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Editorial

Health care costs have been growing rapidly in the past several decades, in some countries the total health care expenditure per capita has increased three to fourfold. The total health care expenditure in Malaysia also has increased from USD 128 in 2000 to USD 367 in 2010 (WHO, 2010), about threefold increase in 10 years. Next year (2013) the government has allocated 19.2 billion dollars on health sector, an increase of 15% from the year 2012. This amount covers slightly more than half of the expected total health care expenditure of the country. Thus patients and private health financing bodies have to contribute to the deficit.

The primary drivers for the increase in health care cost include the changes in diseases pattern and the escalation of drug's price. Improvements in the socioeconomic and technology advancement have influence the life style of the public, and subsequently, the incident of life style associated diseases (Gupta et al., 2012). The use of tobacco, unhealthy diet, insufficient physical exercise and overuse of alcohol contributed to the increase in obesity, diabetes, cardiovascular, cancers, respiratory diseases, mental illness and other non communicable diseases.

Another contributor to the health care cost is the increase in the price of the drugs. The drug prices in Malaysia were higher compared to international reference price, by about 15 to 16 times higher for innovator drugs and 6 to 7 times higher for generic drugs (ZUD Barber et al., 2007). Due to the price difference, most patients and prescribers have shifted to the use of generic drugs (CC Ping et al., 2008), however, the price of the generic drugs in Malaysia also varied depending on the number of generic brands and geographical location (O Fatokun et al., 2011).

To regulate the drug price, the Malaysian Pharmaceutical Services Division has published Medicine Price List which includes the recommended retail price for Non Essential Drugs and Private Sector Retail Price List in 2010 and 2011. The effect of these published lists on the price of drug that a patient has to pay is yet to be evaluated. Until a health policy is formulated and enforced to control and regulate the price of drug in this country, the public will continue to face an ever increasing drug cost.

Editor-in-Chief

Assessment of Malaysian Clinical Practice Guidelines

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Abstract

The Ministry of Health Malaysia (MOH) coordinates the development of Clinical Practice Guidelines (CPGs) in Malaysia, in collaboration with the Academy of Medicine of Malaysia (AMM). This study assessed the methodological quality of 29 Malaysian national CPGs which were developed since 2000 to 2003 using Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument. The study showed high score for only domains on Scope & Purpose as well as Clarity & Presentation (68%, 75% respectively).

Keywords: clinical practice guidelines, AGREE instrument, appraisal of guidelines, Malaysian CPGs.

Introduction

Assessment of the national Malaysian Clinical Practice Guidelines (AMCPG) using Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument was proposed to study the methodological quality in the development of Clinical Practice Guidelines (CPGs) in Malaysia.

The Ministry of Health (MOH) coordinates the development of evidence-based CPGs in Malaysia. This was a collaborative effort between Ministry of Health Malaysia (MOH) and Academy of Medicine Malaysia (AMM). The goal of the CPG development was to increase quality in the delivery of health care services based on clinical evidence with scientific rigor.

This (AMCPG) Project was found to be worthy to be conducted in Malaysia, in view of the fact that Malaysia had developed several CPGs. An evaluation of these developed CPGs could provide more information in improving the development of evidence-based CPGs in Malaysia. It is believed that evidence-based CPGs can help improve the delivery of health care, although proof to such claim has not been consistently demonstrated.

Evaluation of the CPG can be categorized into three levels[3, 4, 5] namely: 1) Examination of the process of guideline development, dissemination and implementation; 2) Measurement of the extent of implementation of the guideline and 3) Assessment of guidelines effect on patient outcomes and health care utilization. Another way of evaluation was to classify into two levels, namely quality of the CPG and later its effectiveness. Good development methodology using current best evidence will determine the quality of the CPG. A "good quality guideline" is the one that ultimately leads to improve patient outcome. However, the

quality of a guideline is indirectly measured by assessing in whatever degree guideline producers minimized potential biases that could occur in the development process and affect validity of its recommendations [6, 7, and 8]. Wrong recommendations affect the health professionals' credibility on guidelines, and consequently, limit their adoption.

In 1999, Shaneyfelt et al. assessed quality of CPG published in Medline between 1985 and 1997 by using systematically developed instrument. The majority of 279 assessed guidelines did not meet the pre-established methodological standards, being rigour of recommendations as one of the most deficiently reported [6, 9]. Similar results were reported by Cluzeau et al. [6, 10], Grilli et al. [6,11] and Graham et al. [6,12] in 1999, 2000 and 2001 respectively. In 2003 the AGREE collaboration (currently the AGREE Research Trust) published the results of the first international project aimed at developing and validating a generic instrument for guidelines assessment[7,8]. This instrument has been translated to different languages and extending its use throughout the world. In recent years, several studies showed methodological deficiencies of using the AGREE instrument in guideline development[6,13-15]

In Malaysia, although many different institutions are interested in CPG development, there is no information about the quality of the guidelines produced. The purpose of this research was to describe trends in guidelines production in Malaysia and to assess their quality by using the AGREE instrument.

Materials and methods

A cross-sectional study was undertaken in 2004 to describe guidelines production in Malaysia between years 2000-2003. Documents were considered as CPG if: 1) they included explicit recommendations targeted to health professional or health providers decision-making in managing diseases or condition, 2) the scope included related to screening and primary prevention, and/or diagnosis, and/or treatment and/or secondary prevention and/or rehabilitation; 3) they contained description of participants or responsible institutions and bibliographic references; 4) they were produced and diffused in the period of study (January 2000 to December 2003) and could be freely accessed. The exclusion criteria were: 1) guidelines targeted to patients (patients 'guidelines) and/or exclusively oriented to health services organization and not to clinical decision-making for managing diseases or conditions; 2) guidelines for which it was not possible to determine if a systematic process was applied in their development such as documents that lacked an explanation of the guideline development methodology that had been used or documents diffused as brief reports which only contained a set of recommendations or documents referred to as guidelines, but were undertaken by only one author without any reference to the methodology applied); 3) guidelines whose year of development could not be established as it was not stated and last but not least 4) guidelines that were not produced by a Malaysian institution (adapted guidelines were included only when the adaptation process was explicitly explained).

All guidelines registered by the Health Technology Assessment units (HTA) in MOH and AMM between January 2000 and December 2003 were selected for this study. The original published CPGs or a photocopy of the original CPGs were retrieved from the HTA unit, the chairman of the guideline developers

group/or downloaded from the Ministry of Health Malaysia website.

Quality guideline assessment was performed using the AGREE instrument. This instrument was the instrument of choice as it covers practically all the relevant dimensions of the evidence-based guideline development process. In addition, it has been internationally validated. The AGREE has fewer items and uses a numerical scale that facilitates the analysis [8, 16,17].

A total of four appraisers were invited to participate voluntarily in the assessment phase. To be considered eligible, professionals should have had at least one of the following criteria: a) previous clinical epidemiology background; and b) knowledge on guidelines development. The professionals who accepted the invitation and fulfilled the eligibility criteria were trained in the use of the AGREE instrument. A learning program was developed in two stages: I. Self-reading of the tool-kit: all participants were provided with the English version of the AGREE instrument, the English version of the Training Manual. II. Pilot assessment - one CPG was assessed independently by all professionals.

All of the 29 copies of the CPGs retrieved were given to each appraiser to be appraised within one month. A data collection form designed on an Excel sheet, accompanied by a user-guide on the AGREE instrument were given to each appraiser. Results of assessments were returned to the researcher team by mail. No assessor received any honorarium.

AGREE consists of 23 key items organized in six domains. Each domain is intended to capture a separate dimension of guideline quality. Domain 1: Scope and purpose (items 1-3) is concerned with the overall aim of the guideline, the specific clinical questions and the target patient population. Domain 2: Stakeholder involvement (items 4-7) focuses on the extent to which the guideline represents the views of its intended users. Domain 3: Rigor of development (items 8-14) relates to the process used to gather and synthesize the evidence, the methods to formulate the recommendations and to update them. Domain 4: Clarity and presentation (items 15-18) deals with the language and format of the guideline. Domain 5: Applicability (items 19-21) pertains to the likely organizational, behavioral and cost implications of applying the guideline. Domain 6: Editorial independence (items 22-23) is concerned with the independence of the recommendations and acknowledgement of possible conflict of interest from the guideline development group.

Each item is rated on a 4-point scale ranging from 4 ‘Strongly Agree’ to 1 ‘strongly Disagree’, with two mid points: 3 ‘Agree’ and 2 ‘Disagree’. The scale measures the extent to which a criterion (item) has been fulfilled. ‘Strongly Agree’ means that the appraiser was confident that the criterion has been fully met, and if the appraiser was confident that the criterion has not been fulfilled at all or if there is no information available then he/she should answer ‘Strongly Disagree’. If the appraiser was unsure that a criterion had been fulfilled, for example because the information was unclear or because only some of the recommendations fulfill the criterion, then he/she should answer ‘Agree’ or ‘Disagree’, depending on the extent to which he/she thought the issue had been addressed.

According to the AGREE Collaboration the domain scores of each CPG were individually considered. Scores of individual items in each domain were

summed and standardized as a percentage of the maximum possible score for that domain, taking into account the number of appraisers. Domain scores can be calculated by summing up all the scores of the individual items in a domain and by standardizing the total as a percentage of the maximum possible score for that domain [6].

The internal consistency of each domain was evaluated using Cronbach's alpha. The Reliability between appraisers was determined for each question and each domain of the AGREE. Intraclass correlation coefficients (ICC) were calculated within each pair of appraisers and across the pool of appraisers. ICCs and Cronbach's alpha values above 0.75 were considered to represent good reliability while values at 0.40–0.75 were considered moderate and value of <0.40 was of poor reliability.

Results

A total of 29 documents were retrieved either from HTA unit or chairman of the guideline developers group or from the MOH or AMM websites. All the 29 CPGs were published locally. The financial sponsor for all these CPGs was mainly MOH. There were no pharmaceutical drug companies influencing our researches. Those developing the CPGs consist of a mixture of professionals mainly from the universities and private professional bodies like the AMM. The development process usually took about 1 to 2 years.

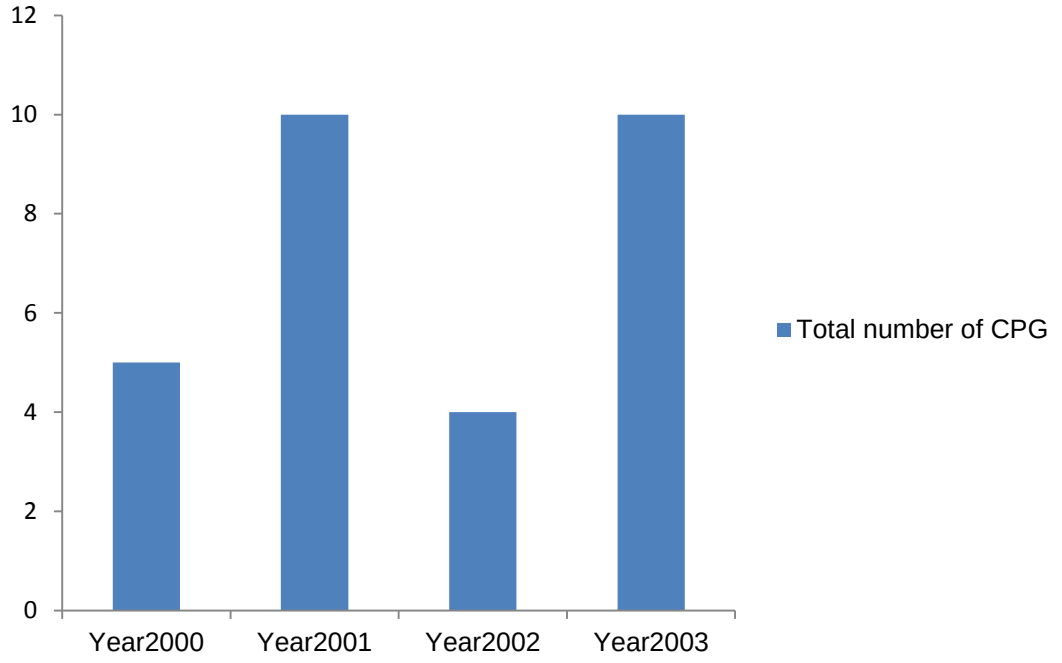
All the 29 documents fulfilled the inclusion criteria. All the 29 CPGs were assessed by 4 assessors. On the item Scope and purpose, only thirteen guidelines (13/29) covered diagnosis, nine guidelines (9/29) covered management, four guidelines (4/29) covered treatment, one guideline (1/29) covered prevention and one (1/29) guideline covered screening.

CPG production was found to increase from year 2001 to year 2003 (Figure 1). Ministry of Health was the principal CPG producer during this period of time. A CPG should be strongly recommended if it was rated high (3 or 4) on the majority of items and most domain scores were above 60% indicating the CPG had a high overall quality. A CPG should be recommended with provisos or alterations if it was rated high (3 or 4) or low (1 or 2) on a similar of items and most domain scores were between 30% and 60% indicating the CPG had a moderate overall quality. A CPG should not be recommended if it was rated low (1 or 2) on the majority of items and most domain scores were below 30% indicating the CPG had a low overall quality.

Domains corresponding to *Clarity and Presentation* (overall score was 75%) and *Scope and Purpose* (overall score was 68%) (Figure 2) were high. The majority of the CPG assessed received moderate scores in nearly all domains such as *Editorial Independence* (the overall score was 56%), *Stakeholder Involvement* (the overall score was 50%) and for *Rigor of Development* (the overall score was 48%). However for *Applicability (*the overall score was 26%) the score was low. In comparison to the results of the other domains, *Clarity and Presentation* was the best scored and *applicability* was the worst scored aspect of the 29 CPGs.

There was no statistically significant difference observed in the standardized domain scores corresponding to *Applicability* and *Editorial Independence.* Statistically significant

Figure 1: Total number of CPG produced per year



differences were observed among scores corresponding to the *Scope and Purpose*, *Clarity and Presentation*, *Stakeholder Involvement* and *Rigor of Development* (Figure 3 and table 2).

Since the distribution of the items scored were skewed, the median value was used which can be a good way to determine an approximate average. Analysis by item showed median values lower than 3 in 13 of the 23 items of the AGREE instrument: 2 items received the lowest possible score (1) (table 1).

The Malaysian CPGs did show significant improvement from 2000 to 2003 for Scope & Purpose; Rigor & Development, Stakeholder involvement and Applicability using AGREE (Fig. 4) However Clarity and presentation and Editorial independence showed lowering in values from 2002 to 2003.

Inter-rater reliability is an estimation based on the correlation of scores between/among two or more raters who rate the same item, scale, or instrument and Intraclass correlation coefficient (ICC) was used to measure the inter-rater reliability of the four appraisers. It may also be used to assess test-retest reliability. ICC may be conceptualized as the ratio of between-groups variance to total variance. ICC measured the extent to which there was agreement consistency among the appraisers. When interpreting ICC <0.4 represents poor reliability, 0.40 -0.75 represents fair to good reliability and >0.75 represents excellent reliability. For the domain, *Rigor of Development* (ICC=0.67`) and *Scope & Purpose* (ICC= 0.60) the score was moderate (Table 3). The ICC for the other domains in the Malaysian CPGs was low (ICC $\leq$ 0.40).

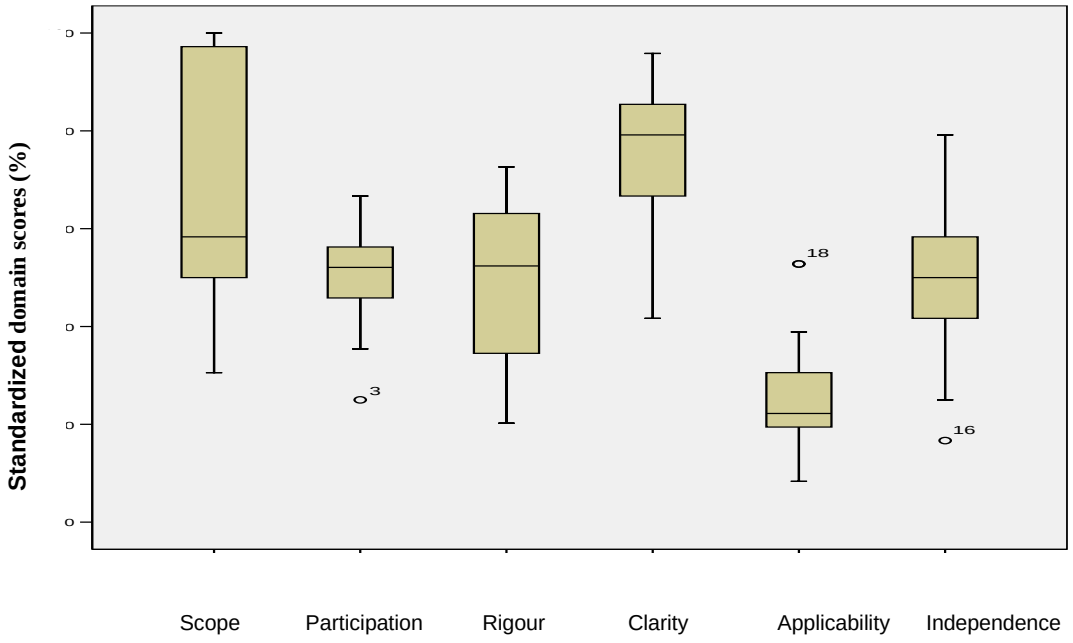
Cronbach's alpha being the most common form of internal consistency reliability coefficient, was used to measure the extent to which item responses correlate with each other. Alternatively, it can be interpreted as the correlation of the observed scale with all

possible other scales measuring the same thing and using the same number of it.

For the domain, *Rigor of Development* (Cronbach's alpha = 0.68) and *Scope & Purpose* (Cronbach's alpha = 0.63), the score was moderate (Table 3). Cronbach's alpha for the other domains in the Malaysian CPGs were low (Cronbach's alpha ≤ 0.40).

There seems to be variability of individual scores between the appraisers on items of the AGREE instrument and some of the variability may be due to differences in interpretation of several items where the instructions were broad.

Figure 2: Results of analysis of the 29 CPGs on the six AGREE instrument domains



differences were observed among scores corresponding to the *Scope and Purpose, Clarity and Presentation, Stakeholder Involvement* and Rigor *of Development* (Figure 3 and table 1).

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Cronbach's alpha was also used to test for internal consistency reliability coefficient to measure the extent to which item responses correlate with each other. Alternatively, it can be interpreted as the correlation of the observed scale with all possible other scales measuring the same thing and using the same number of it. When interpreting Cronbach's alpha magnitudes: <0.4 represents poor reliability, 0.40 -0.75 represents fair to good reliability and >0.75 represents excellent reliability. For the domain, *Rigor of Development* (Cronbach's alpha = 0.68) and *Scope & Purpose* (Cronbach's alpha = 0.63), the score was moderate (Table 3). Cronbach's alpha for the other domains in the Malaysian CPGs were low (Cronbach's alpha ≤ 0.40).

Figure 3: Temporal evolution of the median standardized score for each AGREE instrument domain

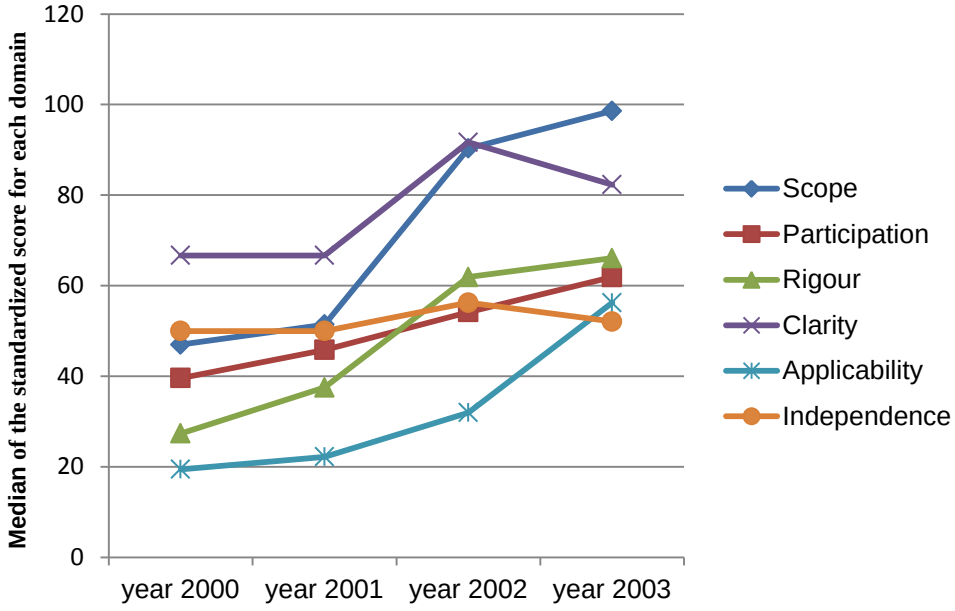


Table 1: Comparison of the CPG quality according to independent variables

	Median [Interquartile range] of standardized domain scores					
	Scope	**Participation**	**Rigour**	**Clarity**	**Applicability**	**independence**
2000-03 (n=29)	58% (49%)	52% (11%)	52% (33%)	79% (20%)	22% (13%)	50 (17%)
Year 2000 (n=5)	47% (11%)	40% (20%)	27% (20%)	67% (29%)	19% (10%)	50% (19%)
Year 2001 (n=10)	51% (8%)	46% (9%)	38% (16%)	67% (24%)	22% (15%)	50% (22%)
Year 2002 (N=4)	90% (40%)	54% (10%)	62% (13%)	92% (8%)	32% (29%)	56% (35%)
Year 2003 (n=10)	99% (15%)	56% (7%)	66% (8%)	82% (8%)	25% (7%)	52% (11%)
P value	0.000	0.000	0.000	0.002	0.413	0.904

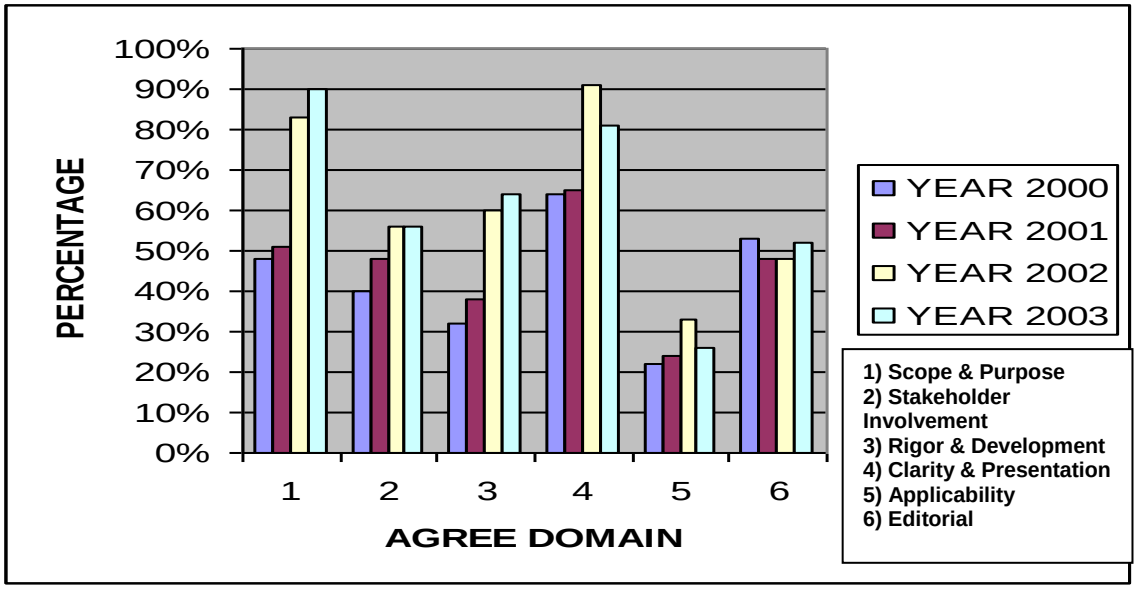
There seems to be variability of individual scores between the appraisers on items of the AGREE instrument and some of the variability may be due to differences in interpretation of several items where the instructions were broad.

