medical devices and novel preventive strategies. *Recent Pat Drug Deliv Formul* 2010; 4: 153-173

Microbial colonization of medical devices and novel preventive strategies

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Abstract

Upon implantation or insertion into patient's body for exerting the intended purpose like salvage of normal functions of vital organs, the medical devices are unfortunately becoming the sites of competition between host cell integration and microbial adhesion. Moreover, since there is an increased use of implanted medical devices, the incidence of biofilm-and medical devices-related nosocomial infections is also increasing progressively. To control microbial colonization and subsequent biofilm formation of the medical devices, different approaches either to enhance the efficiency of certain antimicrobial agents or to disrupt the basic physiology of the pathogenic microorganisms including novel small molecules and antipathogenic drugs are being explored. In addition, the various lipid-and polymer-based drug delivery carriers are also investigated for applying antibiofilm coating of the medical devices especially over catheters. The main intention of this review is therefore to summarize the major and/breakthrough inventions disclosed in patent literature as well as in research papers related to microbial colonization of medical devices and novel preventive strategies. This review starts with an overview of the preventive strategies followed by a short description about the potential of different lipidic-and polymeric-drug delivery carriers in eradicating the biofilm-associated infections from the medical devices.

Key words: Catheters, colonization, implants, liposomes, microbial biofilm, medical devices, quorum sensing

Tamilvanan S, Ajith Kumar B, Senthilkumar SR, Raj Baskar, Raja Sekharan T. Stability assessment of injectable castor oil-based nano-sized emulsion containing cationic droplets stabilized by poloxamer–chitosan emulsifier films. AAPS PharmSciTech 2010; 11: 904-909

Stability assessment of injectable castor oil-based nano-sized emulsion containing cationic droplets stabilized by poloxamer–chitosan emulsifier films

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Abstract

The objectives of the present work were to prepare castor oil-based nano-sized emulsion containing cationic droplets stabilized by poloxamer–chitosan emulgator film and to assess the kinetic stability of the prepared cationic emulsion after subjecting it to thermal processing and freeze–thaw cycling. Presence of cryoprotectants (5%, w/w, sucrose +5%, w/w, sorbitol) improved the stability of emulsions to droplet aggregation during freeze–thaw cycling. After storing the emulsion at 4°C, 25°C, and 37°C over a period of up to 6 months, no significant change was noted in mean diameter of the dispersed oil droplets. However, the emulsion stored at the highest temperature did show a progressive decrease in the pH and zeta potential values, whereas the emulsion kept at the lowest temperatures did not. This indicates that at 37°C, free fatty acids were formed from the castor oil, and consequently, the liberated free fatty acids were responsible for the reduction in the emulsion pH and zeta potential values. Thus, the injectable castor oil-based nano-sized emulsion could be useful for incorporating various active pharmaceutical ingredients that are in size from small molecular drugs to large macromolecules such as oligonucleotides.

Key words: castor oil, chitosan, nano-sized emulsion, poloxamer, stability

Tan KL. Mother-infant bed-sharing in Klang District, Peninsular Malaysia. *Asean-Oceanian J Pediatr and Child Health* 2010; 7: 6-16

Mother-infant bed-sharing in klang district, peninsular Malaysia

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Abstract

The aims of the study were to determine the prevalence and identify factors associated with mother-infant bed-sharing among one, three and six-month-old infants in Klang District, Peninsular Malaysia. This was a cross-sectional study involving 682 mother-infant pairs with infants aged one, three and six months attending government clinics in Klang district, Peninsular Malaysia. Data were collected by face-to-face interview using a pretested structured questionnaire for a four-month period in 2006. Data regarding maternal factors, infant factors and breastfeeding practice were collected. Data on bed-sharing were based on practice in the past one month period. Bed-sharing was defined as an infant sharing a bed with mother, and infant must within arm's reach from the mother, whereas a bed was defined as either a sleeping mattress placed on a bed frame or placed on the floor. The overall prevalence of bed-sharing among mothers with infants aged between one and six months was 73.5% (95% confidence interval: 70.0, 76.7). The prevalence of bed-sharing among infants aged one, three and six months were 74.8%, 69.9% and 75.6% respectively. On multivariate analysis; area, maternal ethnicity, maternal smoking status and breastfeeding practice seemed to have the strongest association with bed-sharing.

Key words: Bed-sharing, Mother-infant, Breastfeeding, Peninsular Malaysia

Tan NH, Fung SY, Ponnudurai G. Enzymatic and immunologic properties of Bungarusflaviveps (red-headed krait) venom. J Venom Anim Toxins incl Trop Dis 2010; 16(1), 147-154

Enzymatic and immunological properties of Bungarus flaviceps (red-headed krait) venom

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Abstract

Bungarus flaviceps (red-headed krait) venom presents an intravenous LD50 of 0.32 µg/g and exhibits enzymatic activities similar to other Bungarus toxins. ELISA cross-reactions between anti-Bungarus flaviceps and a variety of elapid and viperid venoms were observed in the current study. Double-sandwich ELISA was highly specific, since anti-B. flaviceps serum did not cross-react with any tested venom, indicating that this assay can be used for species diagnosis in B. flaviceps bites. In the indirect ELISA, anti-B. flaviceps serum cross-reacted moderately with three different Bungarus venoms (9-18%) and Notechis scutatus venom, but minimally with other elapid and viperid toxins. The results indicated that B. flaviceps venom shares common epitopes with other Bungarus species as well as with N. scutatus. The lethality of the B. flaviceps venom was neutralized effectively by antiserum prepared against B. candidus and B. flaviceps toxins and a commercial bivalent elapid antivenom prepared against B. multicinctus and Naja naja atra venoms, but was not neutralized by commercial antivenoms prepared against Thai cobra, king cobra and banded krait. These data also suggested that the major lethal toxins of B. flaviceps venom are similar to those found in B. multicinctus and B. candidus venoms.

Key words: Bungarus flaviceps venom, enzymes, ELISA, neutralization.

Teoh ML, Chu WL, Phang SM. Effect of temperature change on the physiology and biochemistry of algae: a review. *Malaysian J Sci* 2010; 29(2): 82-97

Effect of temperature change on physiology and biochemistry of algae: a review

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Abstract

The productivity and survival of algae are strongly affected by their physiological and biochemical processes, as well as biotic and abiotic factors in the environment. In recent years, global climate change such as increased temperature and elevated ultraviolet radiation (UVR) due to ozone depletion has huge impact on organisms particularly the ones in the marine ecosystem. It has been demonstrated that the global temperature increased steadily over the last decade, with an average of 0.74°C. In the coming years, climate model projections summarized by the Intergovernmental Panel of Climate Change (IPCC) indicate that average global surface temperature will likely rise a further 0.5 to 1.6°C by 2030, and rising to 1.1 to 6.4°C by 2100. As algae serve as the primary producer of food chain in both marine and terrestrial ecosystems, it is of great significance to understand the impact of temperature change on their physiological and biochemical processes. This review provides the information on how algae respond to temperature change based on their growth, biochemical composition and fatty acid composition.

Key words: Global warming, algae, temperature, biochemical composition, fatty acid

Teoh M, Narayanan P, Moo KS, Radhakrishman S, Pillappan R, Bukhari NI, Segarra I. HPLC determination of imatinib in plasma and tissues after multiple oral dose administration to mice. *Pak J Pharm Sci* 2010; 23: 35-41

HPLC determination of imatinib in plasma and tissues after multiple oral dose administration to mice

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Abstract

Imatinib inhibits Bcr-Abl, c-KIT and PDGFR kinases. It is approved for the treatment of chronic myeloid leukemia (CML), gastrointestinal stromal tumors (GIST) and has further therapeutic potential. Male ICR mice were given imatinib PO (50 or 25 mg/kg, 5 doses every 2 h); euthanized 2 h after the last dose administration; plasma, liver, brain, spleen and kidney were collected and imatinib concentration measured by an optimized HPLC method for quantification in tissues. Methanol (1:1 v/v plasma) and pH 4, 40:30:30 (v/v/v) atermethanol- acetonitrile at 5 ml/g (brain) and 10 ml/g (spleen, kidney, liver) ratio was added to the samples, homogenized, sonicated, centrifuged (15,000 rpm, 5 min, 2°C) and the supernatant injected into an Inertsil® CN-3 column (4.6 mm x 150 mm, 5 µm) using 64:35:1 (v/v/v) water-methanol-triethylamine (pH 4.8), flow rate 1 ml/min, 25°C. Imatinib eluted at 7.5 min (268 nm). Linearity: 0.1-50 µg/ml; precision, accuracy, inter- and intra-day variability was within 15%. Recovery was above 95% (plasma), 80% (brain) and 90% (kidney, liver, spleen). Imatinib tissue concentrations were 6-8 folds higher than plasma except brain, where the ratio decreased from 0.24 to 0.08 suggesting limited brain penetration, likely due to blood brain barrier efflux transporters. The extensive distribution supports the expansion of therapeutic applications.