Table 2: Scores by Item of the AGREE instrument

Domain and items of the AGREE instrument	Median Value	Interquartile Range
Domain 1: Scope and Purpose		
1. The overall objectives of the guideline is (are) specifically described	3	2
2. The clinical question(s) covered by the guideline is (are) specifically described	3	2
3. The patients to whom the guideline is meant to apply are specifically described	4	1
Domain 2: Stakeholder involvement		
4. The guideline development group includes individuals from all the relevant professional groups	4	1
5. The patients' views and preferences have been sought	1	1
6. The target users of the guideline are clearly defined	3	1
7. The guideline has been piloted among end uders	1	2
Domain 3: Rigour of Development		
8. The systematic methods were used to search for evidence	2	2
9. The criteria for selecting the evidence are clearly described	2	3
10. The methods used for formulating the recommendations are clearly described	2	2
11. The health benefits, side effects and risks have been considered in formulating the recommendations	3	2
12. There is an explicit link between the recommendations and the supporting evidence	3	2
13. The guideline has been externally reviewed by experts prior to its publication	2	2
14. A procedure for updating the guideline is provided	2	2.25
Domain 4 : Clarity and Presentation		
15. The recommendations are specific and unambiguous	4	1
16. The different options for management of the condition are clearly presented	4	1
17. Key recommendations are clearly identifiable	3	1
18. The guideline is supported with tools for application	3	2

Domain 5: Applicability			
19.	The potential organizational barriers in applying the recommendations have been discussed	2	1
20.	The potential cost implications of applying the recommendations have been considered	2	1
21.	The guideline presents key review criteria for monitoring and / or audit purposes	2	1
Domain 6: Editorial Independence			
22.	The guideline is editorially independent from the funding body	3	2
23.	Conflicts of interest of guideline development members have been recorded	2	2

Figure 4: Results of 4 Reviewers based on AGREE instrument



Discussion

The results of the study showed that through the years, development of guidelines in Malaysia had progressively increased. The quality of guidelines in Malaysia was practically unknown. To our knowledge, this was the first guideline appraisal in Malaysia. From this research, the quality of the 29 Malaysian guidelines was far from ideal: scores were moderate and low in all domains.

Variability of individual scores between the appraisers on items of the AGREE instrument, was noted as evidenced by the low Cronbach's alpha and ICC. On the other hand, the Argentinean study, by María Eugenia Esandi and Zulma Ortiz et al, ICC and Cronbach's alpha for each domain were in all cases moderate or high (0.46–0.74), except for Editorial Independence which showed very low values.

First, low quality could have been the result of the absence of an explicit policy

TABLE 3: Reliability Scores of the AGREE instrument

	Single rater ICC (95% CI)	Reliability Measures Average of raters ICC (95% CI)	Cronbach alpha	P value
Scope	0.27 (0.17 to 0.38)	0.60 (0.44 to 0.71)	0.63	0.00
Participation	0.05 (0.003 to 0.10)	0.19 (- 0.12 to 0.43)	0.34	0.00
Rigour	0.20 (0.14 to 0.27)	0.67 (0.57 to 0.75)	0.68	0.00
Clarity	0.1 (0.04 to 0.18)	0.36 (0.1 to 0.55)	0.43	0.00
Applicability	0.12 (0.04 to 0.21)	0.36 (0.13 to 0.53)	0.39	0.00
Editorial Independence	-0.80 (-0.16 to 0.01)	- 0.3 (-1.3 to 0.2)	- 0.33	0.96

for guidelines production (especially development of evidence-based CPGs) and evaluation during the period under assessment. There was also no clear guidance on the integration of multiple stakeholders. Most of the guidelines did not have enough multidisplinary representatives in the development process. In order to balance the interests, preferences and knowledge of different stakeholders whose participation in the guideline development process is required, a more integrated approach is required.

Secondly, low quality scores of the Malaysia guidelines could be explained by a slower penetration and consolidation of the evidence-based medicine concept in comparison to developed countries. Before the year 2002, the awareness of evidence-based medicine concept amongst the healthcare practitioners was still low in Malaysia. In the United States, the Consensus Development Program at the National Institute of Health developed its first guideline in 1977. In the last 30 years, all these organizations have accumulated a vast experience in guideline development, dissemination and implementation. Currently, principles of evidence-based-medicine dominate almost all of these national guideline programs. The creation of international networks, like the Guidelines International Network (G-I-N), as well as the establishment of projects like the AGREE, have clearly contributed to the improvement and standardization of these processes in the participating countries. Contrastingly, Malaysia, did not take part in any of these activities except until recently. Diffusion and dissemination of appropriate methods for evidence-based guidelines development is limited in Malaysia. This study found that until 2003, this process was not systematized and the development of CPGs still relied heavily on the opinion of experts. The manual development of evidence-based CPGs was drafted in 2003.

Thirdly, limited accessibility to updated biomedical literature can negatively impact on the use of relevant and important evidence to support guidelines recommendations. Most of the government facilities had very limited accessibility to current biomedical literature due to the financial constrain. Even after the broad agreement on the need for systematic reviews to inform recommendations, this type of evidence was rarely referred in Malaysian guidelines. Therefore, networking activities between guideline producers should also be promoted.

Another factor that could have influenced the quality of Malaysian guidelines is the lack of economical and human resources devoted to guideline production. Since the cost of producing evidence-based guidelines is relatively high, a systematic methodology to adapt international guidelines would be an efficient way of improving not only the quantity but also their quality [18]. Internationally developed guidelines can be adapted to the local context, representing a considerable saving of money. However, an explicit and systematic adaptation process should be performed as guidelines' applicability and transferability can be strongly influenced by different factors, such as population needs (prevalence of disease, baseline risk status), setting (availability of resources) and other factors that modify translation of recommendations into practice [19].

Although many of the Malaysian guidelines were classified as evidence-based, a thorough review of their quality utilizing the AGREE instrument led to the authors to recommend the guidelines only with provisos or alterations. Overall, almost all the guidelines performed poorly with respect to applicability. Most of the guidelines failed to address issues of barriers to implementation, monitoring criteria, and evidence of pilot testing.

On the other hand, the study on the clinical practice guidelines in Argentina (1994–2004) [7] by María Eugenia Esandi and Zulma Ortiz et al. scored lower in the overall standardized scores. Overall standardized score for each domain were: Scope & Purpose (overall score was 39%); *Stakeholder Involvement* (overall score was 13%); Rigor & Development (overall score was 10%); Clarity and presentation (overall score was 42%); *Applicability* (overall score was 6%); *Editorial Independence* (overall score was 0%).

One of the key factors regarding the adequacy of the guidelines pertains to the rigor of development. Many of the guidelines did not clearly delineate the literature review methodology used or the mechanism by which recommendations were formulated. This step is crucial in determining whether the recommendations were truly based on evidence or in understanding how evidence was synthesized.

As in the evidence-based decision making, patient preferences and experiences should be factored into decisions regarding clinical care, especially in diseases such as cancer in which treatments can have significant morbidity and can impact on quality of life. All guideline committees should have patient representatives and all literature reviews specifically addresses quality of life when available.

Finally, findings of this assessment highlighted the need of improving the reporting of the editorial independence of guideline producers. Practically none of the Malaysian guideline reported conflict of interests or funding sources. Lack of transparency was also reported by Papanikolaou et al. in an evaluation of 191 published guidelines: only 7 (3.7%) disclosed potential conflicts of interest [20]. In the case of the Malaysian guidelines, omission could have been unintentional or, on the contrary, intentional (financial ties might have existed in some situations and deliberately hidden by guideline authors). However, regardless of the intent of guideline developers' actions, explicit declaration of conflict of interests at the beginning of the process is strongly recommended by most international organizations as a way of reducing the probability of biased

recommendations and increasing guidelines' credibility [21].

There were several limitations noted in our study. It should be noted that in the AGREE instrument, the appraiser have to choose from four categories (1, 2, 3, 4) for his /her evaluation. Secondly, because we relied on materials reported in the published versions of the guidelines, our findings could be affected not only by the quality of the guidelines themselves but also by the quality of the reporting process. It was possible that in some cases, guideline developers used appropriate techniques but did not report them. We attempted to minimize this by including in our evaluation any background on supporting articles if they were available. However we feel that just as in other medical reports, documentation of methods used is important, and if explicitly stated can help determine the validity of recommendations. Thirdly, using the AGREE instrument, the inter-rater reliability was only poor to moderate. Some of the variability may be due to differences in interpretation of several items where the instructions were broad. Another potential limitation of the AGREE instrument concerns the validity of the responses to the question on the overall assessment of the guideline. Although the reviewers were instructed to consider the domain scores when making a decision about whether or not to recommend the guideline, no clear rules were established.

In Malaysia most practitioners, before the year 2003, were not clear of processes involves in evidence-based medicine approach. Most were still doing with consensus-consulting and agreeing to expert opinions.

To our knowledge this is the first time a study of this kind has been undertaken in Malaysia. Its execution was the first step in the building a network of professionals interested in improving evidence-based CPG development, dissemination and implementation in the country. Its findings have been found to be very useful in improving the methodological quality of developing CPGs in Malaysia.

Conclusion

This study was one of the firsts that systematically employed the AGREE instrument for the critical assessment of guidelines produced in Malaysia. The AGREE instrument can serve as a model to identify improvement opportunities in the guidelines development process of Malaysia. In this sense, this research shows the low quality of guidelines produced and points out areas to which training initiatives should be oriented.

A review of the current Malaysian guidelines demonstrates that many of the clinical topics of interest have been considered by at least one guideline. None covers all the necessary elements. Furthermore, although these guidelines may accurately reflect clinical practice, few adhere to the standards set forth by the AGREE instrument.

Several approaches could be used to improve the quality of guidelines. The guideline producers could become familiar with guideline development standards that have been established and make greater efforts to incorporate them into guidelines, strive to widely adopt and use them.

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Evaluation of the Tablet Splitting Practices among Malaysian Community Pharmacists.

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Abstract

Tablet splitting practices have been shown to reduce the medication cost in many countries. This study was aimed to evaluate the tablet splitting practices among community pharmacists in Penang, Malaysia. A two-month cross-sectional descriptive survey was carried out in forty randomly chosen community pharmacies in Penang. The pharmacists were required to document all their tablet splitting recommendations during the study period. The data collected includes the appropriateness of the tablet splitting recommendations by pharmacists; the extent of communication between pharmacists and physicians when recommending tablet splitting; the physicians' and patients' acceptance towards the tablet splitting; and the documentation of cost-saving achieved from the tablet splitting. The result showed that the tablet splitting was recommended by 31.0% of the pharmacists who receives prescriptions eligible for this practice. Tablets of patent-protected innovator brands were more likely to be recommended for splitting. Majority (92.9%) of the splitting recommendations were appropriate except two cases which involve unscored combination tablet. The pharmacists requested consent from the physicians for 42.9% of the splitting recommendations and majority (91.7%) of the requests were accepted. Meanwhile, the patients' acceptance rate for splitting recommendation was 82.1%. Through acceptance of tablet-splitting, the patients' monthly expenses on drugs reduced by 36.5% and this correspond to a monthly saving of RM39.05 (US$10.30, US$1.00 = RM 3.80) per patient. The study concluded that the tablet splitting is not a common practice among the community pharmacists, however both the physicians and patients highly accept pharmacists' suggestion on splitting. The findings also revealed that tablet splitting can be used as a cost-containment measure for patient as well.

Article Keywords: tablet splitting, community pharmacist, physician, patient, cost-saving

Introduction

Recently, increase in countries' expenditures on prescription drugs has become a worldwide dilemma. In Malaysia, the government fully subsidizes the drugs expenditure in public hospital. However, the government subsidized cost for drugs in public hospital increased from RM 200 million in 1995 to RM 800 million in 2005 with an annual increment of 10%-15%, thus this had affected the government's ability to sustain

pharmaceutical financing in the future (1,2)· Besides, 56% of Malaysian consumers perceived drugs in private sector as expensive and 68% urged that prices should be reduced (3). The high drugs cost may generate prescription non-compliance and thus in return will further increase healthcare costs (4).

Many studies highlighted that tablet splitting resulted in significant cost-saving (5-10). For instance, introduction of tablet splitting by a health plan in North Caroline generated annual savings of US$342,000 (5). However, tablet splitting is contraindicated for extended release formulation and enteric-coated tablet (11-14). Unscored tablet and combination tablet are generally not mean to be split, but some tablets without scoring may be split easily with tablet-splitting device (11-12). Unacceptable weight variation can be resulted from tablet splitting and may be clinical significant for narrow therapeutic drug (15-17). Therefore, this practice only suitable for drugs with wide therapeutic range and long half life (7,12,14-18). Previous studies had shown that majority of the patients' compliance was not hindered after introduction of tablet splitting (19-21). Nevertheless, tablet splitting is not suitable for cognitively and functionally impaired patients who could lead to confusion and incorrect dosing (13,14).

In the current context of pharmacy practice in Malaysia, there is no dispensing separation policy been implemented between private general practitioners and community pharmacists. There is also no tablet-splitting guideline for health professionals in Malaysia. Under these circumstances, little is known about the pharmacist's tablet splitting practices and the response of physician and patient toward the splitting recommendation.

Aim of the study

This study aims to document the tablet splitting practices among Malaysian community pharmacists with the focus on the appropriateness of the tablet splitting recommendations; the extent of communication between pharmacists and physicians while recommending tablet splitting; the physicians' and patients' acceptance towards the tablet splitting; and the cost-saving resulted from the tablet splitting practices.

Method

This is a cross-sectional descriptive survey study using a self-completed data form for pharmacists to fill in. This data form was modified from the data collection form obtained from previous study undertaken in Scotland (22). This data form has been tested for face and content validity by five pharmacy academics and 10 pharmacists. The sample of the form is shown in Appendix 1.

The population of community pharmacists in Penang state was stratified into urban and rural area. The sampling frame was the pharmacies list provided by State Pharmacy Enforcement Department. Thirty and ten outlets were randomly chosen from the urban and rural area respectively and resulted in total of 40 community pharmacies as the sample.

This study includes patients who brought prescriptions written in branded or generic name to the community pharmacies. These drugs are available in various strengths which are eligible for tablet splitting. The pharmacists were requested to document their tablet splitting recommendation to the patient, including the brand name of the drug involved, the strength, the dosage regimen, the cost and selling price of the

drug, the decision either to consult or not consult the physician with regards to splitting recommendations, and physician and patient's acceptance toward the recommendation made. Patients who have a risk that tablet splitting will impair their understanding and compliance to therapy were excluded from the study.

The researcher sent the data form by personal visit to the selected outlets and detail explanations was given to the pharmacists. The participation of this study was strictly voluntary and no personal data of the participants were reported. The duration of data collection was 2 months period from 22nd February 2005 to 22nd April 2005. Follow-up and data collection were done by monthly personal visit by the researcher. All the collected data was entered into SPSS® version 11.5 for analysis.

Results

From the chosen sample of forty pharmacies (one pharmacist in each outlet), 34 pharmacists (85.0%) agreed to participate in this study. At the end of the study, only 9 (26.5%) pharmacists involved in tablet-splitting practices. Five pharmacists (14.7%) did not receive any prescription eligible for tablet splitting. The remaining 20 pharmacists (58.8%) did not recommend tablet splitting although they have the opportunity to do so. In another words, among the 29 pharmacists which received prescriptions eligible for tablet splitting, only 31.0% (9 pharmacists) recommended tablet splitting to their patients.

Total numbers of patients involved in tablet splitting recommendation were 28. There were 28 items involved and one item was considered as one case of tablet splitting recommendation. Besides, the cases involved 13 drugs and 17 products with different strength (Table 1).

Analysis of tablet splitting practices

Majority of the cases involved antihyperlipidemia (42.8%) and cardiovascular drugs (42.8%), followed by antibiotic (3.6%), erectile dysfunction (3.6%), gout (3.6%) and diabetic mellitus (3.6%). Almost all (96.4%) of the cases involved Class B Poison which under the Malaysian Poison Law 1952 can only be sold with a prescription from a registered medical, dental or veterinary practitioners. Only one case (3.6%) involved Class C Poison which under the Malaysian Poison Law can be sold without a prescription by a registered pharmacist in a registered pharmacy premise.

Among the tablet splitting recommendations, 57.2% involved patent-protected innovator brands, followed by 32.2% of off-patent innovator brands which equivalent generic products were available as of the date of this research. Only 10.6% of the cases involved generic products. Zocor® (Simvastatin) was the most popular drug involved in tablet splitting recommendation which consist of 28.6% of the cases and followed by Lipitor® (Atorvastatin) (10.7%) and Norvasc® (Amlodipine) (10.7%) (Table 1).

Detail analysis noticed one unique case of generic substitution occurred concurrently with tablet splitting. In this case, the patient accepted to change the therapy from Zocor® (Simvastatin) 20mg, one tablet daily to Vascor® (manufactured by CCM Pharmaceuticals, a local generic company) 40mg half tablet daily (Table 1). This unique case saved RM62.55 (US$16.50) per month (28 days) for the patient with RM47.60 (US$12.55) of the cost-saving was gained from the generic substitution (Zocor® 20mg, 28 tablets

cost RM93.35; Zocor® 40mg, 14 tablets cost RM78.40; Vascor® 40mg, 14 tablets cost RM30.80; RM3.80 = US$1.00). There was another unique case involved simplified the patient's treatment through tablet splitting. In this case, the patient agreed to change the regime of Apo-Allopurinol® (Allopurinol) 100mg, one and a half tablet daily to become Apo-Allopurinol® 300mg, half tablet daily (Table 1). This recommendation resulted in monthly cost-saving of RM7.80 (US$2.05) to the patient (Apo-Allopurinol® 100mg, 42 tablets cost RM15.60; Apo-Allopurinol® 300mg, 14 tablets cost RM7.80).

In the present study, it was noted that modified release formulation, enteric-coated tablet and narrow therapeutic index drugs were not involved in the splitting recommendations made. Nevertheless, only 32.1% (9 of 28) of the recommendations involved scored tablets with single wide therapeutic drugs which are suitable for splitting (Table 1). The remaining 67.9% (19 of 28) of the cases involved unscored tablets which need further evaluation on its divisibility. All the unscored tablets have symmetrical shape and can be split into two equal halve using appropriate splitting device. Majority (92.9%) of the unscored tablet cases involved single wide therapeutic drug except two cases involved combination tablet which were Co-Diovan® and Fortzaar®. Two drugs in a combination tablet may not evenly distribute throughout the tablet and splitting may not produce equal dose (12). However, the pharmacist requested consent from the physician when recommending splitting of Co-Diovan® and Fortzaar® and these recommendations was agreed by the physician. Analysis shown the manufacturer of Co-Diovan® (Novartis) disallowed splitting by indicating it is "non-divisible" in the product leaflet. Meanwhile, for all other cases, the product leaflet provides information on the tablet characteristics but does not provide any information about its divisibility. As the product leaflet for Fortzaar® do not include any information regarding its divisibility, the researcher had contacted the manufacturer of Fortzaar® (MSD Malaysia branch) to clarify this issue and found that it can't be split. Further analysis on the unscored tablets shows Cozaar® and Zocor® tablet are formulated with a scored line on the lower strength tablet (Cozaar® 50mg and Zocor® 10mg) but are unscored for the higher strength tablet (Cozaar® 100mg and Zocor® 20mg onwards). Besides, studies has shown that tablet splitting for simvastatin and atorvastatin is effective and safe (7,18).