Key words: Imatinib, tissue distribution, brain, HPLC.

Tiong Alexander Kah Lord, Mohandas K, Somanath SD, Ambu S. Multidrug resistant yeasts in synanthropic wild birds. *Ann ClinMicrobiolAntimicrob* 2010; 9:11

Multidrug resistant yeasts in synanthropic wild birds

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Abstract

Background:

The aim of this study was to investigate the presence of multidrug resistant yeasts in the faeces of synanthropic wild birds from the Bangsar suburb of Kuala Lumpur.

Methods:

Species characterisations of yeast isolates and determinations of antimycotic susceptibility profiles were undertaken using the commercial characterization kit, Integral System Yeasts Plus (Liofilchem, Italy).

Results:

Fourteen species of yeasts were detected in the bird faecal samples. *Candida albicans* was present in 28.89% of bird faecal samples, *Candida krusei* (13.33%), *Candida tropicalis* (4.44%), *Candida glabrata* (4.44%), *Candida parapsilosis* (2.22%), *Candida lambica* (2.22%), *Candida stellatoidea* (2.22%), *Candida rugosa* (2.22%) and *Candida lusitaniae* (2.22%). Amongst the non-candidal yeast isolates, *Cryptococcus laurentii* was present in 6.67% of bird faecal samples, *Cryptococcus uniguttulatus* (4.44%), *Saccharomyces cerevisiae* (4.44%), *Trichosporon pullulans* (2.22%), *Trichosporon pullulans/Cryptococcus albidus* (8.89%) and *Rhodotorula rubra/Rhodotorula glutinis* (4.44%). Of the isolated yeasts, 18.1% (or 26/144) were found to be resistant to all 11 antimycotic agents they were tested against i.e. Nystatin, Amphotericin B, Flucytosine, Econazole, Ketoconazole, Clotrimazole, Miconazole, Itraconazole, Voriconazole, Fluconazole 16 and Fluconazole 64. 45.8% (or 66/144) of the bird faecal yeast isolates were resistant to four or more of the 11 antimycotic agents they were tested against.

Conclusions:

This finding is of public health significance as these synanthropic wild birds may be reservoirs for transmission of drug resistant yeast infections to humans.

Tiong KH, Yiap BC, Tan EL, Ismail R, Ong CE. Molecular cloning and functional analysis of cytochrome P450 2A6 (CYP2A6). *Asia Pacific J Molecular Biology and Biotechnology* 2010; 18 (3): 351-357

Molecular cloning and functional analysis of human cytochrome P450 2A6 (CYP2A6)

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Abstract

Human cytochrome P450 2A6 (CYP2A6) is a major hepatic isoenzyme that catalyses the metabolism of nicotine and cotinine. It also contributes, to a certain extent, to the metabolism of pharmaceutical agents (e.g. chlormethiazole) and coumarin-type alkaloids as well as in the metabolic activation of several procarcinogens such as aflatoxin B1. A full-length cDNA clone encoding the wild-type human CYP2A6 has been isolated from human liver total RNA. The CYP2A6 cDNA was amplified using oligonucleotide primers corresponding to 5'- and 3'-ends of the published CYP2A6 nucleotide sequence. The PCR product was inserted into pCWori+, the bacterial expression vector used in subsequent protein expression. The pCW-CYP2A6 construct was subjected to restriction analyses to verify its structure. Sequence analysis of the full-length cDNA revealed that the sequence was identical to that of the reported CYP2A6 wild-type clone. CYP2A6 was subsequently co-expressed with its co-enzyme, NADPH CYP-oxidoreductase (OxR) in *Escherichia coli* DH5 α cells. These two co-expressed proteins were able to form a fully functional NADPH-dependent monooxygenase which metabolized the substrate coumarin in isolated membrane fractions in a fluorescence-based assay. The developed assay serves as a convenient tool to investigate drug metabolism and drug interaction involving this isoenzyme.

Key words: cDNA cloning; Fluorescence-based coumarin 7-hydroxylase assay; Heterologous expression; Human CYP2A6; Kinetic analyses.

Tiong KH, Yiap BC, Tan EL, Rusli Ismail, Ong CE. In vitro modulation of naturally occurring flavonoids on cytochrome P450 2A6 (CYP2A6) activity. *Xenobiotica* 2010; 40(7):458-466

In vitro modulation of naturally occurring flavonoids on cytochrome P450 2A6 (CYP2A6) activity

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Abstract

The effect of flavonoids on coumarin 7-hydroxylation, an activity marker of an important human liver cytochrome P450 isoform, cytochrome P450 2A6 (CYP2A6), was investigated in this study. Coumarin 7-hydroxylase activity was measured fluorometrically in reaction mixtures containing cDNA-expressed CYP2A6, nicotinamide adenine dinucleotide phosphate generating system and 10 μ M coumarin, at various concentrations of flavonoids. Among the 23 compounds tested, most of the active members were from flavonol group of hydroxylated flavonoids, with myricetin being the most potent inhibitor followed by quercetin, galangin, and kaempferol. Further exploration of the inhibition mechanism of these compounds revealed that myricetin, galangin, and kaempferol exhibited mixed-type of inhibition pattern while quercetin was observed to exhibit competitive mode of inhibition. Structure-function analyses revealed that degree of inhibition was closely related to the number and location of hydroxyl groups, glycosylation of the free hydroxyl groups, degree of saturation of the flavane nucleus as well as the presence of the alkoxyated function.

Key words: Flavonoids, coumarin 7-hydroxylation, cDNA-expressed CYP2A6, inhibition

Tiong KH, Yiap BC, Tan EL, Rusli Ismail, Ong CE. Functional characterization of cytochrome P450 2A6 (CYP2A6) allelic variants CYP2A6*15, CYP2A6*16, CYP2A6*21 and CYP2A6*22*. *Drug Metabolism Disposition* 2010; 38:745-751

Functional characterization of cytochrome P450 2A6 allelic variants CYP2A6*15, CYP2A6*16, CYP2A6*21, and CYP2A6*22

Kai Hung Tiong, Beow Chin Yiap, Eng Lai Tan, Rusli Ismail, and Chin Eng Ong

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Abstract

Variation in CYP2A6 levels and activity can be attributed to genetic polymorphism and, thus, functional characterization of allelic variants is necessary to define the importance of CYP2A6 polymorphism in humans. The aim of the present study was to investigate the reported alleles CYP2A6*15, CYP2A6*16, CYP2A6*21, and CYP2A6*22, in terms of the functional consequences of their mutations on the enzyme catalytic activity. With use of the wild-type CYP2A6 cDNA as template, site-directed mutagenesis was performed to introduce nucleotide changes encoding K194E substitution in CYP2A6*15, R203S substitution in CYP2A6*16, K476R substitution in CYP2A6*21, and concurrent D158E and L160I substitutions in CYP2A6*22. Upon sequence verification, the CYP2A6 wild-type and mutant constructs were individually coexpressed with NADPH-cytochrome P450 reductase in *Escherichia coli*. A kinetic study using a coumarin 7-hydroxylase assay indicated that CYP2A6*15 exhibited higher V_{max} than the wild type, whereas all mutant constructs, except for variant CYP2A6*16, exhibited higher K_m values. Analysis of the V_{max}/K_m ratio revealed that all mutants demonstrated 0.85- to 1.05-fold differences from the wild type, with the exception of variant CYP2A6*22, which only portrayed 39% of the wild-type intrinsic clearance. These data suggested that individuals carrying the CYP2A6*22 allele are likely to have lower metabolism of CYP2A6 substrate than individuals expressing CYP2A6*15, CYP2A6*16, CYP2A6*21, and the wild type.

VeJayan J, Shin Yee L, Ponnudurai G, Ambu S, Ibrahim I. Protein profile analysis of Malaysian snake venoms by two-dimensional gel electrophoresis. *J Venom Anim Toxins Incl Trop Dis* 2010; 16: 623-630

Protein profile analysis of Malaysian snake venoms by two-dimensional gel electrophoresis