Extent of communication between pharmacists and physicians

Overall, the pharmacists requested consent from the physician for 42.9% of the splitting recommendations. Further analysis shown 33.3% of the antihyperlipidemia agent cases and 41.7% of the cardiovascular drug cases was recommended with reference to the physicians. Besides, 33.3% and 47.4% of cases involved scored and unscored tablet involved consultation with physicians respectively but the differences in these percentages were not statistical significant (Fisher's Exact Test, $p = 0.687$).

Physicians and patients' acceptance

The physicians' acceptance rate for tablet splitting recommendations was 91.7% with only one case involved Tenormin® 100mg was rejected. In fact, the entire cases involved unscored tablet was accepted by the physicians.

The overall patients' acceptance rate for splitting recommendations was 82.1%. Majority of the patients accepted the

Table 1: Tablet Splitting Recommendations by Community Pharmacists

Therapeutic group	*Drug (generic name)*	*Patient's initial regime (Product name & dose)*	*Tablet splitting recommendation (Product name & dose)*	*Manufacturer (Country of origin)**	*Medication characteristics*†*	*No of case (%)*
1.Antihyperlipidemia	1. Simvastatin	1. Zocor® 10mg, 1 tab ON ‡	Zocor® 20mg, ½ tab ON ‡	Merck Sharp & Dohme (Australia)	Unscored	5(17.9)
		2. Zocor® 20mg, 1 tab ON ‡	Zocor® 40mg, ½ tab ON ‡	Merck Sharp & Dohme (Australia)	Unscored	3(10.7)
		3. Zocor® 20mg 1 tab ON ‡	Vascor® 40mg, ½ tab ON ‖	CCM Pharmaceuticals (Local)	Scored	1(3.6)
	2. Atorvastatin	1. Lipitor® 20mg, 1 tab ON §	Lipitor® 40mg, ½ tab ON §	Pfizer (USA)	Unscored	2(7.1)
		2. Lipitor® 10mg, 1 tab ON §	Lipitor® 20mg, ½ tab ON §	Pfizer (USA)	Unscored	1(3.6)
2. Cardiovascular disease	1. Amlodipine	1. Norvasc® 5mg 1 tab od §	Norvasc® 10mg, ½ tab od §	Pfizer (USA)	Scored	3(10.7)
	2. Atenolol	1. Tenormin® 50mg 1 tab od ‡	Tenormin® 100mg ½ tab od ‡	AstraZeneca (Sweden)	Scored	1(3.6)
		2. Apo-Atenol® 50mg 1 tab od ‖	Apo-Atenol® 100mg ½ tab od ‖	Apotex (Canada)	Scored	1(3.6)
	3. Losartan & Hydrochlorothiazide	1. Hyzaar® (50/12,5) 1 tab od §	Fortzaar® (100/25) ½ ab od §	Merck Sharp & Dohme (Australia)	Unscored	2 (7.1)
	4. Valsartan	1. Diovan® 80mg, 1 tab od §	Diovan® 160mg, ½ tab od §	Novartis (Switzerland)	Scored	2(7.1)
	5. Felodipine	1. Plendil® 2.5mg 1 tab od §	Plendil® 5mg ½ tab od §	AstraZeneca (Sweden)	Unscored	1(3.6)
	6.Losartan	1.Cozaar® 50m 1 tab od §	Cozaar® 100mg ½ tab od §	Merck Sharp & Dohme (Australia)	Unscored	1(3.6)
	7. Valsartan & Hydrochlorothiazide	1.Co-Diovan® (80/12,5) 1 tab od §	Co-Diovan® (160/25) ½ tab od §	Novartis (Switzerland)	Unscored	1(3.6)
3. Antibiotic	1.Cefuroxime	1. Zinnat® 125mg 1 tab bd §	Zinnat® 250mg ½ tab bd §	GlaxoSmithKline (UK)	Unscored	1(3.6)
4. Erectile dysfunction	1. Sildenafil citrate	1. Viagra® 50mg 1 tab prn §	Viagra® 100mg ½ tab prn §	Pfizer (USA)	Unscored	1(3.6)
5. Gout	1. Allopurinol	1. Apo-Allopurinol® 100mg 1.5 tab od ‖	Apo-Allopurinol® 300mg ½ tab od ‖	Apotex (Canada)	Scored	1(3.6)
6. Oral antidiabetic agents	1. Rosiglitazone	1. Avandia® 4mg 1 tab od §	Avandia® 8mg ½ tab od §	GlaxoSmithKline (UK)	Unscored	1(3.6)
Total						*28(100.0)*

* Manufacturer and medication characteristics for products involved in tablet splitting recommendation.

†The medication characteristic of product sold in Malaysia only. The same product that sold in other countries may have different characteristics.

‡Off-patent innovator brand as of April 2005. Equivalent generic products available in the market.

§Patent-protected innovator brand as of April 2005. Equivalent generic products not available in the market.

‖Generic product.

Table 2: Physicians' and Patients' Acceptance towards the Tablet Splitting Recommendation.

	No. of Cases (%)
Pharmacist consult physician	**12 (42.9)**
Physician accepted	11 (91.7)
Patient accepted	11 (100.0)
Patient do not accepted	0 (0.0)
Physician do not accepted	1 (8.3)
Patient accepted	0 (0.0)

recommendations involved anti-hyperlipidemia agents (83.3%) and cardiovascular drugs (75.0%). Meanwhile, the patients' acceptance rate for scored and unscored tablet were 66.7% and 89.5% respectively but there was no statistical differences noted with this regard (Fisher's Exact Test, p = 0.290). The patients refused to accept splitting recommendation in five cases which involve Tenormin® 100mg, Norvasc® 10mg, Apo-Atenol® 100mg, Zocor® 20mg and Zocor® 40mg respectively. For cases involve consultation with prescriber, 91.7% of the cases was accepted by the patients (Table 2). Further analysis shows that the patients strictly (100.0%) followed the decisions of the physicians. In contrast, 75.0% of cases without informing the physicians were accepted by the patients. Nevertheless, there was no statistical significant difference noted in term of patients' acceptance rate between cases involved consultation with the physicians and cases without informing the physicians (Fisher's Exact Test, p = 0.355). **(Insert Table 2 here)**

Pharmacists' cost-saving through the tablet splitting recommendation

The cost-saving was calculated for 21 successful tablet splitting recommendation cases. Five cases which refused by the patients and the Co-Diovan® and Fortzaar® case which not allowed to be split were excluded. The total cost for these 21 cases was RM2071.30 (US$545.10) and RM1236.55 (US$325.40) respectively before and after the splitting recommendation. This means the pharmacists expenses on stocks purchasing were reduced by 40.3% or RM834.75 (US$219.70) through the splitting recommendation.

Pharmacists' monthly cost-saving (per 28 days) for chronic cases

There were 19 successful cases which involved chronic diseases like hyperlipidemia, cardiovascular diseases and diabetic mellitus. The costs of drugs for these cases have been converted to monthly cost (per 28 days). The total monthly cost was RM1586.40 (US$417.45) before the splitting recommendation and reduced by 35.3% to RM 1026.70 (US$270.20) after the recommendation. Total amount of cost-reduction was RM559.70 (US$147.25).

Patients' cost-saving through tablet splitting

From the 21 cases which accepted by the patients, total cost to the patient before tablet splitting was RM2483.00 (US$653.40). After tablet splitting, the patients' total expenses reduced to RM1595.00 (US$419.75). This resulted in cost-saving of RM888.00 (US$233.65), which was 35.8% from the original cost.

Patients' monthly cost-saving (per 28 days) for chronic cases

From the 19 chronic cases within the two months study, the initial total monthly cost of the patients was RM2034.25 (US$535.35), and declined to RM1292.35 (US$340.10) after the tablet splitting. Consequently, the monthly cost-saving achieved was RM741.90 (US$195.25). The percentage of monthly cost-saving was 36.5% and average monthly cost-saving per patient was RM39.05 (US$10.30).

Discussions

For a period of 2 months, only 28 tablet splitting recommendations were performed by 31.0% of the pharmacists that encounter with opportunities for this practice. This finding revealed that tablet splitting is not a common practice among the community pharmacists. Tablets of patent-protected innovator brands were

more likely to be recommended for splitting than the multi-brands drugs. Therefore, the pharmacists may tend to recommend tablet splitting when cheaper generics are not available. This further supported by the concurrent generic substitution study which observed 158 generic substitution recommendations from the same group of pharmacists (23). The combination of tablet splitting and generic substitution is a good cost-containment strategy as shown in the case of converting Zocor® 20mg, one tablet daily to Vascor® 40mg, half tablet daily. The cost-saving achieved was four-fold higher than using tablet splitting alone with 76.1% of the cost-saving was contributed by generic substitution.

Overall, majority (92.9%) of the tablet splitting recommendations were appropriate as there were no sustained-release, enteric-coated or narrow therapeutic drugs involved and the tablets involved mostly contain single wide therapeutic drugs. Although majority of the recommendations involved unscored tablets, their symmetrical shapes enable them to be split into fairly equal halve by using proper device. Besides, studies shown that splitting of tablets contain single wide therapeutic drug are clinically appropriate (7,12,18). Only two cases involved unscored combination tablet (Co-Diovan® and Fortzaar®) were not suitable for splitting. The manufacturers disallowed splitting of these combination tablets because no study being conducted to evaluate patient clinical outcome after the splitting of Co-Diovan® and Fortzaar® tablets. Another interesting finding was only 9.1% (1 of 11) of the manufacturer product leaflets of the unscored split tablets has information on divisibility. This observation was consistent with a finding from primary care centers in Germany where minority (22.5%) of the product leaflet of the unscored split tablets contained information about the divisibility (11). Hence, the pharmacists and physicians have limited information on tablet splitting and this may resulted in inappropriate splitting recommendation. The shape of Zocor® and Cozaar® tablets which are unscored in their higher strength are irrational. The manufacturers should scored all strengths of medications which are clinical appropriate for splitting. A study in USA also observed many tablets are scored only in their lower strengths and urged that manufacturer s be compelled to score all strengths of medication (10).

In this study, the pharmacists tend not to consult the physicians when recommending tablet splitting. However, higher percentage of unscored tablet cases involve consultation with physicians as compared to cases which involved scored tablets. These shown the pharmacists may tend to obtain consent from the prescribers for more critical cases. From physicians' perspective, majority of the physicians agreed with splitting recommendations by pharmacists. This result was consistent with other study in which consultation between pharmacist and physician improved the cost-effectiveness of prescribing (24). Meanwhile, majority of the patients agreed to split their tablet and surprisingly, the acceptance rate for unscored tablet was even higher than scored tablet (89.5% versus 66.7%). The high acceptance rate may due to the benefit of cost-saving. Besides, majority of patients (75.0%) accepted the pharmacists' recommendations which without a consent from the physician. This showed that the Malaysian pharmacists' professional judgment was highly valued by the consumers. Nevertheless, the patients' acceptance rate was higher (91.7%) for cases involved consultation with the physicians. This indicated that co-

operations between pharmacists and physicians are very important in improving patients' treatment.

The present study also showed that tablet splitting may not only reduce patients' expenses on drugs, but it also can reduce pharmacists' inventory costs. The patients' monthly cost-saving of 36.5% was lower than 61.3% of cost-saving achieved from concurrent generic substitution study (23). However, this relatively small amount of cost-saving will become a huge amount when accumulated in long term. In addition, this study also highlighted that while performing dispensing, the pharmacists are capable to helping the patients reduce their expenses on drugs while maintaining the efficacy of treatment.

Study limitations

The relatively small sample size limited the generalization of the study findings. The 34 pharmacies involved in this study represented 21.0% of total 165 pharmacies in Penang state and 2.3% of total 1500 pharmacies in whole Malaysia. The duration of two months study was also not sufficient to collect enough tablet splitting cases. Besides, there was no follow-up on the outcome of patients involved in tablet splitting particularly those involved unscored and combination tablets. Based on this study, there is a need to conduct a larger study in Malaysia, using the similar methodology, with longer duration and documented follow-up on the outcome of patients involved in tablet splitting process in order to give a clear picture of tablet splitting practices among Malaysian community pharmacists.

Conclusions

Although tablet splitting is not a popular practice among the community pharmacists, both the physicians and patients were highly accepted the splitting recommendations by the pharmacists and it resulted in significant cost-saving. There is a need to develop a tablet-splitting guideline for health professionals in order to avoid inappropriate splitting recommendation. Furthermore, the manufacturers should score all the tablets of medications which are clinically appropriate for splitting. Sufficient information on divisibility must also be provided on the medication product leaflet.

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CONFIDENTIAL

APPENDIX 1:
Data collection forms

A) Data collection form Tablet splitting in community pharmacy

Date	Patient Medication Record (PMR) No.	Prescription details (drug name, form, dose and quantity)	Proposed change to prescription details[1] (drug name, form, dose and quantity)	Prescriber informed ? Yes/No (If relevant)	Prescriber acceptance ? Yes/No (If relevant)	Patient acceptance ? Yes/No (If relevant)

1. Tablet splitting recommendation.

B) Form for estimating cost saving Tablet splitting in community pharmacy

Date	***Patient PMR no.***	***Cost of current prescription item***		***Cost of new prescription item***		***Saving per item per script***		***Saving per 28 days (long term therapy)[1]***	
		Cost price (A)	**Selling price (B)**	**Cost price (C)**	**Selling price (D)**	**Cost price (A-C)**	**Selling price (B-D)**	**Cost price**	**Selling price**

1. To calculate cost saving per month: $\frac{\text{Cost saving x 28}}{\text{No. of days on prescription}}$

Stability of Folic Acid in an Extemporaneously Prepared Oral Suspension

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Abstract

Many drugs are not available in suitable dosage forms for paediatric use and have to be extemporaneously prepared by pharmacist for the individual patient. This study is conducted to investigate the physicochemical and microbiological stability of an extemporaneous oral suspension containing 1mg/ml of folic acid. The oral suspension was prepared using commercially available tablets and vehicle from the hospital. The folic acid oral suspension was stored for 60 days at 4ºC (refrigeration) and 25ºC (room temperature) protected from light. The physical, chemical and microbial stability were examined at day 0, 14, 28 and 60. The content of folic acid was determined using HPLC-UV method. The analytical results showed that the content of folic acid was above 90% in all the samples tested throughout the study period. The visual appearance, colour, odour and pH remained fairly unchanged throughout the study period and the oral suspension was not susceptible to microbial contamination. The results indicated that the extemporaneous formulation was stable at both temperatures and 60 days expiration date could be recommended for this formulation.

Keywords: Compunding, Extemporaneous preparation, Folic Acid, Stability, Shelf-life

Introduction

Pharmacist plays very important role in pharmaceutical compounding in both hospital and community pharmacy practices. Pharmaceutical compounding known as extemporaneous preparation is important to prepare pharmaceutical product that is not available in suitable dosage form to suit individual patient's need. The demand for this process is increasing to provide the needed products by the patients and healthcare practitioners. Despite its important and useful for patient, there are legitimate concerns about the quality and safety of compounded products as well as concerns about overseeing the pharmacies that compound them (1).

Many drugs are often not available commercially in suitable dosage forms for paediatric and geriatric patients. These products have to be extemporaneously prepared by pharmacist to suit individual need of the patient. However, the information related to the extemporaneous formulations and the stability of the final products are lacking (2,3). The methods of extemporaneous preparation for the same drug were significantly different among hospitals throughout Europe (2,4). There is no harmonization of compounding methods and the availability of suitable licensed

paediatric products varied among European countries (2,5). Due to the paucity of information, many pharmacists are facing problems to find a fully validated formulation for extemporaneous preparation. When deciding on whether to formulate an extemporaneous preparation in these circumstances, the pharmacist must consider the risk of withholding treatment, as well as the risks inherent in extemporaneous formulation.

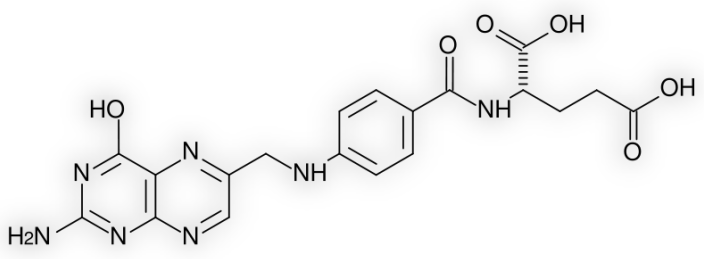
There are many reasons for the lack of commercially available paediatric formulations. The overall size of the paediatric market is much smaller than for adults. Therefore, the pharmaceutical industry is reluctant to invest financially to seek drug licensing for infants and children unless a disease occurs exclusively or frequently in the paediatric population. In addition, the formulation has to have been adequately studied in paediatric patients before it can be registered (6). As such the availability of paediatric formulations varies between countries and very few products are available in countries which constitute a small market (7).

When there is a need to undertake extemporaneous preparation, the pharmacist must choose the best extemporaneous formula. Ideally, the pharmacist should choose formulation used for extemporaneous preparation with validated stability and proven shelf-life (5,8). However, in the absent of published data, stability studies should be carried out on the formulations used in practice. The most stable formulation is then can be recommended as the standard formula for all the hospitals.

Folic acid oral suspension is one of the commonly prepared extemporaneous oral preparations in hospital pharmacies and has been selected for this study. In paediatric, folic acid has been used as folate supplement in neonates who have megaloblastic anaemia due to folate deficiency, haemolytic anaemia and prophylaxis of folate deficiency in dialysis (9).

Folic acid (**Figure 1**) is a yellowish or orange crystalline powder. It is practically insoluble in water and in most organic solvents. It dissolves in dilute acids and in alkaline solutions. Folic acid is a member of the vitamin B group. In the body, it will be reduced to form tetrahydrofolate, a coenzyme for various metabolic processes including the synthesis of purine and pyrimidine nucleotides, and hence in the synthesis of DNA; it is also involved in some amino-acid conversions, and in the formation and utilisation of formate (10).

Figure 1: Folic Acid



A few extemporaneously prepared liquid formulations of folic acid have been reported in literatures. In a recent study, a folic acid liquid preparation was prepared using folic acid powder and combined solvents of sorbitol, glycerine and propylene glycol. The result from this study showed that the liquid preparation was stable at pH range of 5 and 5.5 and no significant degradation when the liquid preparation was stored for 2 years at room temperature (11). The study did not mention about microbial stability of the liquid preparation and the use of preservative. In another study, an oral suspension of folic acid with a concentration of 50g/ml in glass container was physically and chemically stable, at least 14 days, when stored under refrigeration (2 to 8ºC) and under light protection (12).The author acknowledged that an evaluation of the microbiologic stability of this kind of extemporaneous preparations (contain no preservatives) is critical to ensure safe use in paediatric patients and is particularly required for an extemporaneous oral formulation to be stored at room temperature over an extended period (12).

The folic acid powder in small doses can be repacked into powder papers from commercially available tablets or capsule contents. In the survey conducted by Teixeira de Barros *et al*, folic acid powder papers were the most frequently prepared extemporaneous preparation in an oral powder form (14.7%) in Portuguese hospitals (4). This dosage form has its own limitations. The powder need to be reconstituted immediately prior to drug administration by the caregiver. Consequently, it will increase the risk of inconsistency of the preparation for each dose (6,7).

In New Zealand, a survey conducted by Kairuz *et al.* found that suspensions are the most frequently compounded dosage form in a number of hospitals (13). In a survey conducted by Lowey and Jackson to established the top 50 extemporaneously prepared oral preparation in Yorkshire, the North-East and London, they found that the most commonly prepared oral dosage forms were aqueous suspensions (66.2 %) and solutions (22.2 %) (8). At the same time, they also found that the evidence base to support extemporaneous preparation was generally poor.

Oral liquid preparations are often the dosage form of choice in paediatric and geriatric population (14). Most problems associated with the stability of these preparations have been attributed to the interaction between drug substance and excipients (tablet and formulation) rather than the degradation of the drug substance by standard routes (14). An extensive survey of literature and investigation of 83 liquids extemporaneously prepared from commercial available products revealed that only 7.2% of these liquids exhibited instability due to interactions between the drug substance and the excipients rather than degradation of the active pharmaceutical ingredient (6).

To address the lack of stability data on the formulation faced by pharmacists in the hospital practice, a liquid formulation using the commercial drug product and vehicle in the hospital practice should be prepared and the extemporaneous formulation can be validated. The formulation of the extemporaneous preparation should be designed as simple as possible. The result from this study will provide the stability data and the protocol can be standardized in the prescribing and compounding practices among the hospitals to provide a safe, effective and quality extemporaneous preparation to the patients.

The objective of this study is to evaluate the stability of extemporaneously prepared folic acid oral suspension at 4ºC (refrigeration) and 25ºC (room temperature) and to determine the shelf-life and storage condition of the extemporaneous preparation. This information is important to ensure that the extemporaneous preparation remains stable and efficacious during the course of their use. When there is supporting stability information of the specific preparation, the expiry date may be exceeded rather than a short 14 days shelf-life when stored at cold temperature if limited information or no supporting data available according to *USP 34-NF 29 Chapter <795>, Pharmaceutical Compounding – Nonsterile Preparations*(15).

Drug product stability encompasses chemical, physical, microbiological, therapeutic and toxicological stability. Stability studies should be performed for desired drug concentration and in real storage conditions (storage temperature, duration and type of container). The physical stability is assessed from changes in appearance, colour or odour, while the chemical stability is determined using an adequate analytical method for drug quantification. Microbiological stability should be conducted in extemporaneous oral formulations containing no or insufficient preservatives and be stored at room temperature over an extended period (7,12).