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Abstract

Snake venoms comprise a highly complex mixture of proteins, which requires for their characterization the use of versatile two-dimensional electrophoresis techniques. In the present study, venoms obtained from eight snakes (*Ophiophagus hannah*, *Naja kaouthia*, *Naja sumatrana*, *Bungarus fasciatus*, *Trimeresurus sumatranus*, *Tropidolaemus wagleri*, *Enhydrina schistosa* and *Calloselasma rhodostoma*) commonly found in Malaysia were separated based on two independent properties, isoelectric point (pI) and molecular weight (MW). Many differences in snake venoms at the inter-family, inter-subfamily, inter-genus and inter-species levels were revealed. Notably, proteins from individuals of the Viperidae family – *Trimeresurus sumatranus*, *Tropidolaemus wagleri* and *Calloselasma rhodostoma* – were found to be numerous and scattered by the two-dimensional gel electrophoresis (2DE) specifically in regions between 37 and 100 kDa compared to the Elapidae venom proteins. The latter were clustered at the basic and lower molecular mass region (less than 20 kDa). Trains of spots were commonly observed, indicating that these proteins may be derived from post-translational modifications. *Ophiophagus hannah* (Elapidae) revealed a great amount of protein spots in the higher molecular mass range when compared to *Enhydrina schistosa*, *Naja kaouthia*, *Naja sumatrana* and *Bungarus fasciatus*. Overall 2DE showed large differences in the venom profile of each species, which might be employed as an ancillary tool to the identification of venomous snake species.

Key words: snake venom, protein profile analysis, two-dimensional gel electrophoresis, SDS-PAGE.

Wan YC. Student nurses' perceptions towards the learning of biological sciences: a comparative study between a teaching and a private hospital. J Malaysian Nurses Association 2010; 4: 3-9

Student nurses' perceptions towards the learning of biological sciences: a comparative study between a teaching and a private hospital

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Abstract

The Diploma in Nursing Program provides nursing students with the knowledge of biological, social and behavioural sciences. The majority of students expressed difficulties and anxieties in learning the biological sciences. A study was carried out to explore first year students' perceptions of their learning of the biological sciences in nursing. The study consisted of 108 nursing students (97.3% response rate) from a teaching hospital and 82 respondents (96.4% response rate) from a private hospital. Resulting data were computed to the SPSS 11.0 system. The majority, 88.9% (96) and 81.7% (67) from the teaching and private hospitals respectively expressed that it was very important to have a good background of basic sciences (biology, chemistry, physics) prior to their enrollment in nursing and would influence their learning of the biological sciences. Some 35.2% (38) and 58.5% (48) of the respondents from the teaching and private hospitals respectively, described their abilities in the learning of the biological sciences as average. The majority, 47.2% (51) and 48.8% (40) from the teaching and private hospitals respectively, expressed themselves as only moderately satisfied with their grades obtained from the biological science subjects' assessment results. Spearman's rank order correlation analysis indicated that respondents with science background had increased abilities in learning biological sciences and were more satisfied with overall assessment results ($p < 0.05$). The majority respondents 74.0% (80) and 57.4% (47) from the teaching and private hospitals respectively commented that there was too much detail and insufficient time in the biological sciences' curriculum. Respondents commented that learning objectives, pre-reading lists, lecture notes were helpful and revealed a strong preference for the lecture-oriented approach. Implications of the findings were discussed. Strategies such as reviewing students' entrance criteria, course organisation and appropriate teaching modalities should be considered.

Key words; Biological sciences, perceptions, nurse education, student nurses

Wong NL, Achike FI. Gender discrimination in the influence of hyperglycemia and hyperosmolarity on rat aortic tissue responses to insulin. *Reg. Peptides*, 2010; 163: 113-119

Gender discrimination in the influence of hyperglycemia and hyperosmolarity on rat aortic tissue responses to insulin

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Abstract

Hyperglycaemia initiates endothelial dysfunction causing diabetic macro- and micro-vasculopathy, the main causes of morbidity and mortality in diabetes mellitus. The vasculopathy exhibits gender peculiarities. We therefore explored gender differences in comparing the effects of hyperglycaemia (50 mM) per se with its hyperosmolar (50 mM) effects on vascular tissue responses to insulin. Endothelium-intact or denuded thoracic aortic rings from age-matched male and female Sprague–Dawley rats were incubated for 10 min or 6 h (acute versus chronic exposure) in normal, hyperglycaemic or hyperosmolar Krebs solution. Relaxant responses to insulin (6.9×10^{-7} – 6.9×10^{-5} M) of the phenylephrine-contracted tissues were recorded. Endothelium denudation in both genders inhibited relaxation to insulin in all conditions, more significantly in female than in male tissues, suggesting the female response to insulin is more endothelium-dependent than the male. Acutely and chronically exposed normoglycemic endothelium-intact or -denuded tissues responded similarly to insulin. Chronic hyperglycemic or hyperosmolar exposure did not alter the endothelium-denuded tissue responses to insulin, whereas the responses of the endothelium-intact male and female hyperosmolar, and male hyperglycemic tissues were enhanced. The results show that insulin exerts an endothelium-dependent and independent relaxation with the female tissue responses more endothelium-dependent than the male. The data also suggest that hyperosmolarity per se enhances aortic tissue relaxant responses to insulin whereas hyperglycemia per se inhibits the same and more so in female than male tissues. These effects are endothelium-dependent.