Materials and methods

Commercial Drug and Vehicle

Sourcing the active pharmaceutical ingredient in powder form is not always practical or possible thus commercially available tablets are used in compounding oral liquids. Similarly, the use of commercially available vehicles containing a combination of sweeteners, flavours, suspending agents and preservatives is encouraged and is considered an excellent choice for making the extemporaneous preparation's simple for the inexperienced pharmacist (5). Commercial vehicles are considered a convenient choice especially since various practice settings may not hold a wide variety of excipients (such as suspending agents, flavours, sweeteners or preservatives) in stock (16).

Tablets containing 5mg of folic acid (Pharmaniaga Folic Acid 5mg Tablet) manufactured by Duopharma (M) Sdn Bhd, Malaysia were used for the compounding of folic acid oral suspension. X-temp Oral Suspension System marketed by Pharm-D Sdn Bhd, Malaysia was selected for this extemporaneous preparation. X-temp Oral Suspension System contains specialized suspending system formulated to assist in extemporaneous preparation of oral liquid, non-soluble (suspended), aqueous dosage form and is orange flavoured, sweetened, sugar-free vehicle containing suitable preservatives.

Extemporaneous Preparation

A folic acid oral suspension with the concentration of 1mg/ml was prepared using tablets containing 5mg of folic acid. Tablets were grounded to a fine powder in a mortar with a pestle. A portion of the vehicle was used to levigate the fine powder and a uniform paste was prepared. Additional vehicle was added to the mortar in small portions and then transferred to a graduated container and more vehicles were added to make the total volume required.

Twenty-four bottles of folic acid oral suspension (1mg/ml) were packed into 100ml semi-transparent plastic bottles and were fitted with white plastic screw cap. Twelve bottles were stored at 4 ± 2ºC (refrigeration) and the other twelve bottles at 25 ± 2ºC (room condition) in the absence of light.

Analytical Method

The content of folic acid was measured by HPLC-UV method after the extemporaneous preparation was made and throughout the stability study period. Samples were collected from each individual bottle on days 0, 14, 28 and 60. The assay method was developed with the reference to the British Pharmacopoeia 2009 and the content of folic acid was set at 90 to 110% of the stated amount (17). An ASEAN reference standard of folic acid was obtained from National Pharmaceutical Control Bureau (NPCB).

The HPLC system used for the analysis was an Agilent 1100 HPLC instrument with quaternary pump, autosampler, UV/VIS detector and chemstation. The chromatographic separation used was Zorbax Eclipse XDB-C18 (4.6mm ID x 150mm, 5μm). The UV/VIS detector operated at 283nm. The mobile phase consisted of a mixture of 93 volumes of 0.05M potassium dihydrogen orthophosphate and 7 volumes of acetonitrile and then adjusted to pH 6 with 5M sodium hydroxide. The mobile phase was delivered at a flow rate of 2ml/min. Samples were filtered before HPLC analysis and the injection volume as 5μL.

Physicochemical Stability Studies

The physical and chemical tests (such as visual appearance, odour, pH and folic acid content) were assessed at time 0, 14, 28 and 60 days during storage at both temperatures. Prior to sample collection, the bottles were agitated on a rotating mixer for 30 minutes. The oral suspensions were examined at each sampling time for any change in appearance or odour. The pH was periodically checked during storage at both temperatures. The preparation is considered stable if physical characteristics have remained fairly unchanged and assay of folic acid has remained equal or above 90% of the original concentration during the storage period.

Microbiological Stability Studies

Microbiological stability of the folic acid oral suspension stored at 4ºC and 25ºC was studied at the interval of days 0, 14, 28 and 60. The microbial limit of total bacteria, total fungi and *E. Coli* was monitored to establish the microbiological quality of this extemporaneous preparation and test methods was developed according to the British Pharmacopoeia 2010 for non-sterile products (18).

Results and discussion

Physicochemical Stability

The visual appearance, odour and pH at 4 ºC and 25 ºC of the extemporaneous preparations remained the same (Table 1,2 and 3). In practice, the visual appearance, smell, taste and mouth feel of the pharmaceutical preparations will influence the patient's acceptance and compliance, especially in the paediatric patients. These factors are important to be considered in the development of a suitable oral extemporaneous preparation (5).

The folic acid concentration remained in the extemporaneous preparations collected at 0, 14, 28 and 60 days were all above 90% for both storage conditions (Figure 2). Although previous

study found that the rate of chemical degradation usually increases with temperature (7), this study showed no significant differences in the concentration of folic acid remained in the suspension in both storage conditions. (Figure 2).

In aqueous solution, folic acid is stable up to 10 hours at 100ºC, in a pH range of 5 to 12 and protected from light. The degradation rate increases at pH below 5 (19). However, this study found no significant degradation in the folic acid prepared in oral suspension dosage form even though the pH were consistently below 5 throughout 60 days. Drugs in solution are more susceptible to chemical degradation than drugs in solid state (such as suspensions), thus suspensions are more stable than solutions (7). This may explain why the folic acid remained stable even at pH lower than 5.

Table 1: Visual appearance of folic acid oral suspension

Time (Days)	0	14	28	60
4ºC	Colour: orange yellow Clarity: opaque	Colour: orange yellow Clarity: opaque	Colour: orange yellow Clarity: opaque	Colour: darker orange Clarity: opaque
25ºC	Colour: orange yellow Clarity: opaque	Colour: orange yellow Clarity: opaque	Colour: orange yellow Clarity: opaque	Colour: darker orange Clarity: opaque

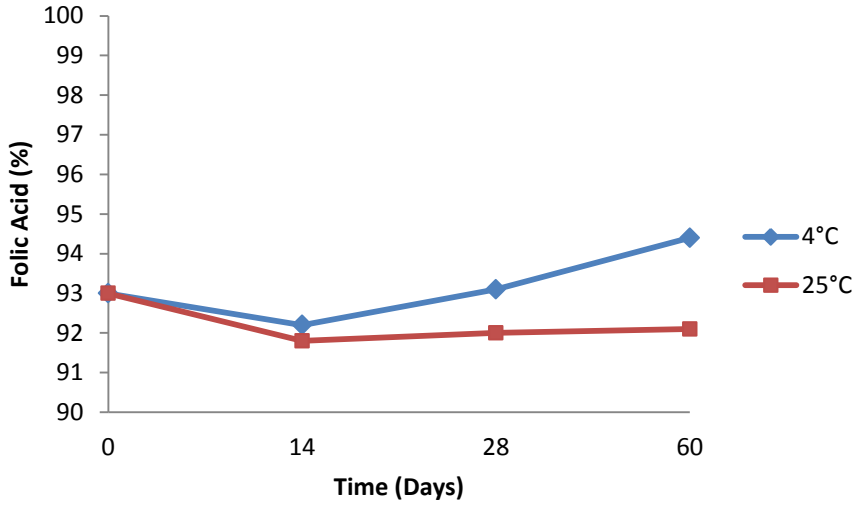
Table 2:Odour of folic acid oral suspension

Time (Days)	0	14	28	60
4ºC	Orange	Orange	Orange	Orange
25ºC	Orange	Orange	Orange	Orange

Table 3:pH of folic acid oral suspension

Time (Days)	0	14	28	60
4ºC	4.341	4.347	4.384	4.371
25ºC	4.341	4.348	4.369	4.374

Figure 2:Stability of folic acid oral suspension at 4ºC and 25ºC



It is important to understand that the tablet dosage forms used for extemporaneous preparations also contain many other excipients. These excipients are compatible in the tablet form but may have the potential to interact with both in solution or suspension. These excipients alter the pH of the final product during storage and increase the degradation rate (7). Consequently, it may affect the stability of the drug and on the shelf-life of the final preparation (16).

Microbiological Stability

The results from the microbiological stability study of folic acid oral suspension showed that the microbial quality was within the established specifications during the study period for both temperatures (Table 4 and 5). The total viable aerobic count was kept low and total yeast and mould count was minimal. *E. coli* was absent throughout the 60 days period. This result shows that the preservatives used in this extemporaneous preparation were effective against bacteria and fungi and the folic acid oral suspension is microbiologically stable.

Effective preservative systems require rigorous evaluation which is seldom performed on extemporaneous formulations. Many factors can reduce the effectiveness of the preservative including use of contaminated materials, chemical degradation, binding of preservative to suspending agents or tablet excipients, incorrect storage or unhygienic use of the extemporaneous preparations (7).

Table 4: Microbial results of folic acid oral suspension (4ºC)

Time (Days)	0	14	28	60
Total aerobic bacteria (Not more than 200cfu/g)	<10cfu/g	<10cfu/g	<10cfu/g	<10cfu/g
Total yeast & mould (Not more than 20cfu/g)	<10cfu/g	<10cfu/g	<10cfu/g	<10cfu/g
E. coli (Absence in 1g)	Conforms	Conforms	Conforms	Conforms

Table 5: Microbial results of folic acid oral suspension (25ºC)

Time (Days)	0	14	28	60
Total aerobic bacteria (Not more than 200cfu/g)	<10cfu/g	<10cfu/g	<20cfu/g	<20cfu/g
Total yeast & mould (Not more than 20cfu/g)	<10cfu/g	<10cfu/g	<10cfu/g	<10cfu/g
E. coli (Absence in 1g)	Conforms	Conforms	Conforms	Conforms

As the physicochemical and microbiological stability results were within the acceptable specifications throughout the study period, the study concluded that the extemporaneous formulation of folic acid oral suspension is stable for up to 60 days when stored at both 4ºC and 25ºC. The extemporaneous preparation of folic acid in the form of suspension has a few advantages over solution or oral powder. The insoluble drugs such as folic acid may be more palatable and stable in suspension than solution and the suspended insoluble powders are easy to swallow or administer than the reconstitution of oral powder in water which may not form readily into a suspension (20). The method of extemporaneous preparation in suspension form enables easy administration of folic acid to paediatric well as the patient compliance and acceptance will be much better than oral powder papers.

This information on formulation and stability data should be made accessible to both pharmacists and paediatricians so that patients can receive the highest quality preparations. Although this study have addressed some of the risks associated with extemporaneous compounding such as non-validated stability of the product, there are still other inherent risks in compounding which include using incorrect formulation and calculations, selecting incorrect drugs and using incorrect quantities (21).Therefore, proper guidelines that focus on the quality assurance and quality control practices should be made available for every compounding pharmacy in order to deliver consistent, safe and quality products (1).

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Self-medication practices among Malaysian consumer: A questionnaire-based study

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Abstract

This study was carried out to assess the prevalence of self-medication practice among Malaysian consumers who visit to community pharmacies. The data was collected using structured questionnaires which were randomly distributed to 500 consumers who visited to 10 conveniently selected community pharmacies in Sungai Petani, Kedah between August to October 2007. Out of the 500 questionnaire distributed, 105 responses were received for a response rate of 21.0%. Approximately 45% of the respondents have practiced self-medication in the preceding six months. The respondents mainly practiced self-medication for fever (35.2%), colds and flu (35.2%) and cough (31.4%). The most popular classes of medicines used by the consumers were analgesic/NSAIDs (32.4%), cold and flu medicines (23.8%) and antacids (18.1%). Only 27.6% of respondents were confident in self-managing medications or dietary supplements. The consumers mostly agreed that more advice on medications should be given by pharmacist (75.2%) and pharmacist has high level of professionalism on medication (65.7%). The study concluded that the practice of self-medication mostly involved management of minor ailments using non-prescription and over-the-counter medicines.

Keywords: self-medication, consumer, community pharmacy, pharmacist, minor ailment

Introduction:

Self-medication is a common practice among the consumers, particularly for those in developing countries (1). It can be considered as the most common form of self-care in health. It is defined as the use of a drug product for the treatment of a disease or symptom or for the disease prevention or promotion of health, without a professional prescription (2) or obtaining and consuming medicines without the advice of a physician or pharmacist either for diagnosis, prescription or surveillance of a treatment (1).

Over the last decade, the economical, political, and cultural factors have contributed to a constant increase in self-medication worldwide, leading this practice into a major public health concern. The huge amount of medicines currently available in the market does not equate with an improvement in quality of life (2). The main concerns regarding self-medication are the risk of

inadequate use of drugs and the occurrence of side-effects and accidents related to this practice (2). For instance, the use of non-prescription medications and dietary supplements by elderly patients in USA has causes concern (3). This geriatric population uses more prescription medications and have higher potential risk of developing harmful medication-related problems than the younger adults. Various reports have shown that 40% to 87% of community-dwelling adults older than 65 years were using at least one OTC product regularly and 5.7% were taking five or more non-prescription medications and/or dietary supplements daily (3).

Patients turn to purchase medicines frequently through drugstore sales personnel, in an attempt to save time and money on a medical appointment that fails to meet their expectations (2). Several studies have documented that community pharmacies are not the only sites where medicines are bought and sold, they are also places where information and advice on health problems and treatment is sought (4). Some studies have found that it is fairly routine for the patient to seek the advice of pharmacists and medicine shop attendants for common ailments. Such consultations are convenient; they save time, money and the opportunity cost of waiting to be seen by a doctor (4).

Since medicines are widely used in the population to reduce morbidity and mortality (3), it is important to ensure that the non-prescription medicines and OTC are used appropriately during self-medication. The patient's self-medication practice must be evaluated to provide the information which enables health care providers to educate the patients on issues around self-medication. In order to maximize the therapeutic outcome and provide safe and quality medical care, a better understanding of the patient demand and factors affecting patient's self-medication practices is required. Nevertheless, currently there is lack of study on self-medication and factors contributing to consumer's practice of self-medication with community pharmacies services in Malaysia. Thus, a study is warranted to investigate the practices of self-medication with community pharmacies in Malaysia. Consequently, strategies and action plans can be developed to improve the community pharmacy services on the issue around consumer self-medication. Therefore, this study was carried out to obtain baseline data on self-medication practices among the Malaysian consumers and factors influencing self-medication.

Method

This is a cross-sectional descriptive study using a structured questionnaire. The questionnaire was adapted and modified from a survey instrument formulated by Shankar et al. (1). The questionnaire was designed in three different languages (English, Malay and Mandarin) to cater for the language proficiency differences among the Malaysian consumers. The questionnaire was initially examined by an expert for its face and content validity. Subsequently, internal consistency and reliability were tested by assigning 20 customers to answer the questionnaire. The consumers consisted of Malay, Chinese and Indian who visited a community pharmacy in the state of Penang, Malaysia. A Cronbach's alpha of 0.73 was obtained (value of > 0.70 is considered acceptable reliability).

This final questionnaire comprised of 5 sections. The first section contained questions on demographic and socioeconomic background of respondents. The second section contained questions on distance from residency to nearest pharmacy, type of pharmacy the respondents used to visit and frequency of visit. The third section assesses the consumer self-medication practice for the past 6 months, reason for not consulting doctor, main use of the medicines and main symptoms that being experienced. The forth section was the details of medicine taken and medical conditions that had been suffered. The last section was to assess the consumer's opinion towards self-medication. Respondents were requested to describe the level of agreement on self-medication based on 10 statements which formulated in a 5-point Likert scale (1 = Strongly disagree; 2 = Disagree; 3 = Not sure; 4 = Agree; 5 = Strongly agree).

A convenient sample of 10 community pharmacies in Sungai Petani city, state of Kedah, Malaysia was chosen as the study stations. The study population consisted of consumers who visited to the selected pharmacies. The consumers must be aged over 18 years and literate. A total of 500 questionnaires were sent by personal visit by the researcher (Ooi GS) to the selected pharmacies and detail explanation had been given to the pharmacists-in-charged. The questionnaires were then randomly distributed to the consumers who visited to the selected pharmacies by the pharmacists-in-charged. The respondents were requested to complete the questionnaire and returned it to the pharmacists before they leave the pharmacy. Participation in this study was strictly voluntary and written informed consent was obtained from the respondents. Once the completed questionnaire was received, all identifying information had been removed to protect anonymity.

Data analysis

Data analysis was performed by using SPSS version 15.0. Chi-square statistic was used to investigate differences in the consumers' tendency to practice self-medication between different groups of consumers (age, gender, race, martial status, educational level, monthly income and insurance coverage), based on their responses to question 3A: "Have you purchased medicines of your own without consulting either a doctor or a pharmacist in the preceding six months?". The sub-groups with less than ten respondents were excluded from the analysis. Odds ratio were calculated for variables which showed significant differences based on Chi-square analysis. Student t-test was used to investigate differences between consumers' monthly health care expenditure between those who practiced self-medication and those who did not practice in this way. A significant level of less than 0.05 was used for all analytical statistic analysis.

Results

Demographic characteristics

Of the 500 questionnaire distributed, 105 responses were received for a response rate of 21.0%. The respondents were mostly female (57.1%) and aged between 20-29 years old (31.4%). In terms of ethnicity, the majority of the respondents were Chinese (57.1%). Approximately two-third (64.8%) of the respondents were married and around half (51.5%) were either graduated from primary or

secondary school. Most of the respondents were employed (86.7%) with a monthly income within RM1,500-RM5,000 (47.6%). Around six out of ten (57.0%) of the respondents spent RM0-RM99 per month on health care and only 7.7% spent RM300 and above (Table 1).

Table 1: Demographic characteristics of the responding consumers

Characteristic	*n*	*%*	*Characteristic*	*n*	*%*
Age group			**Educational level**		
20-29	33	31.4	Primary or secondary	54	51.5
30-39	24	22.9	Collage/Technical school	20	19.0
40-49	20	19.0	University	30	28.6
≥ 50	28	26.6	No formal education	1	1.0
Gender			**Monthly income (RM)**		
Male	45	42.9	< 800	16	15.2
Female	60	57.1	800-1500	20	19.0
			1500-3000	25	23.8
Race			3000-5000	25	23.8
Malay	26	24.8	> 5000	5	4.8
Chinese	60	57.1	Unemployed	4	3.8
Indian	18	17.1	Retired	10	9.5
Others	1	1.0			
			Monthly health care expenditure (RM)		
Marital status			0-99	60	57.0
Single	36	34.3	100-199	24	22.9
Married	68	64.8	200-299	13	12.4
Widowed	1	1.0	≥300	8	7.7

Details of pharmacy visit

Majority of the respondents (81.0%) were able to assess the nearest pharmacy from residency within 15 minutes (Table 2). The respondents visited independent pharmacy (63.8%) more frequently than chain pharmacy (36.2%). Most of the respondents (51.4%) visit to pharmacies once or twice a month.

Self-medication for the preceding six months

Approximately 45% of the respondents have practiced self-medication in the preceding six months (Table 3). The purchased medicines were mainly for their own used (84.8%), followed by for their parents (25.7%) and children (24.8%). The respondents mainly experience fever (35.2%), colds and flu (35.2%) and cough (31.4%). Allopathic medicines (73.3%) and supplements (67.6%) were predominantly used by the respondents. Respondents' main reasons for not consulting a doctor including do not think it is necessary to do so (52.4%) and feel expensive (34.3%). Majority (95.2%) of the respondents purchased their medicines from pharmacy. When specifically looking at the main use of the purchased medicines, the respondents mostly used it for treatment (69.5%) and health maintenance (36.2%).

Table 2: Details of pharmacy visit among the responding consumers

Survey question	*n*	*%*
2A. Distance from residency to nearest pharmacy		
< 5 min	32	30.5
5-15 min	53	50.5
15-30 min	15	14.3
> 30 min	5	4.8
2B. Which types of pharmacy do you visit most?		
Chain (has 4 or more stores under common ownership)	38	36.2
Independent (has 3 or fewer stores under common ownership)	67	63.8
2C. How frequent do you visit pharmacy?		
More than once a week	6	5.7
Once a week	8	7.6
Twice a month	23	21.9
Once a month	31	29.5
Once every 2-3 months	16	15.2
Once every 6 months	13	12.4
Once a year	8	7.6

Differences in the tendency of self-medication between different demographic groups

Chi-square analysis showed no significant differences ($p > 0.05$) in the tendency of self-medication between consumers with different age, gender, race, martial status, educational level and monthly income. However, consumers with insurance coverage were 3.45 times (Odds ratio) more tend to practice self-medication than those without insurance coverage (chi-square value $X^2 (1) = 8.20$, $p = 0.004$).

The mean monthly health care expenditure among consumers who practiced self-medication (RM127.02 ± 140.45) was slightly higher than those who consulted with doctor or pharmacist when purchasing medicines (RM91.29 ± 115.23). However, t-test analysis showed that the different was not significant ($p = 0.122$).

Medical condition of the respondents

Around 58% of the responding consumers do not have underlying medical condition (Table 4). For those who have one underlying disease (34.3%), the main conditions were allergy (9.5%), hypertension (5.7%) and diabetes (4.8%). About 8% of the respondents have two underlying medical conditions, which predominantly were hypertension and diabetes (2.9%).

Details of medicines taken during self-medication

The three most popular classes of allophatic drugs used by the respondents during self-medication were analgesic/NSAIDs (32.4%), cold & flu medicines (23.8%) and gastrointestinal medications/antacids (18.1%). When assessing the type of supplements normally used during self-medication, vitamin C (30.5%), multivitamin (25.7%) and fish oil/Omega 3 (10.5%) were the most popular supplements (Table4).