Key words: Hyperglycemia; Osmolarity; Insulin vasorelaxation; Gender differences

Wong SF, Mak JW. *Candida parapsilosis*-specific monoclonal antibodies and their use for detection of candida antigens in experimental systemic candidiasis. *Hybridoma* 2010; 29(6): 539-546; Doi: 10.1089/hyb.2010.0049

Candida parapsilosis-specific monoclonal antibodies and their use for detection of candida antigens in experimental systemic candidiasis

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Department of Pathology, International Medical University, Kuala Lumpur, Malaysia

Abstract

Candida parapsilosis has emerged as one of the most common causes of bloodstream infection worldwide. The diagnosis of invasive candidiasis etiological agents to the species level remains a laboratory and clinical challenge. Thus, specific monoclonal antibodies to detect systemic candidiasis and to identify *Candida* virulence factors and associated pathogenesis through immunohistochemistry would be very useful. Inbred Balb/c mice were immunized with *C. parapsilosis* antigens, and blood was checked for the presence of reactive antibodies using ELISA. Fusion was performed using the harvested spleen cells and NS1 myeloma cells, and the clones were screened for the presence of antibody producing hybrid cells by dot-blot. The 1B11 clone secreted IgG2a monoclonal antibody that was reactive with the *C. parapsilosis* antigen at MW of 59 kDa and cross-reacted with *C. tropicalis* but not with other fungal and bacterial antigens tested. Another 3D1 clone secreted IgG1 monoclonal antibody that was reactive with *C. parapsilosis* antigen at MW of 30 kDa. The 3D1 monoclonal antibody was found to be species specific. Experimental systemic candidiasis in rats was induced through intravenous injection of *C. parapsilosis*, and all the vital organs were collected for immunohistochemistry study. These monoclonal antibodies were reactive against surface epitopes on the yeast cells, pseudohyphae, and immune complexes in tissue sections. Sandwich ELISAs using these antibodies were developed and were able to detect circulating antigens in experimental candidiasis in rats at 0.2 µg/µL. These monoclonal antibodies may have potential as primary capture antibodies for the development of rapid diagnostic test for human systemic fungal infection.

Wong RSY, Shar Mariam M, Nadarajah VD, Tengku Alma T Ibrahim.
Characterisation of the binding properties of *Bacillus thuringiensis* 18 toxin on leukaemic cells. *J Exp Clin Cancer Res* 2010; 29:86

Characterisation of the Binding Properties of *Bacillus Thuringiensis* 18 Toxin on Leukaemic Cells

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Abstract

Background:

Various strains of *Bacillus thuringiensis* (Bt) have been found to produce parasporal proteins that are cytotoxic to human cancer cells. This study aims to establish the binding affinity of purified Bt 18 toxin for CEM-SS (T lymphoblastic leukaemia cell line), to determine if competition exists between the toxin and commercial anticancer drugs for the binding site on CEM-SS and to localise the binding site of the toxin on CEM-SS.

Methods:

In homologous competitive binding study, the purified toxin was labelled with biotin and allowed to compete with unlabelled toxin for binding sites on CEM-SS and its dissociation constant (Kd) was determined. Comparisons were made with CCRF-SB, CCRF-HSB-2 and MCF-7. In heterologous competitive binding study, biotinylated toxin competition was determined with two other Bt toxins (crude Btj and crude Bt 22) and anticancer drugs (cisplatin, doxorubicin, etoposide, navelbine and methotrexate). To localise the binding site under the confocal microscope, the biotinylated toxin was tagged with FITC-conjugated streptavidin.

Results:

Homologous competitive binding assays revealed decreasing binding affinity of Bt 18 toxin for CEM-SS, CCRF-SB, and CCRF-HSB-2 with Kd of 8.44 nM, 14.98 nM and 17.71 nM respectively. Kd for MCF-7 was not determined as the inhibitory concentration (IC₅₀) was not reached. Heterologous competitive study showed little competition (< 30%) between biotinylated Bt 18 toxin and all test compounds used. Confocal microscopy revealed binding of toxin at the periphery of the cell.

Conclusions:

It was postulated that purified Bt 18 toxin binds on the cell surface of CEM-SS and the mechanism of cell death may differ from that of Btj toxin, Bt 22 toxin and all five anticancer drugs used in this study, since it did not significantly compete with these compounds for the same binding site.

Yadav H. Breastfeeding practices in a rural community in Kedah, JUMMEC 2010; 13(1): 38-44

Breastfeeding practices in a rural community in Kedah

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Abstract

Breast feeding has been actively encouraged in Malaysia in the last few years in all public hospitals. This study proposes to find out the prevalence of breast feeding in three villages in a rural community in Kedah, Malaysia. This was a cross sectional study on breastfeeding practices in Kubang Pasu, a district of Kedah. Majority of the mothers initiated breast feeding but exclusive breastfeeding was only 21% for four months and predominant breastfeeding was about 12.6%. The breastfeeding practice was more prevalent among women from the higher educational strata and higher income than those from the lower strata and lower income ($p < 0.05$). Mothers with a positive attitude on breastfeeding and those who possess a higher knowledge were associated with a longer mean total duration of breastfeeding ($p < 0.05$). Spouse and family members played an important role in building up a mother's confidence to breast feed her child. Majority of the mothers received breast feeding information before birth from mainly the doctors and nurses. Older mothers, house wives and mothers with formal education practiced a longer duration of breast feeding ($p < 0.05$). The study also showed that there is an increase in the knowledge of breast feeding among the mothers and that they have a positive attitude to breastfeeding. Most of the mothers initiated breast feeding early and they received support on breastfeeding from the nurses and doctors.

Key words: exclusive breastfeeding, predominant breastfeeding, rural Malaysia

Yeap Swan Sim, Emily Man Lee Goh, Das Gupta E. Knowledge about osteoporosis in a Malaysian population. *Asia Pac J Public Health*, 2010; 22: 233-241

Knowledge about osteoporosis in a Malaysian population

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²Gleneagles Intan Medical Centre, Kuala Lumpur

³International Medical University, Seremban, Malaysia

Abstract

To determine the depth and sources of knowledge about osteoporosis (OP) among the public in Malaysia. A self-administered questionnaire was distributed to attendees of health-related public forums. A total of 87.1% of the attendees had heard of OP. Of these, 89.5% were concerned about getting OP. Significantly more women than men ($P=.015$), those with more than 10 years of schooling ($P<.001$), and those earning more than \$US285 per month ($P=.022$) had heard of OP. Knowledge of OP risk factors was good: 97.1% identified low calcium intake, 87.8% lack of exercise, 80.0% family history of OP, and 75.8% postmenopausal status. A total of 38.7% of the attendees thought that OP was more serious than cancer and 35.1% more serious than heart disease; 55.7% obtained information about OP from newspapers and 46.6% from magazines. In this self-selected population, women, the better educated, and those earning higher incomes were more aware of OP. Knowledge of OP was obtained mainly from printed materials.

Key words: Asian, knowledge, osteoporosis, public

Yeo JL, Tan TCB, Achike FI. Exploring the mechanism of endothelial involvement in acidosis-induced vasodilatation of aortic tissues from normal and diabetic rats. *Eur J. Pharmacol* 2010; 642:99-106

Exploring the mechanism of endothelial involvement in acidosis-induced vasodilatation of aortic tissues from normal and diabetic rats

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Abstract

Acidosis modulates physiologic and pathophysiologic processes but the mechanism of acidotic vasodilatation remains unclear. We therefore explored this in aortic rings from normal and streptozotocin-induced diabetic Sprague–Dawley rats. Phenylephrine (PE)-induced contraction in endothelium-intact and -denuded rings were recorded under normal and acidotic pH with or without drug probes. Acidosis exerted a relaxant effect in endothelium-intact and -denuded euglycaemic and diabetic tissues. L-NAME or methylene blue partially inhibited acidotic relaxation in these endothelium-intact but not the -denuded tissues, with greater inhibition in the diabetic tissues, indicating that acidosis induces relaxation by endothelium-dependent and -independent mechanisms, the former being EDNO-cGMP mediated. Indomethacin had no effect on the tissues, indicating that cyclooxygenase products are neither involved in acidosis-induced vasodilatation nor in the modulation of phenylephrine-contraction. In euglycaemic tissues under normal pH, no K⁺ channel blocker altered phenylephrine-contraction, but all (except glibenclamide) enhanced diabetic tissue contraction, indicating that normally, these channels (K_{ir}, K_v, BK_{Ca}, K_{ATP}) do not modulate phenylephrine-contraction, but they (except K_{ATP}) are expressed in diabetes where they attenuate phenylephrine-induced contraction and modulate acidosis. Only the K_{ir} channel modulates acidotic relaxation in euglycaemic tissues. Only tetraethylammonium and iberiotoxin enhanced phenylephrine-induced contraction in endothelium-denuded diabetic tissues indicating that BK_{Ca} attenuates phenylephrine-contraction and that acidotic relaxation in this condition is modulated by a tetraethylammonium-sensitive mechanism. In conclusion, acidosis causes vasodilatation in normal and diabetic tissues via endothelium-dependent and -independent mechanisms differentially modulated by a combination of a NO-cGMP process and K⁺ channels, some of which are dormant in the normal state but activated in diabetes mellitus.