Table 3: Self-medication for the preceding six months among the responding consumers

Survey question	*n*	*%*
3A. Have you purchased medicines of your own without consulting either a doctor or a pharmacist in the preceding six months?		
Yes	47	44.8
No	58	55.2
3B. To whom is the medicine meant for?*		
Self	89	84.8
Parents	27	25.7
Children	26	24.8
Spouse	13	12.4
Others	6	5.7
Missing data	1	1.0
3C. What was the main symptoms did you experience?*		
Fever	37	35.2
Colds and flu	37	35.2
Cough	33	31.4
Headache/migraine	30	28.6
Gastric pain	27	25.7
Muscle pain	23	21.9
Sore throat	21	20.0
Stomach discomfort	19	18.1
Allergic	11	10.5
Others	13	12.4
3D. What type of medicine(s) did you use?*		
Allopathic (modern) medicines	77	73.3
Supplements	71	67.6
Cosmetics	48	45.7
Herbal medicines	36	34.3
Nutritional products	8	7.5
Missing data	1	1.0
3E. What was your main reason for not consulting a doctor?*		
Not necessary	55	52.4
Expensive	36	34.3
Inconvenience	14	13.3
Far	7	6.7
Not effective	4	3.8
Others	10	9.5
3F. Which type of premises does you usually go to purchase your medication?*		
Pharmacy	100	95.2
Chinese medical hall	11	10.5
Medical hall	4	3.8
Malay traditional clinic	3	2.9
Others	3	2.9
3G. State the main use of the medicines that you purchased on your own:*		
Treatment	73	69.5
Health maintenance	38	36.2
Prevention	19	18.1
Others	2	1.9
Missing data	2	1.9

**Note: ***The respondent (n = 105) can answer more than one answer

Table 4: Medical condition of the respondents and details of medicines taken during self-medication

Survey item	***n***	***%***
4A. Medical condition of the responding consumers		
Consumer without underlying medical condition	***61***	***58.1***
Consumer with one underlying medical condition	***36***	***34.3***
Allergy	10	9.5
Hypertension	6	5.7
Diabetes	5	4.8
Gastric	3	2.9
Cardiovascular disease	3	2.9
Migraine/headache	2	1.9
Dysmenorrhoea / Period pain	2	1.9
Hyperlipidemia	1	1.0
Others	4	3.8
Consumer with two underlying medical conditions	***8***	***7.6***
Hypertension & Diabetes	3	2.9
Hypertension & hyperlipidemia	2	1.9
Allergy & Gastric	1	1.0
Diabetes & cardiovascular disease	1	1.0
Gastric & others	1	1.0
4B. Class of allophatic / modern drug(s) normally used by the responding consumers during self-medication*		
Analgesics or NSAIDs	34	32.4
Cold & flu	25	23.8
Gastrointestinal medications / antacids	19	18.1
Cardiovascular medications	17	16.2
Allergy medications	16	15.2
Diabetes medications	10	9.5
Antibiotics	6	5.7
Others	1	1.0
4C. Class of herbal medicine(s) normally used by the responding consumers during self-medication*		
Chinese herbal medicines	20	19.0
Malay herbal medicines	11	10.5
Indian herbal medicines	5	4.8
4D. Type of supplements normally used by the responding consumers during self-medication*		
Vitamin C	32	30.5
Multivitamin	27	25.7
Fish oil / Omega 3	11	10.5
Vitamin B complex	8	7.6
Calcium	8	7.6
Vitamin A, C & E	7	6.7
Evening primose oil	6	5.7
Vitamin E	4	3.8
Others	15	14.3

**Notes: ***The respondent (n = 105) can answer more than one answer

Consumers' opinion towards self-medication

The respondents' responses towards questions assessing their opinion on self-medication were shown in Table 5. Majority of the consumers (69.5%) were either strongly disagreed or disagreed that prescription medication can be purchased without professional's assistance. Only 27.6% of respondents were confident in self-managing medications/dietary supplements. Additionally, approximately one in every three consumers were either strongly agreed or agreed that non-prescription medications/dietary supplements can be purchased without assistance. Most of the respondents (62.9%) held positive opinion that non-prescription medications/dietary supplements help maintain health. The consumers mostly agreed that more advice on medications/dietary supplements should be given by pharmacists (75.2%) and pharmacist has high level of professionalism on medications (65.7%). However, the responding consumers predominantly held a neutral opinion about whether more prescription medicines should be switched to pharmacy or over-the-counter status (45.7%). Around half of the respondents (53.4%) expressed disagreement upon the sharing of medicines among family members as compared to 16.2% who in favour with this practice. Majority of the consumers disagreed that the leftover medicines stored at home can be used when needed (78.1%). The consumers generally disagreed that originally prescribed dosage can be changed according to their own judgment (80.0%).

Table 5: Responding consumers' opinion towards self-medication

Survey question/Statement	*Frequency (%)*					
	1	**2**	**3**	**4**	**5**	**Missing data**
1. Prescription medications can be purchased without professional's assistance.	42 (40.0)	31 (29.5)	23 (21.9)	8 (7.6)	1 (1.0)	0 (0.0)
2. I am confident in self-managing medications/dietary supplements.	7 (6.7)	16 (15.2)	53 (50.5)	19 (18.1)	10 (9.5)	0 (0.0)
3. Non-prescription medications/dietary supplements can be purchased without assistance.	13 (12.4)	24 (22.9)	33 (31.4)	24 (22.9)	11 (10.5)	0 (0.0)
4. More advice on medications/dietary supplements should be given by pharmacist.	2 (1.9)	3 (2.9)	20 (19.0)	40 (38.1)	39 (37.1)	1 (1.0)
5. I think non-prescription medications/dietary supplements help maintain health.	5 (4.8)	8 (7.6)	26 (24.8)	40 (38.1)	26 (24.8)	0 (0.0)
6. I think pharmacist has high level of professionalism on medications.	2 (1.9)	11 (10.5)	23 (21.9)	32 (30.5)	37 (35.2)	0 (0.0)
7. Medicines can be shared among family members	32 (30.5)	24 (22.9)	32 (30.5)	15 (14.3)	2 (1.9)	0 (0.0)
8. The leftover medicines stored at home can be used anytime when needed.	47 (44.8)	35 (33.3)	16 (15.2)	6 (5.7)	1 (1.0)	0 (0.0)
9. Originally prescribed dosage can be changed according to my own judgement.	47 (44.8)	37 (35.2)	15 (14.3)	5 (4.8)	1 (1.0)	0 (0.0)
10. More prescription (doctor) medications should be switched to pharmacy or over-the-counter status.	6 (5.7)	21 (20.0)	48 (45.7)	13 (12.4)	17 (16.2)	0 (0.0)

Note: 1 = Strongly disagree; 2 = Disagree; 3 = Not sure; 4 = Agree; 5 = Strongly agree

Discussion

This study revealed that self-medication practices were prevalent among the Malaysian consumers who visited community pharmacy. About 45% of the surveyed respondents had purchased medicines without consulting either a doctor or pharmacist in the previous six months. This percentage was lower compared with a recent study undertaken among consumers in Kuala Lumpur, the capital city of Malaysia where 62.7% had practiced self-medication in the preceding week (5). However, the prevalence of self-medication in the present study was slightly higher than study findings from Jordan (42.5%) (6) and Southwest Ethiopia (39.2%)(7).

Consumers from different demographic background found to have no significant differences in their tendency of self-medication. The only factor which indicated higher probability for practising self-medication among the consumers was insurance coverage. However, the present study did not evaluate the reasons behind this observation. Around half of the responding consumers expressed "not necessary" as their main reason for not consulting a doctor. This finding may be due to the fact that the respondents mostly performed self-treatment for minor ailments like fever, cold and flu and cough which can be managed by non-prescription medicines. Study from other countries also found similar trend where consumers were confident with self-medication for minor ailments. For instance, a recent study in Canada found adolescents' self-administration of acetaminophen for pain is common with 50% to 75% of junior high students reporting that they use acetaminophen for pain relief without first checking with any healthcare provider (8). Nevertheless, self-treatment practice without proper information given may increase risk of misuse or over-consumption of non-prescription medicines. The Malaysian consumers should be educated on the dangers of self-medication and advised doing it only for minor ailments and to seek medical treatment if unsure (5).

The present study highlighted the important role of community pharmacist in providing advice and professional consultation to the consumers who practice self-medication. Majority of the surveyed consumers viewed that more advice on medications should be provided by pharmacists. Further, the respondents generally viewed pharmacists as having high level of professionalism on medication. Therefore, community pharmacists must be equipped themselves with the skills of educating the consumers on the appropriate and quality use of non-prescription and over-the-counter medicinal products. Indeed, educational intervention by pharmacist is needed to correct the inappropriate practices observed among some consumers in the present study, for instance, the sharing of medicines among family members and the keeping of leftover medications. The development of professional standards of practice among the community pharmacists is needed in the area of self-medication (5). This could be achieved via structured training and establishment of guidelines to assist the community pharmacists in providing professional consultation to the consumers with regards to self-medication.

Study limitation

The selection bias cannot be ruled out due to the convenience sampling and self-reported information obtained in the present study. The small sample size and low response rate further reduced the generalisability of the study findings.

Future study should include a larger representative sample size of the Malaysian consumers who visit to community pharmacies.

Conclusion

Self-medication is prevalent in Sungai Petani with approximately 45% of surveyed consumers using some form of self-medication in the past 6 months of the study. The practice of self-medication mostly involved management of minor ailments using non-prescription and over-the-counter medicinal products. Pharmacist is responsible to limit the potential risks involved in self-medication by educating the consumers regarding the medicines and its appropriate use, and instructions to received medical treatment if they are unsure.

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ABSTRACTS FROM THE MALAYSIAN PHARMACEUTICAL SOCIETY PHARMACY SCIENTIFIC CONFERENCE 2012

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PHARMACY: LEADING & MANAGING CHANGE

Jointly organised by the Malaysian Pharmaceutical Society, the Department of Pharmacy of the University of Malaya and the Pharmaceutical Services Division of the Ministry of Health, Malaysia

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PPM7	R A Rahman	Analgesic and Antipyretic Activity of *Manihot esculenta* crantz Extracts

PPM8	A M Saleem	Involvement of Opioidergic and Serotonergic Pathways in the Analgesic Activity of *Cissus quadrangularis* L. (Patah Tulang) Stem Extract in Mice
PPM9	P Hassandarvish	Investigation of Gastro-Protective Activity of Schiff Bases Complexes and their Mechanisms
PPM10	L Z A Salim	Anti-leukemia Effect of Thymoquinone Isolated from *Nigella sativa*
PPM11	M Taher	Study on Antidiabetic Plants Cocktail Containing *Andrographis paniculata*, *Cinnamomum burmannii* and *Tinospora crispa*
PPM12	Y Pan	*In Vitro* Effect of Various Herbal Active Constituents on Cytochrome P450 2E1
PPM13	A M Saleem	Analgesic Activity of *Cissus quadrangularis* (Patah Tulang) Stem Extracts in Mice
PPM14	A M Saleem	Antibacterial Activity of Methanolic Extract of *Clinacanthus nutans* (Sabah Snake Grass) Leaf
PPM15	A J Sunilson	Hepatoprotective Activity of *Swietenia macrophylla* Fractions in CCl_4 Intoxicated Rats
PPM16	S E A Saad	Analgesic Effect of *Ruta graveolens* in Albino Mice and Rats
PPM17	A K Balaraman	Antidiabetic Effect of Steroidal Compound Isolated from *Melothria maderaspata*
PPM18	S C Ng	Effects of Hopea Extracts on Human Colorectal Cancer Cell Proliferation via Induction of Apoptosis
PPM19	Y S Chia	Inhibition of Human Estrogen Dependent Breast Carcinoma Proliferation by *Hopea odorata* and *Hopea ponga*
PPM20	L Y Foong	*In Vitro* Cytotoxic Effects of *Hopea odorata* and *Hopea ponga* on Estrogen Independent Breast Cancer
PPM21	K H Tan	Antiproliferative Property of *Hopea odorata* and *Hopea ponga* Extracts on Human Cervical Cancer Cells
PPM22	P K Boey	Antiproliferative Activity of *Hopea ponga* and *Hopea odorata* Leaves and Stem Bark on Leukemia Cancer Cell Lines (CEMss)
PPM23	F Y Tan	The Cytotoxic Activities of *Hopea odorata* and *Hopea ponga* Extracts on Human Ovarian Cancer Cells

PHARMACEUTICAL TECHNOLOGY

No	**Presenting Author**	**Title**
PPT1	A R Tapas	Preparation of Carvedilol Spherical Crystals Having Solid Dispersion Structure by the Emulsion Solvent Diffusion Method and Evaluation of Its *in vitro* Characteristics
PPT2	R Sheshala	Comparative Evaluation of Different

		Spreadability Techniques on Extemporaneously Prepared *Cocos nucifera* Topical Dosage Forms
PPT3	B H Ng	Erosion and Dissolution Performance of Intermediate Molecular Weight HPMC Controlled Release Polymers
PPT4	K Dua	Aqueous Solubility Enhancement of Ketoconazole Using Solid Dispersion and Complexation Technique
PPT5	M Razavi	Formulation and Evaluation of Gastroretentive Matrix Tablets of Metformin Hydrochloride with Xanthan and Tamarind Gum
PPT6	S Rajesh	Formulation and *In-vitro* Evaluation of Matrix Type Transdermal Patches of Captopril
PPT7	N S Ashikin Wan Hussin	Effect of Polymer Concentration on Plasticity of Hot Air-Dried Guluronate- and Mannuronate-Rich Alginate Films
PPT8	A Abdellah	People Perception towards Impact of Good Manufacturing Practice Implementation in Malaysia

ORAL PRESENTATIONS

PHARMACY EDUCATION

OPE1 (000044)

Assessing Stress among Undergraduate Pharmacy Students in University of Malaya

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Health care students including pharmacy students are believed to experience a higher level of stress as compared to their age-matched peers. However, stress among pharmacy students in Malaysia has not been well documented. This cross-sectional study aimed to determine the prevalence and sources of stress among the undergraduate pharmacy students in the University of Malaya (UM). All UM pharmacy students (n = 273) completed a well validated measure, the Derogatis Stress Profile. The response rate was 100%. Our findings showed that although these students did not demonstrate significant levels of stress, their perceived stress levels were significantly higher (mean = 53.55 ± 7.87; $p < 0.001$) than the general population. Academic-related stress was rated as the most common source of stress. Stress was significantly associated with ethnicity and place of stay, with Malay students and students living off-campus having higher levels of stress. There was a significant negative correlation between stress and grade point average (GPA) ($r = -0.159$, $p = 0.009$) indicating that as stress levels increases, students GPA decreases. Second year students were found to be the most stressed although stress levels did not significantly differ across academic years. Thus, targeted interventions may be an effective way of dealing with stress during the transition from second year to third year training.

OPE2 (000051)

Evaluation of Multimedia and Conventional Counselling in Metered Dose Inhaler (MDI) Technique Education and Time-efficiency in Sibu Hospital

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Multimedia has shown to be a useful tool in medical device education. This study evaluated whether recorded counselling on touchscreen computer, that is multimedia counselling is as effective and time-efficient in promoting patient understanding of metered dose inhaler (MDI) with or without valved-holding chamber (VHC) technique as conventional way. MDI users were recruited and randomly allocated into either multimedia or conventional counselling group. Inhalation technique was assessed before and after counselling using checklists. Time spent to reach perfect inhalation technique was recorded to determine the time-efficiency of the counselling methods. Both multimedia and conventional groups showed significant improvement with average of 44.3% (standard deviation (SD): 22.1; $P<0.001$) and 26.9% (SD: 17.6; $P<0.001$),

respectively in the inhaler technique score. However, there was no significant difference in the technique improvement between both groups (P=0.122). Similarly, there was no significant difference between time spent in both groups to reach perfect inhalation technique (14.3 minutes, SD: 7.8 vs 11.5 minutes, SD: 5.3; P=0.114). In conclusion, both multimedia and conventional counselling improved patient MDI (with or without VHC) technique significantly. Both counselling methods had similar effectiveness and time-efficiency in MDI (with or without VHC) technique education.

OPE3 (000074)

Perception of Nurses towards Generic Medicines: Qualitative Groundwork

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Nursing is a major supporter of the health care system in Pakistan. The study is aimed to explore nurses' views towards generic medicines and their substitution. The study was conducted among nurses of two medical wards in a large private sector, tertiary care hospital (700-bed) in Karachi, Pakistan. Nurses who agreed to participate were interviewed personally (n=11) using a semi-structured interview guide. The tape recorded interviews were held during the summers of 2009 in the hospital. Thematic analysis of the interviews identified four major themes: Understanding of the terms "generic medicine", "switching between the medicines", "quality of locally manufactured generics", and "information about locally manufactured generic medicines". None of the respondents showed understanding about generic medicines and they understand the term generic medicines as locally manufactured medicines available only by their chemical names in the market. Nearly all the respondents reported frequent switching between those medicines that contain the same active compound of similar potency. More than half of the respondents raised doubts about the safety and efficacy issues in locally manufactured medicines. All the respondents suggested to be better informed about locally manufactured generic medicines. Understanding about generic medicines is lacking among nurse. Nurses expressed their suspicion about locally manufactured generics and therefore incorporation of generic medicine information in nursing education is required to build trust for locally manufactured medicines.

OPE4 (000100)

It is Not as Simple as I Thought: Motivating Students to Learn Non-Prescription Preparations More Effectively through Action Research

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As a diligent lecturer, spending time finding resources and effective methods to transfer knowledge to students is hard work. Spurring and motivating students in taking up and

maintaining their interest in an elective course on Non-Prescription Preparations is not an easy task, as this course is not commonly chosen by the pharmacy students as one of their elective courses due to various reasons. Hence, action research was conducted as the research technique to improve on the teaching method, hoping that the course will become more interesting for students to sign up in future. Series of written feedback and one verbal feedback were obtained from the students enrolled in the course using "Start-Stop-Continue" theme. Students were free to give feedback and suggestion on whether to start, to stop or to continue with the new teaching method employed and new course content incorporated into the course. No doubt, action research methodology requires a lot of patience and effort to conduct as it requires constant improvement and continuous change throughout the whole research period. Furthermore, a lot of persuasion is needed to encourage students to speak up. Meanwhile, as the researcher who is also the lecturer, it was almost impossible to teach the students and carry out observation concurrently. This oral presentation will discuss how the researcher practiced flexibility and the challenges faced when conducting this action research in motivating students to learn Non-Prescription Preparations more effectively and in an enjoyable learning environment.

OPE5 (000026)

Pharmacy Students' Assessment of an Objective Structured Clinical Examination (OSCE) in International Islamic University Malaysia (IIUM)

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An Objective Structured Clinical Examination (OSCE) is an objective method of assessing students' clinical, practical and technical skills. The aim of this study is to determine the effectiveness of an OSCE for assessing 4th year pharmacy students' skills in International Islamic University Malaysia (IIUM). Six OSCE stations (5 active and one rest stations) were designed and implemented in the 2011-2012 academic year as part of the assessment methods for a clinical pharmacy course. The broad competencies tested in the OSCE included: demonstration of the correct technique of measuring blood pressure (station 1), screening and validation of a prescription (station 2), identification and resolution of Drug Related Problems (DRPs) (station 3), demonstration of the correct technique of blood glucose testing (station 4), and improving glycaemic control (station 5). After all the students completed the OSCE, they filled a questionnaire containing items on understanding written instructions, difficulty of the tasks, degree of learning gained and needed, adequacy of time given to accomplish tasks and the appropriateness of reference materials used. More than 50% of the students felt that the written instructions provided at the second station were difficult to understand. Approximately 70% of the examinees felt that the fifth station were difficult. A majority of the students felt that a higher degree of learning was needed to accomplish the fifth station. About 50 to 60% of the students reported that the 10 minutes allocated for completing fourth and last stations (station 5) was inadequate. Clearer instructions at OSCE stations, sufficient time and higher degree of learning should be provided for students.

OPE6 (000023)

Honey Compared to Silver Sulphadiazine Dressing for Acute Wounds: A Systematic Review

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While both honey and silver sulphadiazine dressing (SSD) are commonly used for acute wounds, their relative effectiveness remains unclear. The aim of this review was to compare the effectiveness of honey to SSD. We searched the Cochrane Central Register of Controlled trials, MEDLINE, EMBASE, EBSCOhost and other databases without date or language restriction for randomised controlled trials (RCTs) that compared the effectiveness of honey with SSD for acute wounds. We also checked the reference lists of included studies and related reviews for additional studies. Two reviewers extracted and summarised details of eligible trials and assessed the methodological quality of each trial using the Cochrane risk of bias tool assessments independently. From the initial 1028 search titles obtained, we identified eight eligible RCTs involving 649 patients. Only six out of the eight trials reported quantifiable outcome. Overall, the risk of bias in the included trials was fair. Pooled analysis showed that honey compared to SSD significantly reduced healing time for (i) superficial thickness wound [WMD -4.62 (95% CI: -7.37 to -1.88) and (ii) partial thickness wounds, [WMD -2.76 (95% CI: -4.36 to -1.15)]. While the results provide marginal evidence that honey is superior to SSD in term of shorter healing time for acute wound, additional robust trials is needed before a firm conclusion can be made.

CLINICAL PHARMACY & PHARMACY PRACTICE

OPP1 (000012)

The Incidence and Clinical Management of Adverse Events Due to FOLFOX Chemotherapy in Colorectal Cancer Patients

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FOLFOX chemotherapy has become the standard regimen for advanced colorectal cancer (CRC) but data on its adverse events profile within clinical practice, particularly in Malaysia, are scarce. This study aimed to describe the incidence and clinical management of FOLFOX-related adverse events (AEs) in CRC patients at a tertiary-care referral hospital in Malaysia. Chemotherapy records from mid-2007 to mid-2011 were screened to identify patients who received FOLFOX chemotherapy. Data were collected for 111 patients who met the inclusion criteria, from the start of FOLFOX chemotherapy up to 1

year post-treatment. Grades 3&4 FOLFOX-related AEs, graded according to NCI CTCAE v4.0 definitions, occurred in 45% of patients, with the key AEs being neutropaenia (41%), thrombocytopaenia (5%), anaemia (5%), diarrhoea (4%) and neuropathy (2%). Chemotherapy dose delays and dose reductions due to AEs occurred in 66% and 32% of patients, respectively. AEs also led to chemotherapy discontinuation (6%) and treatment-related deaths (2%). Clinical management of AEs varied between patients, with symptomatic approaches generally employed based on clinical judgement. No statistically significant association was found between clinical characteristics of patients and grades 3&4 FOLFOX-related AEs. The incidence of haematological FOLFOX-related AEs observed were similar to published data from clinical trials of FOLFOX chemotherapy but were lower for non-haematological AEs, likely due to incomplete documentation. Wide variations of clinical management strategies for FOLFOX-related AEs were observed. To optimise patient safety and clinical outcomes, thorough documentation of all chemotherapy-related AEs and the development of institution-specific treatment protocols on the clinical management of chemotherapy-related AEs are recommended.

OPP2 (000015)

Adverse Events Profile and Clinical Management of Malaysian Breast Cancer Patients on FEC+Docetaxel Chemotherapy

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Sequential chemotherapy with fluorouracil, epirubicin and cyclophosphamide followed by docetaxel (FEC+docetaxel) has led to improved clinical outcomes in breast cancer patients, but there is currently little data describing its adverse events profile within clinical practice. This study aimed to describe the adverse events profile and clinical management of breast cancer patients on FEC+docetaxel chemotherapy in a Malaysian tertiary-care hospital. Chemotherapy records from 2007 to 2011 were reviewed to identify patients who received FEC+docetaxel chemotherapy. Data were collected for 201 patients who met the inclusion criteria. Adverse events (AEs) due to FEC+docetaxel chemotherapy were graded according to NCI CTCAE v4.0. The highest incidences for haematological AEs were neutropaenia (48%), anaemia (20%) and febrile neutropaenia (18%), and for non-haematological AEs were nausea and vomiting (54%), nausea only (34%), and oral mucositis (34%). Chemotherapy dose delay, dose reduction and discontinuation due to AEs occurred in 33%, 28% and 9% of patients respectively. Haematological AEs were generally managed with chemotherapy dose delays or reductions, prophylaxis with GCSF and antibiotics, blood transfusions and haematinics. Wide variations of symptomatic clinical management strategies for non-haematological AEs were given to 84% of patients, generally based on clinical judgement. The incidence of FEC+docetaxel-related AEs differed from published data from clinical trials but direct comparisons were not possible due to incomplete documentation and grading of AEs in the study population's medical records. To optimise patient safety and clinical outcomes, thorough documentation of chemotherapy-related AEs and the development of institution-specific treatment protocols on the clinical management of chemotherapy-related AEs are recommended.

OPP3 (000108)

Can the Community Pharmacists Detect Drug Related Problems (DRPs)?

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Pharmacists are making improvements in pharmaceutical care, especially detecting drug related problems (DRPs). The study was aimed to develop a checklist to detect DRP among patients with allergy. The study involved preliminary phase which involved study literature, preliminary survey and adaptation of validated questionnaire and PCNE checklist from previous studies. Then the created checklist was tested in Phase 1 where it was used in a community pharmacy to get it validated. Four professionals agreements, predictive values, sensitivity and specificity tests were done to validate the checklist. This validated checklist was then field tested in Phase 2 which consisted of two groups to test the reliability of the checklist. Results: During Preliminary Phase, some inputs which were based on patients own experience of DRPs differed from the PCNE checklist. Prevalence of DRPs detected was 12.96%. In Phase 1, significant DRPs ($p<0.05$) were therapy failure, untreated indication and in need of additional therapy whereas significant causes of DRPs ($p<0.05$) were food/drug interaction, dispensing error and polypharmacy. In Phase 2, Group1 (with validated checklist) obtained results similar to Phase 1 whereas Group 2 (without validated checklist) was unable to detect DRPs. Discussions: The study managed to develop a checklist which can be used as a detection method for DRPs among patients with allergy. There were similarities of DRP types and causes correlation statistics with studies from other countries. This study revealed that improvement had to be made in DRPs detection methods to improve pharmaceutical care and help community pharmacists play a major role in our healthcare system.

OPP4 (000018)

Outcome of Pharmacist Involvement in the Therapeutic Management of Rheumatoid Arthritis Patients in Hospital Sultanah Bahiyah (HSB)

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This study aimed to evaluate the outcome of pharmacist involvement in the therapeutic management of rheumatoid arthritis (RA) patients at the rheumatology clinic in Hospital Sultanah Bahiyah (HSB). A prospective interventional study was conducted from July to November 2011. Patients were recruited at the rheumatology clinic with two subsequent monthly follow ups at the specialist clinic pharmacy. Assessments at entry and at 2 months included quality of life (QOL) using SF-12 questionnaire and symptoms of RA. Medication adherence, drug knowledge, and adverse drug reaction (ADR) were also assessed. At each encounter, patients were counselled on medication adherence and interventions highlighted to physicians where necessary. Data was analysed using SPSS Version 16 with statistical tests which included Friedman's test (RA symptom, pain score, adherence), Wilcoxon Signed Rank test (knowledge), Pearson chi-square (ADR), and paired t-test (quality of life). Thirty-four RA patients were recruited but only

30 completed two months of follow up. At the end of follow-up, significant improvement in medication adherence and knowledge were observed with 54.7% reduction in mean Morisky score ($p = 0.006$) and 11.2% increase in knowledge score ($p<0.05$), respectively. There was a significant reduction of complaints of ADR at the end of follow-up. In quality of life assessments, physical component scores showed a significant increase of 5.70% ($p = 0.04$) while mental component scores increased 0.62%, though this was not statistically significant ($p = 0.81$). This showed that pharmacist intervention had a positive impact on therapy management of RA patients.

OPP5 (000096)

De-escalation of Carbapenem Therapy in Sarawak General Hospital (SGH): How Far Do We Put It Into Practice?

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De-escalation of antibiotics is one of the strategies in an antibiotic stewardship programme to reduce the overuse of antimicrobials and prevent the emergence of multidrug resistant organisms. Our objectives were to study the empirical versus targeted use of carbapenems (meropenem, imipenem and ertapenem) in SGH, to determine the rate of de-escalation in empirical therapy, to identify factors associated with absence of de-escalation and to suggest measures to overcome barriers to its implementation. All patients more than 12 years old who received more than one dose of carbapenems from April to August 2012 were identified from computerised in-patient pharmacy records. Site of infection, regime and course of antibiotics, culture and sensitivity (C&S) results were determined from their medical records. Failure of de-escalation was defined as the continued usage of carbapenems without de-escalation to a narrower spectrum antibiotic following the availability of C&S results. Out of the 65 identified cases, 42 prescriptions (64.6%) were empirical and the rest were definite therapy. Of the empirical therapy, eight patients were excluded from the study giving the rate of de-escalation of 44.1% (15 cases). Mean days of therapy to de-escalation was 5.53 days whereas mean days from the reported date of C&S results to de-escalation was 2.62 days. Absence of de-escalation in the remaining 19 cases (55.9%) was mainly attributed to the unavailability of C&S results as guidance (57.9%). The practice of de-escalation of carbapenem therapy in SGH is considered satisfactory but can be improved with the recent introduction of an institutional antibiotic policy to create awareness of antibiotic de-escalation.

OPP6 (000024)

An Evaluation on Over the Counter Medications (OTC) and Vitamins Use Among Pregnant Women: A Single Center Study from Malaysia

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Globally, over-the-counter (OTC) medications and vitamins utilization have increased in pregnant women. However, little is known about such practice among the Malaysian obstetric population. This study aimed to evaluate the utilization of OTC medications and vitamins among the Malaysian pregnant women. This was a cross-sectional survey conducted via face-to-face interview using validated and pilot-tested structured questionnaire from the period of April-May 2012. A total of 181 pregnant women who attended follow-up at Seberang Jaya Health Clinic were approached. Chi-square test and odd ratio were used to assess the impact of demographic characteristics on the use of OTC medications. A total of 175 pregnant women (96.6%) agreed to be interviewed. Slightly more than half (54.9%) of the respondents had used OTC medications, mostly to treat fever (24%) and flu (20.6%). Paracetamol was the most commonly utilized product followed by topical analgesics. All respondents had used at least one vitamin. Among the most commonly consumed vitamins were folic acid, vitamin C, vitamin B and iron. The main reasons for using vitamins were to improve general health (57.1%) and immune system (51.4%). The tendency of OTC medications use were noted more in working (OR:2.80; CI:1.36-5.79) and higher educated pregnant women (OR:2.04; CI:1.11-3.75). Besides, the usage of such products were significantly higher in 3rd trimester than 1st trimester (OR:2.89; CI:1.24-6.50). In conclusion, the use of OTC medications and vitamins are prevalent among Malaysian pregnant women. Therefore, integrated monitoring and education are the core of safe use of any products during pregnancy.

OPP7 (000028)

Medication Reconciliation during Hospital Admission and Discharge: Evaluating Discrepancies

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Lack of medication reconciliation at transition points of care is associated with discrepancy-related errors. This study aims to determine the clinical impact of unintentional medication discrepancies in the medical wards of Hospital Seri Manjung. All patients admitted from March-June 2010 were included in this study. Patients were excluded if they were readmitted, discharged during weekends or public holidays, transferred to another hospital or intra-hospital ward, died, or absconded. At admission, patients' medication histories were obtained by pharmacists and compared with ward prescriptions. Upon discharge, patients' discharge prescriptions were evaluated for unintended discrepancies. Discrepancies were clarified with the prescribers and documented. Severity of the discrepancy was classified as minor, significant, serious, and

life-threatening errors. Of the total 1242 potential study subjects identified, 400 patients were excluded based on exclusion criteria, and 342 patients had incomplete data. Out of 500 subjects studied, 170 (34%) had at least 1 unintended discrepancy; the remaining 330 had either intended discrepancy or no discrepancy. A total of 206 unintended discrepancies were identified. Overall rate of unintended discrepancies was 0.41 per patient. Most discrepancies occurred at admission (130, 76.5%) compared to discharge (60, 35.3%). The most common discrepancy at admission (44.7%) and discharge (20.6%) was drug omission. The most frequent medication class associated with discrepancies was antihypertensive drugs (32.3%). Majority of the discrepancies at admission (57.6%) and discharge (27.6%) were significant errors, while 9 (5.3%) patients experienced life-threatening errors. Unintended discrepancies at admission were 2 times higher than at discharge. Medication reconciliation by pharmacists may help to prevent unintended discrepancies.

OPP8 (000038)

Causality Assessment of Spontaneous Adverse Drug Reaction Reports: Comparison of the Results Obtained from Published Algorithms with WHO-UMC System

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A major issue in pharmacovigilance is that it is difficult to establish causal association between suspected drugs and the adverse drug reactions (ADRs). Causality assessment of ADRs is important in order to provide early warning signals and evaluate risk-benefit ratio of drugs. The aim of this study was to evaluate the agreement between causality assessments of ADRs obtained from two published algorithms with WHO-Uppsala Monitoring Centre (WHO-UMC) system. All ADR reports submitted between 2007 to August 2011 involving cardiovascular drugs were retrieved from the database of the Malaysian Adverse Drugs Reactions Advisory Committee (MADRAC). We selected at random ten percent (n = 506) of the total reports retrieved. Based on the information provided in the ADR report form, we determined the causality assessment with two published algorithms and compared with the WHO-UMC system. The degree of agreement between WHO-UMC system with both algorithms was poor ($\kappa = 0.181$; $p < 0.001$ for Naranjo and $\kappa = 0.010$; $p = 0.720$ for Koh & Li). Both algorithms presented high rates of sensitivity (99.6% for Naranjo and 91.3% for Koh & Li) but low rates of specificity (both were 0%) due to poor quality reports. Our study highlights the need to improve the quality and standard of reporting so that algorithms could be used to have more objective causality assessments compared to the WHO-UMC system.

OPP9 (000043)

The Effect of *Hibiscus sabdariffa* on Blood Lipids: A Systematic Review

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Hibiscus sabdariffa is claimed to be effective in lowering blood lipids, however the evidence of its effectiveness is still not clearly defined. The aim of this study was to evaluate the effect of *Hibiscus sabdariffa* on lipid profiles. Electronic databases including Cochrane Central Register of Controlled Trials, MEDLINE, and publisher databases were searched up to June 2012 for randomized controlled trials (RCTs) of *Hibiscus sabdariffa* for dyslipidemia. Journal papers and conference proceedings were also searched. The risk of bias of included studies was assessed and statistical pooling of the results from similar studies was undertaken. Four RCTs assessing effect of *Hibiscus sabdariffa* on dyslipidemia, involving 312 participants were considered eligible for inclusion. These studies varied in terms of the doses of *Hibiscus sabdariffa* used, controls, and duration of trials. *Hibiscus sabdariffa* did not produce any statistically significant reduction in total cholesterol levels [WMD 12.8; 95% CI -10.9736.57], triglyceride levels [WMD -4.35; 95% CI -29.2620.56] or an increase in high density lipoprotein levels [WMD 0.59; 95% CI -2.533.71] when compared to its control. As pooled studies are of poor to moderate quality, firm conclusion cannot be made at present on the beneficial effects of *Hibiscus sabdariffa* on blood lipids.

OPP10 (000045)

Evaluation of Parents' Perception toward Antibiotics Prescribing for Treating Their Children in Emergency Department, Hospital Kepala Batas

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The lack of knowledge and awareness on appropriate antibiotic usage may contribute to antibiotic over-prescription hence contributing towards antibiotic resistance. This study aimed to evaluate parental beliefs and practices towards antibiotics prescription for their children. This cross-sectional study took place at the pharmacy unit and involved parents who were collecting medication(s) for their out-patients children. A one-page questionnaire was used. Analysis was performed using SPSS Version 16.0. Majority of the respondents were Malay (93.7%), followed by Chinese (2.6%) and Indian (2.6%). The most common reasons for parents to bring their children to Emergency Department were fever, cough and flu. More parents with educational level up to secondary schooling and below (86.2%) significantly believed that antibiotics were free of side effects, compared to (those who attained tertiary education (13.8%) (c^2=6.4, p=0.041). Parents who believed that antibiotics can cure all infections were more likely to demand for antibiotics prescription to treat their children (c^2=8.723, p=0.013) and more likely to comply with the antibiotics regimen for their children (c^2=9.431, p=0.009). This study has shown that parental perception and attitude influence the antibiotic prescribing practice to some

extent. It is essential to raise awareness among parents to facilitate appropriate antibiotic prescribing practice. Such interventions include distribution of pamphlets and counselling on rational antibiotic use by pharmacists during dispensing sessions.

OPP11 (000057)

Health-related Quality of Life (HRQoL) Among Non-prescription Medicine Customers in Malaysia

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This study was aimed to assess the health-related quality of life (HRQoL) among non-prescription medicine customers in Malaysia and the factors that affected it. A nationwide cross-sectional survey was conducted among pharmacy customers in 59 randomly selected community pharmacies in Malaysia. The self-administered questionnaire includes the EuroQoL EQ-5D, the EQ-VAS, non-prescription medicines purchased and questions related to demographics. Data were analyzed using the multivariate analysis of variance and multiple logistic regression. A total of 2729 customers enrolled in this study with a mean EQ-5D score of 0.92 (SD = 0.15) and mean EQ-VAS score of 69.92 (SD = 24.80). In comparison to Malaysian adult population, non-prescription medicines customers have lower mean EQ-5D score ($t = -4.49$, $p < 0.01$) and EQ-VAS score ($t = -25.87$, $p < 0.01$). We found that pain/discomfort (25.6%) and anxiety/depression (13.7%) were the major HRQoL problems. Locality, age, ethnicity, household income per month, type of occupation and type of non-prescription medicine purchased were associated with the health status of non-prescription medicine customers [$F(22, 5286) = 2.555$, Wilks Lambda = 0.979, $p < 0.01$]. In conclusion the HRQoL of non-prescription medicine customers is lower compared to general Malaysian population. The HRQoL is affected by their age, ethnicity, locality, types of occupation, household income and types of non-prescription medicine purchased.

OPP12 (000062)

Health Screenings and Assessment of Social-economic Status among Aboriginal Peoples (Orang Asli) in Kampung Air Bah, Grik, State of Perak, Malaysia

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Health screenings of Orang Asli population in remote areas provide insights on their quality of life as they are disadvantaged groups with limited accessibility to healthcare services. A health campaign was conducted in Kampung Air Bah, Perak on 16th April 2011 whereby screening tests and interviews for assessment of social-economic status were performed in two different sessions. Of the 57 subjects screened in the first session, only 12.3% were obese (BMI $\geq 27.5 kg/m^2$) while 8.3% and 20.0% of male and female respectively had high body fat percentage. The prevalence of diabetes mellitus (7.0%) and hypertension (12.3%) was low among the population. However, three subjects were found

to have high blood sugar which warranted for further diagnostic investigations. In the second session, 53.8% of the 13 subjects interviewed were uneducated. Majority (69.2%) of the subjects were working with an average monthly income of RM 550. Approximately 31% of the subjects consumed less than 3 meals per day. Around 56% of them obtained treatment from government clinics or hospitals when sick and their average monthly healthcare expenditure was RM 55. Utilization of herbs as medicines were found to be high among the population and 84.6% of subjects thought that traditional medicines do not pose harms. The subjects screened were generally in good health. However, their educations should be emphasized for a better future considering their current poor income and quality of life. Further research on the traditional medicines utilization among the population is warranted for better understanding of the impact on their health.

OPP13 (000068)

Comparison Studies of Clinical Status Improvement and Weight Gain Among Premature Infants in Hospital Sultanah Bahiyah (HSB) Who Had Received Soybean-oil Based Emulsion and Fish-oil-enriched Emulsion in Total Parenteral Nutrition (TPN)

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INTRODUCTION: Fat emulsions are one of the essential components of parenteral nutrition regime. Soybean-oil based emulsion is a conventional lipid emulsion based on soybean oil only. Fish-oil-enriched emulsion is a newer formulation consisting of soybean oil, medium chain triglycerides, olive oil and fish oil. Soybean-oil based emulsion has been totally replaced by fish-oil-enriched emulsion for neonates receiving TPN in neonatal intensive care unit (NICU), HSB in 2011. However, the clinical outcomes of neonates receiving TPN with either soybean-oil based emulsion or fish-oil-enriched emulsion, have not been assessed or compared before. OBJECTIVE: To examine and compare the outcomes of neonates receiving TPN with either fish-oil-enriched emulsion or soybean-oil based emulsion in HSB. METHODS: This is a retrospective clinical study conducted in HSB. SMOFLIPID® 20% was used as fish-oil-enriched emulsion and INTRALIPID® 20% soybean-oil based emulsion. Data were traced from electronic-Hospital Information Service (e-HIS) and patients' clinical notes. The data collected were analyzed descriptively using Microsoft® Excel, and statistically using SPSS 16.0. Differences in baseline or changes in each variable (e.g. total bilirubin, AST, ALP, etc) were analyzed using independent t-test and Mann-Whitney U test. Statistical significance was set at $p<0.05$. RESULTS AND DISCUSSION: A total of 60 neonates were included in this study: 27 males and 33 females. Among them 21 weighed between 500 – 1000g and 39 weighed between1000 – 1500g. Indirect bilirubin ($p=0.046$) and ALP level ($p=0.013$) were found to significantly reduced after receiving fish oil-enriched emulsion as compared to soybean-oil based emulsion. The mean of TPN administration days for soybean-oil based emulsion was 11 days whereas for fish-oil enriched emulsion, was 9 days. There were no significant differences in clinical status improvement or weight gain among premature neonates in HSB who had received soybean-oil based emulsion or fish-oil-enriched emulsion. CONCLUSION: Fish-oil-enriched emulsion was found to be beneficial for neonates with high indirect bilirubin and ALP level compared with soybean-oil based emulsion.

OPP14 (000071)

Cardiac and Behavioural Impact of Cardiac Rehabilitation Medication Therapy Adherence Clinic on Post-myocardial Infarction Patients

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Coronary heart disease that commonly manifests as myocardial infarction (MI) is the single largest but preventable cause of disability and premature death globally and in Malaysia. Cardiac Rehabilitation Medication Therapy Adherence Clinic (CR-MTAC) in Hospital Kuala Lumpur is the first of its kind led by pharmacists to manage post-MI patients. CR-MTAC patients were assessed for medication adherence, counseled on non-pharmacotherapy and pharmacotherapy approaches and given medication supply in the clinic itself. These services, however, were not given at Usual Care (UC). Drug related issues were also identified and solved along with drug information provision. This study is aimed to evaluate the clinical and behavioural impact of pharmacist-managed Cardiac Rehabilitation MTAC on post-MI patients compared to UC. This cross-sectional, observational study was conducted between January and April 2011. A total of 45 patients from CR-MTAC and 43 patients from UC were randomly selected and medical records were evaluated retrospectively for two years. Baseline patient characteristics were similar between both groups. CR-MTAC was associated with a significant mean reduction in low-density lipoprotein cholesterol (LDL-c) (-0.98 ± 0.87mmol/L) and total cholesterol level (-1.04 ± 1.04mmol/L) compared to UC (-0.32 ± 0.73mmol/L and -0.14 ± 0.84mmol/L, respectively) ($p<0.01$). CR-MTAC showed significant increment in percentages of patients achieving target lipid goals for all the lipid parameters while UC only had significant improvement for LDL-c target goal and target lipid profile ($p<0.05$, within-group comparisons). Only six patients in each group achieved target lipid profile (all the target lipid goals). CR-MTAC and Usual Care patients who did not achieve the primary LDL-c target goal had similar average doses of simvastatin equivalents, which implied failure to achieve the target goal may be associated with medication non-adherence. CR-MTAC demonstrated a statistically significant higher percentage of adherent patients (Modified Morisky Scale (MMS): 86.7%, 'A Single Question' (ASQ): 95.6%) compared to UC (MMS: 41.9, ASQ: 53.5%) ($p<0.01$). Better medication adherence was associated with lower LDL-c levels and higher reductions ($p<0.01$). In conclusion, CR-MTAC showed statistically significant positive clinical and behavioural impact on post-MI patients compared to UC.