Key words: Acidosis; EDRF; Potassium channels; Diabetes mellitus

Zeeshan F, Bukhari NI. Development and evaluation of a novel modified-release pellet-based tablet system for the delivery of loratadine and pseudoephedrine hydrochloride as model drugs. *AAPS Pharm Si Tech* 2010; 11: 910-916

Development and evaluation of a novel modified-release pellet-based tablet system for the delivery of loratadine and pseudoephedrine hydrochloride as model drugs

Farrukh Zeeshan and Nadeem Irfan Bukhari

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Abstract

Modified-release multiple-unit tablets of loratadine and pseudoephedrine hydrochloride with different release profiles were prepared from the immediate-release pellets comprising the above two drugs and prolonged-release pellets containing only pseudoephedrine hydrochloride. The immediate-release pellets containing pseudoephedrine hydrochloride alone or in combination with loratadine were prepared using extrusion-spheronization method. The pellets of pseudoephedrine hydrochloride were coated to prolong the drug release up to 12 h. Both immediate- and prolonged-release pellets were filled into hard gelatin capsule and also compressed into tablets using inert tableting granules of microcrystalline cellulose Ceolus KG-801. The *in vitro* drug dissolution study conducted using high-performance liquid chromatography method showed that both multiple-unit capsules and multiple-unit tablets released loratadine completely within a time period of 2 h, whereas the immediate-release portion of pseudoephedrine hydrochloride was liberated completely within the first 10 min of dissolution study. On the other hand, the release of pseudoephedrine hydrochloride from the prolonged release coated pellets was prolonged up to 12 hr and followed zero-order release kinetic. The drug dissolution profiles of multiple-unit tablets and multiple-unit capsules were found to be closely similar, indicating that the integrity of pellets remained unaffected during the compression process. Moreover, the friability, hardness, and disintegration time of multiple-unit tablets were found to be within BP specifications. In conclusion, modified-release pellet-based tablet system for the delivery of loratadine and pseudoephedrine hydrochloride was successfully developed and evaluated.

Key words: extrusion–spheronization; loratadine; modified-release multiple-unit tablet; pseudoephedrine hydrochloride.

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Malaysia Shape of the Nation (MySoN): a primary care based study of abdominal obesity in Malaysia

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Abstract

Abdominal obesity (AO), measured by waist circumference (WC), is a stronger predictor of subsequent development of cardiovascular disease (CVD) than generalised obesity, which is measured by body mass index (BMI). This study aimed to measure WC and prevalence of AO in Malaysians visiting primary care physicians. 1893 patients between the ages of 18 and 80 attending primary care clinics in Malaysia were recruited over two days for this multi-centre cross-sectional study. Pregnant women were excluded, their medical history, weight, height and WC were examined. The prevalence of co-morbidities were as follows: (1) CVD-4%, lipid disorder-17%, hypertension-26%, diabetes-14% and any of the clinical characteristics of CVD/lipid disorder/hypertension/diabetes-38%. The mean BMI for men and women was 25.62 +/- 4.73 kg/m² and 26.63 +/- 5.72 kg/m², respectively. Based on WHO criteria for BMI (overweight, 25-29.9 kg/m²; obese, > 30 kg/m²), 34.2% were overweight and 20.4% were obese. The mean WC for men and women was 89.03 +/- 13.45 cm and 84.26 +/- 12.78 cm, respectively. Overall, 55.6% had AO and there was higher prevalence among women (based on International Diabetes Federation criteria: WC > or = 90 cm for men and > or = 80 cm for women). AO was present in approximately 71% patients with lipid disorder, in 76% with hypertension and in 75% with diabetes. Patients with AO were also at a higher risk of developing co-morbidities. Malaysia has a high prevalence of AO and associated cardiovascular risk factors. This needs to be addressed by public health programs, which should also include routine measurement of WC.