PHARMACEUTICAL CHEMISTRY / PHARMACOLOGY / TRADITIONAL & COMPLEMENTARY MEDICINE

OPM1 (000008)

Functionalized Aurones as Inducers of NAD(P)H:Quinone Oxidoreductase 1 (NQO1) that Activate AhR-XRE and Nrf2-ARE Signalling Pathways: Synthesis, Evaluation and SAR

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The chemopreventive potential of functionalized aurones and related compounds as inducers of NAD(P)H:quinone oxidoreductase 1 (NQO1, EC 1.6.99.2) are described. Several 4,6-dimethoxy and 5-hydroxyaurones induced NQO1 activity of Hepa1c1c7 cells by 2 fold at submicromolar concentrations, making these the most potent inducers to be identified from this class. Mechanistically, induction of NQO1 was mediated by the activation of AhR/XRE and Nrf2/ARE pathways, indicating that aurones may be mixed activators of NQO1 induction or agents capable of exploiting the proposed cross-talk between the AhR and Nrf2 gene batteries. QSAR analysis by partial least squares projection to latent structures (PLS) identified size parameters, in particular those associated with non-polar surface areas, as an important determinant of induction activity. These were largely determined by the substitution on rings A and B. A stereoelectronic role for the exocyclic double bond as reflected in the E_{LUMO} term was also identified. The electrophilicity of the double bond or its effect on the conformation of the target compound are possible key features for induction activity. These findings provide the lead for the future development of aurones as cancer chemopreventive agents.

OPM2 (000032)

Synthesis and Evaluation of Benzalacetophenone Derivatives in Inhibiting Human Colorectal Cancer Proliferation through Peroxisome Proliferator-activated Receptor Gamma (PPARg)

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Several lead compounds which suppress cancer proliferation through peroxisome proliferator-activated reactor gamma (PPARg) were previously identified. A series of 46 benzalacetophenone derivatives, containing various electron withdrawing and/or donating functional groups on aromatic rings were synthesised and evaluated for their activity on human colon cancer (HT-29) cell lines. We found that 25 of the 46 synthesised

compounds had IC50 less than 100 µM. Structure-activity relationship studies revealed that the presence of electron withdrawing groups on either of the aromatic rings or both increased the potency of these compounds. In silico molecular docking also supported this finding and indicated that benzalacetophenone derivatives to interact with the PPARg ligand-binding domain. PPARg knockdown studies confirmed the PPARg activity of benzalacetophenone derivatives. Therefore, our findings suggest that the colorectal cancer antiproliferative effects of benzalacetophenones are to be mediated through activation of PPARg.

OPM3 (000082)

Development of A New Two-Tier Method for Drug Pre-Screening Analysis; A Spectral Database Study

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This research was initiated as part of the fight against the public health problems of rising counterfeit, substandard, and poor quality medicines and herbal products. A simple, quick and cost-effective drug screening procedure using incremental near infra-red (NIR) spectral database of common medicines in combination with principal component analysis (PCA) was developed to facilitate drug analysis without depending on standard compounds or products from manufacturers. The novelty of the approach is demonstrated by this two-tier method which allowed applications in product identification, drug quality study, herbal analysis, and the detection of counterfeit and adulterated medicines. The NIR spectra database consisted of almost 4000 spectra from 15 types of medicines and 3 types of herbal preparations, acquired and stored in the database throughout the study. The optimization works on the database produced a search strategy using correlation and first derivative correlation algorithms on the full spectrum. The cut-off points of the hit quality index (HQI) were determined to classify the unknown sample in four categories; similar batch/ match (Type 1, <0.0001), same brand/different batch (Type 2, <0.01), same type of medicine/ different brand (Type 3, <0.1) and different type of medicines (Type 4, >0.2). This method was proven successful when challenged firstly using simple compound drugs followed by complex mixtures of herbal preparations and then using alleged counterfeit and adulterated samples. This method has allowed samples to be identified without known background information which was difficult to do using other NIR qualitative techniques that required reference products for comparison.

OPM4 (000030)

Pharmacodynamic Interaction Potential of Glimepiride with Ginger in Type 2 Diabetic Rats

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Certain foods, dietary supplements and specific nutrients in food stuff, if ingested concurrently with some drugs, may affect the overall pharmacodynamics, pharmacokinetics and therapeutic efficacy of the medications. These effects may lead to treatment failure or severe adverse effects. Therefore, it is important to evaluate the effects of individual food on drug efficiencies to avoid harmful effects. The present study was aimed to evaluate pharmacodynamic interaction potential of glimepiride with ginger (*Zingiber officinale*). Type 2 diabetes mellitus was induced in overnight fasted Wistar rats by streptozotocin and nicotinamide. Six groups of rats viz. group 1 (normal control), group 2 (diabetic control), group 3 (standard) and group 4, group 5, group 6 (groups having standard drug glimepiride with aqueous extract of ginger i.e. 125 mg/kg, 250 mg/kg and 500 mg/kg body weight, respectively) were employed in study and each group contains seven animals. The blood glucose, cholesterol, triglycerides and HDL levels were estimated from 1st to 28th day, demonstrated significant reduction in such biochemical parameters and showed hypoglycaemic and anti-hyperlipidaemic potential with co-administration of glimepiride and ginger at a dose of 250 mg/kg and 500 mg/kg body as compared to glimepiride alone ($p<0.05$). As in this study; use of glimepiride with ginger treatment not only resulted in glycaemic control but also provide beneficial hypolipidaemic effects in diabetic rats. This study revealed that a drug interaction may also provide some beneficial effects.

OPM5 (000055)

A Systematic Approach to Evaluate the Receptor Profiles of a Novel Opioid Ligand with a Mixed Agonist/Antagonist Activity Using a Vas Deferens Assay

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Before the discovery of the cell-cultured based assays, the isolated tissues have been widely used to evaluate the pharmacological activities of the opioid-related drugs at the different types of opioid receptors. Despite providing a more physiological environment, the isolated tissues assay also can be used to study the pharmacodynamics of drug-receptor interaction such as drug reversibility. The aim of this study is to explain the systematic methods of evaluating the pharmacological profiles of a novel opioid ligand

(with a mixed agonist/antagonist activities) and also to discuss the strategies of optimizing the experimental techniques using the isolated tissues. In this project, we had successfully characterized few ligands using different assay systems ([^{35}S]GTPγS, receptor binding assay and isolated tissues) at different types of opioid receptors (μ-, κ- and NOP). Using the vas deferens tissues (rat vas deferens (μ- and NOP) and mouse vas deferens (κ-), few ligands have been further evaluated to measure their binding affinities (K_B) and potencies (pA_2) at each individual opioid receptors. These parameters were calculated using Schild analysis and Schild equation. While the binding affinities of the ligands are comparable (< 30 fold difference), none of the ligands shows efficacy in the vas deferens compared to the [^{35}S]GTPγS assay (eg: BU10136, partial agonist ([^{35}S]GTPγS, μ-), antagonist (rat vas deferens, μ-). From our experiments, we have concluded that the isolated tissues assay is a good alternative to measure the receptor binding affinities of a mixed agonist/antagonist opioid besides giving additional information about the drug behaviours at the receptor levels.

OPM6 (000118)

Gastroprotective Effect of Dictamnine Against Ethanol Induced Stomach Ulceration

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Dictamnine (DC) is a naturally occurring furoquinoline alkaloid which was isolated from leaves of *Melicope latifolia* T.G Hartley (Rutaceae). In the present study we have evaluated the antiulcer property of dictamnine (DC) against ethanol induced gastric ulcers in animal model by gross microscopic lesions and histological evaluation were taken in consideration. Experimental groups were orally pre-treated with two different doses of DC in 5% Tween 80 solution. Ulcer control groups were pre-treated with vehicle solution and reference group was orally pre-treated with 20 mg/kg Omeprazole. After 30 min, all groups received absolute ethanol to generate gastric mucosal injury. After an additional 30 min, all rats were sacrificed and ulcer areas of gastric wall were determined. Histological studies of gastric wall of ulcer control group revealed severe damage of gastric mucosa, along with edema and leucocyte infiltration of sub-mucosal layer compared to rats pre-treated with either omeprazole or DC. Serum levels of creatinine and liver enzymes aspartate (AST) and alanine transaminases (ALT), in the rats exposed to ethanol induced ulceration have been altered. Administration of DC modulates the acute alterations of AST, ALT and creatinine level. The level of gastroprotection of DC 5mg/kg and 10mg/kg doses was 88.13% and 56.35%, respectively. This finding suggests that DC promotes ulcer protection as ascertained by the comparative decreases in ulcer areas, reduction of edema and leucocyte infiltration of the sub mucosal layer.

OPM7 (000136)

Effect of Treatment Duration of *Morinda citrifolia* Fruit Juice on Blood Coagulation and Liver Functions in the Rat

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Morinda citrifolia , noni or mengkudu have traditionally been used as a herbal remedy for many conditions and is believed to have extensive therapeutic properties, including an anticoagulant effect. We have found the fruit juice from a commercial source (McC) to prolong the coagulation profile of human volunteers when ingested for 6 weeks with transient effect on liver enzymes. Studies reported by others on liver toxicity were inconclusive. The objective of this study was to determine the treatment duration of McC on the blood coagulation and liver functions in the rat. Nine groups of 6 rats each were orally fed daily, either saline or the McC (0.5mL/kg or 1mL/kg) for 7, 14 or 21 days. Blood coagulation was assessed with clotting time (CT), thrombin time (TT), prothrombin time (PT) and activated partial thromboplastin time (aPTT). Liver function was assessed by serum aspartate transaminase, alanine transaminase and gamma-glutamyl transferase and liver histology. Means + SEM were compared between groups using ANOVA and T test. The results show a prolongation of clotting time, TT, PT and aPTT significant difference in coagulation time between study groups and control. No significant change in the levels of liver enzymes or liver histology was noted. Treatment with McC (0.5mL/kg) in rats seemed to optimally affect blood coagulation. The findings showed that McC affects coagulation profile in the rat at the doses studied without causing any toxicity on the liver.

OPM8 (000039)

The Anti-Cholinergic and Anti-Adrenergic Effects of *Radix saussurea* on the Contraction of the Rat Ileal Smooth Muscle and Frog Cardiac Muscle

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Radix saussurea is a medicinal herb that is widely used in traditional chinese medicine to treat a variety of gastrointestinal problems. Several in vitro and in vivo pharmacological studies have demonstrated that the herb has significant antagonistic activity on various muscle types. Due to the multiple biological activity of the herb, it therefore has immense potential to be developed into a potential therapeutic agent. This study investigates the anti-cholinergic and anti-adrenergic effects of *Radix saussurea* on the ileal smooth muscle of the rat and the cardiac muscle of the frog heart. This provides some insight to the antagonistic effects of the herb and explain its use in traditional medicinal system to treat a variety of illnesses. Isolated tissue preparations were used to observe any significant antagonistic effects of the crude extract of *Radix saussurea* on smooth muscle and cardiac muscle. The contractions of the tissue preparations were measured using a

force transducer and the readings obtained were recorded with a PowerLab program. ANOVA was performed on all the data to establish the significance of the results. In both the isolated rat ileum and frog heart preparations, the *Radix saussurea* extracts demonstrated significant antagonism on the action of acetylcholine and adrenaline on the rat ileal smooth muscle and frog cardiac muscle. The ANOVA test confirmed that the crude extract produced significant antagonism on the acetylcholine and adrenaline induced effects of the smooth muscle and cardiac muscle. The crude extract demonstrated either a competitive-reversible or a non-competitive type of antagonism on the rat ileal smooth muscle and frog cardiac muscle. As the exact type of antagonism could not be confirmed in this study, further research is required to establish this relationship.

OPM9 (000116)

Gastroprotective Study of *Mucuna pruriens* on Experimentally Induced Gastric Hemorrhagic Mucosal Lesions in Rats

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Mucuna pruriens is a traditional medicinal plant. The investigation was carried out to evaluate the gastroprotective effects of ethanolic extract of *M. pruriens* leaves against ethanol induced gastric mucosal injuries in rats. Rats were divided into 8 groups. The negative control and the ulcer control groups were orally administered with carboxymethylcellulose (CMC). The extract control groups received 500 mg/kg of the extract. The reference group was orally administered with 20 mg/kg of omeprazole. The experimental groups received 62.5, 125, 250 and 500mg/kg of the extract by oral administration, respectively. After 1 h, CMC was given to the negative control and the extract control groups, orally. The other groups received absolute ethanol. Rats were sacrificed after 1h. The gastric wall mucus, ulcer areas and histology and immunohistochemistry of the gastric wall were assessed. Prostaglandin E2 (PGE2), superoxide dismutase (SOD) and malondialdehyde (MDA) content also were measured. The ulcer control group exhibited significant mucosal injuries with decreased gastric wall mucus and severe damage to the gastric mucosa compared with the experimental groups. The extract causes upregulation of Hsp70 protein, down-regulation of Bax protein and intense periodic acid schiff (PAS) uptake of glandular portion of stomach. A significant increase in antioxidant defence enzymes (PGE2 and SOD) in the gastric mucosal homogenate was observed, while MDA was significantly decreased. The acute toxicity test did not showed any signs of toxicity or mortality. The results suggest that plant extract affords protection against ethanol-induced hemorrhagic mucosal lesions and suggested the applicability as a gastroprotective agent.

OPM10 (000129)

Extraction, Phytochemical Screening and Hypoglycemic Effects of *Aquilaria malaccensis* (Gaharu) Leaves

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The objective of this study was to perform preliminary screening to identify the phytochemical groups in *Aquilaria malaccensis* (Gaharu) leaves and also to investigate its hypgoglycemic effects on rats. The leaves were extracted with water in maceration at 60^{o}C. Different fractions were administered to rats to investigate the hypoglycemic effect by Intra-Peritoneal Glucose Tolerance Test (IPGTT). Preliminary phytochemical screening carried out on the aqueous and ethanolic extracts of *A. malaccensis* leaves confirmed the presence of tannin, glycoside, saponin, alkaloid, anthraquinone, terpenoid and flavonoid. The proximate analysis showed a moisture content of 9.83% implied that the plant can be stored for longer period with lower chances of microbial attack or growth. The water soluble extractive value of 44.72% was higher than the alcohol soluble extractive value of 23.66%. The total ash value of 8.79% implied that the plant had low inorganic components probably as salts or complexes and a high organic component. Water-soluble ash content was 8.93%. The low acid-insoluble ash of 1.01% suggested that a large portion of the ash content is acid soluble and hence may be physiologically important as salts in the body when consumed. It is also indicative of high digestibility of the plant when eaten. The extracts exhibited glucose lowering effects which are comparable to Metformin and Glibenclamide at 30 and 45 minutes after intra-peritoneal injection of glucose. The results showed that *A. malaccensis* leaves might possess medicinal and therapeutic value.

OPM11 (000114)

Investigation of the *In Vitro* Antioxidant Activities and *In Vivo* Acute Toxicity of Ethanol Extract of *Vitex pubescens*

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The traditional medicinal plant *Vitex pubescens* (*V. pubescens*) was evaluated for antioxidants properties. The ethanol extract of plant leaves was used in determination of ferric-reducing /antioxidant power (FRAP), the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assays, the total phenolic content (TPC), total flavonoid content (TFC). The results exhibited antioxidant activities. In this study, the acute toxicity of *V. pubescens* was investigated in vivo. Both sexes of Sprague Dawley (SD) rats were administered with high and low doses. The crude extract did not produce toxic symptoms in rats.

OPM12 (000122)

Animal Study of Schiff Base Derived Copper (II) Complex in Acute Gastric Lesions

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Copper is an essential element in various metabolisms. The investigation was carried out to evaluate acute gastroprotective effects of the Copper (II) complex against ethanol-induced superficial hemorrhagic mucosal lesions in rats. Rats were divided into 7 groups. Group 1 and 2 were orally administered with Tween 20. Group 3 was orally administered with 20 mg/kg omeprazole. Groups 4-7 received 10, 20, 40 and 80 mg/kg of the Copper (II) complex, respectively. Tween 20 was given orally to group 1 and absolute ethanol was given orally to groups 2-7, respectively. Rats were sacrificed after 1 h. Group 2 exhibited severe superficial hemorrhagic mucosal lesions. Gastric wall mucus was significantly preserved by the pre-treatment complex. The results had showed that significant increase in glutathione (GSH), superoxide dismutase (SOD), nitric oxide (NO) and Prostaglandin E2 (PGE2) activities and decrease in malondialdehyde (MDA) level. Histology showed marked reduction of hemorrhagic mucosal lesions in groups 4-7. Immunohistochemical staining showed up-regulation of Hsp70 and down-regulation of Bax proteins. PAS staining of groups 4-7 showed intense stain uptake of gastric mucosa. The gastroprotective effect of the Copper (II) complex may possibly be due to preservation of gastric wall mucus, increase in PGE2 synthesis, GSH, NO and SOD up-regulation of Hsp70 protein, decrease in MDA level and down-regulation of Bax protein.

OPM13 (000124)

Evaluation of Chemopreventive Effects of *Andrographis paniculata* on Azoxymethane-Induced Colorectal Cancer in Rats

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Cancers of colon and rectum are among the most common cancers in Malaysia. About 3600 new cases are diagnosed every year. *Andrographis paniculata* is a grass leaves used in traditional Malaysian medicine. It has a broad range of pharmacological use. Aim of the study was to evaluate the antiproliferative activity of the crude extract of *Andrographis paniculata* on azoxymethane (AOM) induced colon cancer in rats. Male Sprague Dawley rats were divided into 5 equal number groups. Two groups were orally administrated of leaf crude extract by different doses of received colon-specific carcinogen, azoxymethane (AOM). Another three groups are induced non treated,

fluorouracil treated, and none induced non treated groups . After sacrificing, colons were examined for lesion, aberrant crypt foci (ACF). *Andrographis paniculata* significantly reduced the numbers of ACF and aberrant crypts.

PHARMACEUTICAL TECHNOLOGY

OPT1 (000002)

Effect of Polymers on Buccoadhesive Compacts of Enalapril Maleate

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The buccal route has long been advocated as a possible route of delivery of drugs having poor oral bioavailability because of high first pass metabolism or degradation in the gastrointestinal tract. The purpose of this research is to develop and evaluate buccacoadhesive compacts (BC's) of Enalapril maleate using Carbopol 934P and different viscosity grades of HPMC. The effects of polymer types, proportion and combination were studied based on the drug release rate, release mechanism and mucoadhesive strength of the prepared formulations. BC's were made by direct compression and characterized for physical parameters, *ex vivo* residence, stability studies in human saliva and mechanism of release. Relative antihypertensive activity and *in vivo* mucoadhesion studies of the optimized formulation were evaluated in rabbits. Results of the physical characteristics were found within limits. Drug release, mucoadhesive strength and swelling index were found to be dependent upon polymer types, proportion and viscosity. The formulations prepared using HPMC100KM showed maximum mucoadhesion. The release mechanism of most formulations was found to be of anomalous non-Fickian type. *In vivo* antihypertensive studies of the selected formulation in rabbits demonstrated significant reduction in hypertension. *In vivo* mucoadhesion studies showed that the designed tablets adhered well to the buccal mucosa for more than 8 hours without causing any discomfort. The stability studies revealed that there is no significant decrease in the drug content of Formulation 2 (F2). It may be concluded that the designed buccoadhesive controlled release tablets have the potential to overcome the disadvantage of poor and erratic oral bioavailability.

OPT2 (000011)

Acetazolamide loaded Dendrimer based Nano-Architectures for Effective Glaucoma Management

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Glaucoma is becoming an increasingly important cause of blindness. The challenging objective for pharmaceutical formulators is to develop topically effective ocular delivery system with improved ocular drug retention and reduced systemic side effects. The present investigation was aimed to formulate and evaluate the potential of poly (propylene imine) (PPI) dendrimers as nano-carriers for ocular delivery of acetazolamide (ACZ) in the treatment of glaucoma. PPI dendrimers were synthesized by divergent approach taking ethylenediamine as dendrimer core. The prepared plain and drug loaded dendrimers were characterized by different parameters such as TEM, SEM, NMR and FT-IR spectroscopy. Entrapment efficiency, *in vitro* drug release kinetics, effect of drug-dendrimer system on surface morphology of RBCs and hemolytic toxicity were also determined. *In vivo* studies included the determination of ocular irritation index, ocular residence time and intra-ocular pressure (IOP) reduction profile. *In vivo* study revealed that in lower concentrations the aqueous solutions of formulations were weakly irritant to the eye. The sustained and prolonged reduction in IOP is probably due to the slow, as well as controlled release of drug from formulations. This shows that drug entrapped in dendrimers can be used for higher retention in ocular cul-de sac. The PPI dendrimer based formulation seems to be promising candidate to develop as ophthalmic vehicle with prolonged ocular drug residence time and IOP lowering effect in treatment of glaucoma, more safely, both *in vitro* and *in vivo*.

OPT3 (000021)

Dissolution Enhancement of Ursodeoxycholic Acid (UDCA) by Complexation with Glucosyl-β-Cyclodextrin-Choline Dichloride Coprecipitate

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The objective of the present investigation is to study the *in vitro* dissolution effects of choline dichloride (CDC) co-precipitation of glucosyl-β-cyclodextrin (G1-β-CD) molecular inclusion complexed ursodeoxycholic acid (UDCA). The molecular inclusion complexes of UDCA with Gl-β-CD co-precipitated with CDC were prepared using different methods. Physicochemical characterization and *in vitro* dissolution of pure drug, physical mixtures and inclusion complexes were carried out. Phase solubility studies of UDCA-Gl-β-CD systems in water at 25 °C exhibited typical A_L–type solubility curve. Low values of standard deviation in drug content of cyclodextrin inclusion complexes indicated uniform drug distribution. The average particle size of the Gl-β-CD complexes was found to be within the range of 56.2 µm to 77.5 µm. The scanning electron

microscopy revealed the appearance of binary systems as agglomerates, exhibiting the amorphous nature of the multi-component systems. FT-IR spectroscopy and DSC studies indicated no interaction between UDCA and Gl-β-CD-CDC. Molecular inclusion complexes of ursodeoxycholic acid with co-precipitated Gl-β-CD showed considerable increase in the dissolution rate in comparison with physical mixture and pure drug in 0.1N HCl, pH 1.2 and phosphate buffer, pH 7.4. Dissolution enhancement was attributed to the formation of water soluble inclusion complexes with the precipitated form of Gl-β-CD. The *in vitro* release from all the formulations was best described by first order kinetics followed by Higuchi release model. In conclusion, due to the dual phenomenon of co-precipitation and formation of stable molecular inclusion complex of UDCA with Gl-β-CD in the presence of CDC, the dissolution profile was enhanced significantly, which in turn have potential to produce a faster onset of action and assists in dose reduction.

OPT4 (000037)

Synthesis of Chitosan Nanoparticles Conjugated with TAT-Peptide as a New Potential Delivery System for siRNA

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Chitosan nanoparticles (CN) have shown to protect siRNA from enzymatic degradation. Successful delivery of siRNA into cells however is hampered by its low cellular uptake. In this study, Tat-peptide (Tat) was conjugated to CN as Tat has the ability to penetrate cell membrane. CN was prepared using the ionic gelation method. CN was then conjugated with Tat (CN-Tat) via disulfide linkage by adding N-succinimidyl 3-(2-piridyldithio) propionate (SPDP) and a reducing agent, dithiothreitol (DTT). CN was conjugated with Tat at various Tat to CN weight ratios, from 0.008:1 to 0.125:1. Particle size of the resultant CN-Tat was less than 756 ±76 nm with surface charge varied from +0.3 ± 2 to +1.7 ± 0.2 mV, depending on the Tat to CN weight ratio. HPLC and Raman analysis showed that Tat was successfully conjugated onto CN via disulfide linkage as the peak for S-S bond appeared at 545.52 cm^{-1}. siRNA entrapment efficiency of CN-Tat was 85% and siRNA was strongly bound to CN-Tat as determined by UV-spectrometer and gel electrophoresis, respectively. CN-Tat was relatively non-toxic to living cells with percent of V79 cell viability of more than 90%. The gene silencing study on GAPDH showed higher knockdown of the targeted gene by the siRNA-CN-Tat compared to siRNA-CN. Hence, CN-Tat has great potential as a safe and efficient carrier into cells for siRNA and possibly RNAi-based therapeutic agents.

OPT5 (000080)

Development of Transdermal Patches for the Effective Delivery of Antihypertensive Agent

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The aim of the present study was to develop transdermal patches of Carvedilol, a non-selective beta blocker used in the treatment of arterial hypertension, ischemic heart disease and heart failure with an improved permeation by incorporating natural permeation enhancers. Patches of Carvedilol were prepared with different ratios of Eudragit RL 100 (ERL) and Eudragit RS 100 (ERS) using eucalyptus oil and rice bran oil as permeation enhancers by employing solvent casting technique. Patches were prepared with and without (control) incorporating permeation enhancers and all the prepared patches were evaluated for their physico-chemical characteristics like morphology, thickness, weight variation, folding endurance, drug content and water vapor transmission (WVT) studies. The DSC and IR results suggested that the drug and polymers are compatible. The prepared patches were found to be smooth, flexible and transparent. The weight and drug content of all the patches (n=17 ± 0.225) were found uniform. SEM studies indicated the uniform distribution of drug in the patches and WVT through patches followed zero order kinetics. *Ex vivo* drug permeation study was carried out through rat abdominal skin using Keshary-Chein diffusion cell in phosphate buffer of pH 7.4 for 24 h and analyzed for the concentration of drug using U.V. spectrophotometer at 241 nm. The various permeation parameters such as flux, permeability co-efficient and enhancement ratio were determined. Among the two permeation enhancers studied, eucalyptus oil showed the greater enhancement ratio. Patches containing eucalyptus oil (FE1), showed maximum flux as well as more drug release, than the other formulations. It was observed that 90.52 % of drug was released at the end of 24 h and flux was 3.941×103 mg/cm^2/h. Similarly, patches containing rise bran oil (FR1) exhibited flux value of 3.316×103 mg/cm^2/h. and drug release (82.51%) at the end of 24 h. The formulations FE1 and FR1 showed promising results and the non-allergic nature of the patches were confirmed by skin irritation test on rats. The rate of drug release corresponded best to first order kinetics (0.9760 to 0.9942) and mechanism of drug release was non–Fickian diffusion controlled and followed super case II mechanism. The patches developed in this study could be viable alternative for effective delivery of Carvedilol.

OPT6 (000097)

Public Awareness Towards Pharmaceutical Good Manufacturing Practice in Malaysia

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Good Manufacturing Practice (GMP) in Pharmaceuticals is a concept to ascertain quality, safety and efficacy of manufactured drugs. This study was aimed to know the awareness among Malaysian public towards Pharmaceutical GMP. A public survey questionnaire was prepared by Likert scale method, study was conducted in Kuala Lumpur, Penang and Kota Baru upon Faculty ethical committee approval. Respondents of 20 to 60 years old with the education background from secondary school to university level, as well as uneducated were selected randomly. The data obtained was analyzed using SPSS statistical software version 16. About 544 respondents participated in the study. The results showed that only 23 % of the sample population had an idea about Pharmaceutical GMP and 65 % were aware of the existence of the regulatory body called the National Pharmaceutical Control Bureau. Pertaining to the quality matters, only 7 % understand the information on the medicine package, 94 % checks the expiry date, and 70 % ignored the problems related to the use of medicines in the country. The results also showed that a large number (94 %) of respondents kept medicines at home, 23 % kept medicines for more than six months and 29 % did not read the recommended storage conditions. Statistically P value (0.014) and Cross tab results indicated that the higher the qualification the greater the GMP awareness. The finding in this study suggests a lack of awareness among public is mainly due to poor information about medicine handling. There is a need to balance and sustain the demand and supply to reduce stockpiling of medicines at home.

OPT7 (000098)

Investigation of *In-vitro* Bioadhesive Properties of Natural Gums

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The objective of this study was to investigate the *in-vitro* bioadhesive properties of natural gums, namely Konjac Gum 32H, Konjac Gum 40H, Tara Gum, Xanthan Gum, and their combinations. *In-vitro* bioadhesive strength and work of adhesion were investigated using Texture analyser by employing two different biological membranes, cow intestine and chicken pouch. Flat tablets of 10 mm diameter were prepared, by direct compression method using pure gums and their combination in ratios mentioned below. Seven different time points (1, 2, 3, 5, 7, 9 and 11 min.) were employed to study the impact of contact time on bioadhesive strength. Different gums produced significantly different bioadhesion strength in the order of Xanthan Gum > Konjac Gum 40H > Konjac Gum 40H+Xanthan Gum (1:1) > Konjac Gum 32H+Xanthan Gum (1:1) > Konjac Gum 40H+Xanthan Gum+Tara Gum (1:1:1) > Konjac Gum 32H+Xanthan Gum+Tara Gum (1:1:1) > Konjac Gum 32H > Xanthan Gum+Tara Gum (1:1) > Konjac Gum 40H+Tara

Gum (1:1) > Konjac Gum 32H+Tara Gum (1:1) > Tara Gum. It was observed that the bioadhesion strength was enhanced when the contact time was increased in chronological order of 1 < 2 < 3 < 5 < 7 < 9 < 11 min., and the results obtained are statistically significant ($p < 0.05$) when analyzed using ANOVA. It was concluded that different natural polymers, their combination produced different bioadhesion strength and the two gums, Xanthan and Konjac 40H can be used in bioadhesive drug delivery. There was no significant difference between the bioadhesive values of two membranes used in the study.

POSTER PRESENTATIONS

CLINICAL PHARMACY

PCP1 (000003)

Utilization of Beta Blockers Post-myocardial Infarction

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Beta blockers have been widely studied in post-myocardial infarction (MI) patients. Beta blockers provide both morbidity and mortality benefits for these patients. Despite this, many studies have highlighted that beta blockers are still often underused or used at suboptimal dosages. This was a retrospective observational study conducted between 2005-2006 with the objectives of estimating the proportion of post-MI patients who were receiving beta-blocker therapy in University Malaya Medical Centre (UMMC), assessing the number of post-MI patients receiving beta blockers at optimal dosages and determining the factors associated with beta-blocker prescribing in post-MI patients. 315 case notes of post-MI patients were reviewed. Majority of them were male, Malay and ≤ 65 years old. 77.5% of patients were prescribed beta blockers by the end of the 12-months study period. However, dosages were optimized in only 39.3% of patients. Reasons for not increasing the dosages within the study period were typically not due to the presence of contraindications to beta blockers. Elderly (> 65 years old), ejection fraction (EF) < 40%, a history of cerebrovascular accident (CVA) or mild asthma, use of calcium channel blocker (CCB), digoxin or anti-asthmatic agents were all significantly associated with a reduced rate of beta-blocker prescribing post-MI. In conclusion, overall utilization of beta-blocker therapy post-MI in UMMC patients was satisfactory. However, more effort should be placed in improving its use in specific patient populations. Initiatives to optimize the dosage of beta blockers to recommended dosages that matched those in clinical trials with proven mortality benefits will also need to be intensified.

PCP2 (000005)

A Study of the Effect of Administration of Parenteral Nutrition on Body Weights of Premature Infants in Kuala Lumpur Hospital

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Impaired growth in premature infants such as low body weight and immature immune system, can increase their vulnerability to infectious diseases and their need for ventilator support**.** With parenteral nutrition (PN) supplementation, premature infants show a greater weight gain. The objectives of this study are to measure the changes in body weight of premature infants after receiving parenteral nutrition support, and to assess the impact of amino acid and calories intake on weight gain of premature infants. A prospective study

design with convenience sampling was conducted in Special-Care Nursery (SCN) ward in Kuala Lumpur Hospital from December 2010 to April 2011. Forty six preterm infants (gestational age <37 weeks) were included in the study. The weights of these subjects before starting PN, on Day 1 and Day 7 of PN administration, as well as calorie intake and protein intake on Day 1 and Day 7 of PN were computed. Data were analysed statistically using Friedman ANOVA, Wilcoxon Signed Rank test and Spearman's test, where appropriate, with $p<0.05$ indicating statistical significance. The mean weight before starting PN was 1.13 ± 0.38 kg at postnatal age of 4.22 ± 4.70 days of life. The body weight is significantly increased by PN support (Day 1 = 0.98 ± 0.29 kg, Day 7 = 1.02 ± 0.30 kg; $p=0.001$). There is no significant correlation between protein intake and weight gain (Protein intake on Day 1 versus weight gain on Day 7, $r = -0.101$; $p=0.523$). In addition, there is no significant correlation between calorie intake and weight gain (Calorie intake on Day 1 versus weight gain on Day 7, $r = 0.200$; $p=0.204$). This study does not resemble other studies due to only a small sample size. This study shows that parenteral nutrition supplementation will increase the body weight of premature infants.

PCP3 (000007)

Antibiotic Usage in Surgical Prophylaxis: A Prospective Surveillance at Surgical Wards of Sarawak General Hospital

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The widespread and inappropriate use of broad spectrum antibiotics in surgical prophylaxis has led to reduced treatment efficacy, increased healthcare cost and antibiotic resistance. This study was conducted with the aim to improve the quality of antibiotic usage and to study the adherence to the national antibiotic guideline on surgical prophylaxis. A three-month prospective observational study was conducted in the surgical wards of Sarawak General Hospital (SGH) from 1st July till 30th September 2011. Data collection was facilitated using a standardised surveillance form. Each patient was reviewed for up to 30 days post-operatively to determine the occurrence of surgical site infection (SSI). A total of 87 cases were included within the study period. Nearly 60% of the present cohort were females with the mean age of 54.2 (SD=14.7). The majority of cases were clean-contaminated wounds (60.9%) namely hepatobiliary cases (37.9%) followed by colorectal cases (19.5%). The most frequently used antibiotic was Cefoperazone (63.2%). The choices of antibiotics in 78.2% of the cases were consistent with the guidelines. Around 80% of prophylactic antibiotics were given within 1 hour before operation and 77% were discontinued within 24 hours post-operatively. Of those who received continued therapy for >24 hours, the majority (60%) were for unknown reasons. SSI was documented in 13.8% of the total cases studied. However, there was no significant association between timing of surgical prophylaxis with incidence of SSI ($X^2=3.628$, $p=0.258$). Areas of non-concordance to the guidelines require further exploration to ensure appropriate use of antibiotics in surgical prophylaxis.

PCP4 (000014)

Characteristics, Risk and Outcome of Neonates Prescribed with Empiric Antibiotic Therapy in the Prevention of Early Onset Sepsis in Hospital Pulau Pinang

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Objectives: To describe the characteristics and outcome of neonates treated with empiric antibiotic for suspected early onset sepsis (EOS). **Methods:** This was a cross-sectional study conducted in Hospital Pulau Pinang. Records of neonatal patients admitted within 72 hours of life and prescribed with empirical antibiotic therapy for suspected EOS were reviewed. **Results/Discussion:** 302 cases met the inclusion criteria. Cases were divided into gestational age (premature= <36 weeks; term= ≥37 weeks) and birth weight (Low birth weight (LBW), <2.5 kg; normal body weight (NBW), ≥2.5 kg) groups. Premature (n=162) and LBW (n=149) neonates had significantly higher incidence of prolonged rupture of membrane (>18 hours) and required higher antibiotic therapy during pregnancy, perinatal steroid, surfactant and longer hospital stay (p=0.001). More than 86% of premature and LBW neonates were diagnosed with respiratory distress syndrome, congenital pneumonia and presumed sepsis. Term (n=138) and NBW (n=153) neonates had significantly higher incidence of meconium stained amniotic fluid and perinatal asphyxia which was associated with a higher manifestation of seizures (p=0.001) and higher diagnosis of meconium aspirate syndrome. The incidence of confirmed EOS was 2.98%. C-penicillin plus gentamicin regimen was the standard therapy prescribed in all groups and started within 24 hours of life with a median treatment duration of 3 days. 80% of term and 78% of NBW neonates were discharged well while 61% of premature and 64% of LBW neonates required referrals. **Conclusions:** Both gestational age and birth weight groups presented mainly with respiratory symptoms. The standard empiric antibiotic regimen prescribed was effective to treat EOS.

PCP5 (000042)

Evaluation of Drug Treatment in Patients with Status Epilepticus

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Despite significant improvements in the diagnosis and treatment of status epilepticus (SE) over the past years, it is still associated with a significant morbidity and mortality. The objectives of this study were to evaluate trends of drug treatment for SE in Hospital Universiti Sains Malaysia (HUSM), to determine outcome associated with SE and to evaluate drug related-complications during treatment. A retrospective review of medical records of all patients who were admitted in HUSM between January 2007 and December 2011 was done whereby 85 patients with 123 cases of SE are included in this study. There were 64.4% of children and 73.1% of adult have no previous history of SE. Diazepam, phenytoin, phenobarbitone and midazolam were the drugs that commonly used for SE in

HUSM. The use of newer antiepileptic drugs (AEDs) like valproic acid, levetiracetam and propofol were minimal. The most common group of AED used was combination of diazepam and phenytoin. About 36% of SE episodes were successfully treated with drugs from first-line treatment. In 32% episodes of SE, first-line of treatment was already given at other health facilities. The odd of children having SE aborted using first-line of treatment is 0.677 times less than those of adult. There were 19 cases of ADR reported during this study. The highest was sedation which was associated with the use of diazepam. The risk of children getting ADR was 35.3% less than adult group. As conclusion, even without significant differences, the chances of children having SE aborted with first-line of drug treatment and the risk of them getting ADR was less than adult.

PCP6 (000063)

A One Day Community Health Screening Conducted at SRJK(T) Sungai Pinang, State of Penang, Malaysia

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Non-communicable diseases are raising much concern in Malaysia owing to changing lifestyles parallel to economic development. This can be intervened by community health screening (CHS) which allows early detections, preventions and reductions of chronic diseases and its risk factors. A one day health screening was conducted in April 2012 at SRJK(T) Jalan Sungai Pinang, Penang. A convenient sample of the general public was recruited for screening tests such as body mass index, body fat percentage, blood cholesterol and blood pressure. Out of 76 participants recruited, 54.5% and 48.2% of male and female, respectively were obese (BMI > 27.5 kg/m^2). Body fat percentage was high in 71.4% and 67.3%, respectively of male and female. High visceral fat accumulation (≥ 15) was found in 22% of the participants. Around 8% of the participants had high cholesterol levels (> 6.5 mmol/L), in which 3 of them were newly discovered hypercholesterolemia cases from the present screening. The prevalence of diabetes mellitus (40.4 %) and hypertension (42.1%) was high among our participants. Information and counselling given by the trained healthcare providers during the health screening helps the public to take necessary measures to reduce risk factors while preventing complication resulting from these chronic diseases. Furthermore, referrals to healthcare institutions can be recommended for those with high risks and clinical manifestation of such illnesses. In conclusion, CHS is an important health promotion approaches which benefits the general public while reducing national health cost burden.

PCP7 (000064)

Study on Liver Enzymes among Surgical Patients Receiving Parenteral Nutrition: A Pilot Study

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Lipid is indicated as a source of calories and essential fatty acids for patient requiring parenteral nutrition (PN). Source of fat in parenteral lipid emulsions is one of the contributors in developing hepatobiliary complications. The objectives of this research are to monitor liver enzyme in patient on PN and to compare liver enzymes alanine transaminase (ALT) and alkaline phosphatase (ALP) among patient receiving different lipid in PN postsurgery; long chain triglycerides (LCT) and lipid enriched with fish oil. A prospective study design with convenience sampling was conducted in surgical ward Hospital Kuala Lumpur from January 2012 until June 2012. Eight postsurgical patients receiving PN after surgery were included in the study. The level of liver enzymes ALT and ALP before starting PN (Day 0), on Day 2, Day 9 and Day 12 were computed. Data was analysed statistically using T-test, with $p<0.05$ indicating statistical significance. The mean age and body weight are 62+/-7.51 years old and 55+/-13.20 kg for lipid enriched with fish oil, and 56+/-8.94 years old and 54+/-12.33 kg for LCT. Base line ALT and ALP for lipid enriched with fish oil are 7.00+/-2.65 mmol/l and 77.67+/-41.77 mmol/l respectively. Meanwhile for LCT base line ALT and ALP are 18.60+/-9.40 mmol/l and 91.60+/-37.25 mmol/l respectively. The level of ALT is significantly difference on Day 12 between lipid enriched with fish oil (39.33+/-8.62 mmol/l) and LCT (9.50+/-2.12 mmol/l) with $p<0.05$. There was significant difference for ALT (Day 0: 7.00+/-2.65 mmol/l, Day 12: 39.33+/-8.62 mmol/l) and ALP (Day 0: 77.67+/-41.77 mmol/l, Day 12: 228.67+/-65.62 mmol/l) in lipid enriched with fish oil group on Day 0 and Day 12 with $p<0.05$. This study showed that parenteral nutrition with different lipids will derange the level of liver enzymes (ALT and ALP) in postsurgical patient.

PCP8 (000065)

A Study on Pharmaceutical Interventions in Medical Wards, Kuala Lumpur Hospital

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In the clinical setting whereby a number of medications are prescribed to treat serious conditions, pharmacists play an important role by doing pharmaceutical interventions such as monitoring and identifying drug related problems. Thus, the aim of this study is to analyse clinical pharmacist interventions and evaluate their benefits at Kuala Lumpur Hospital. The objectives of this study are to determine the common types of accepted interventions done by clinical pharmacists, then to identify the common drug class involved subsequently to evaluate the clinical significance of the interventions based on

severity of outcome. From 2nd to 21st April 2012, 127 accepted interventions were randomly collected in retrospective manner from three female medical wards. However, only 67 interventions with complete data were analysed. The interventions were then evaluated by two independent reviewers to determine the significance of each intervention based on the severity of outcome. From this study, the type of intervention that has the highest frequency is inappropriate dose/frequency (43%) followed by inappropriate drug (38.8%). One-third of the interventions done involved the use of antibiotics. While 15.9% of the interventions are related to nutrition and blood system followed by cardiovascular system (13.0%). With moderate agreement (Kappa = 0.41) between the two reviewers, 57 out of 67 interventions done by clinical pharmacists has clinical significance whereby 50.7% has major/moderate possible clinical outcome. From this study, although clinical pharmacists did not necessarily save lives, they did bring about change, which directly improved the quality of patient care.

PCP9 (000081)

Evaluation of Knowledge, Practice and Adherence to Asthma Guidelines among General Practitioners (GPs) and Community Pharmacists (CPs) in the State of Penang, Malaysia

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Background: Asthma worldwide is under-diagnosed and under-treated, creating a burden to individuals and families. Adhering to evidence-based guidelines, in diagnosis and medical intervention, may raise the asthma control to optimal levels. The objective of this study was to assess and compare the knowledge, practice and adherence of general practitioners (GPs) and community pharmacists (CPs) in Penang, Malaysia to asthma management guidelines. **Methods**: A survey research, through cross-sectional, descriptive study using a validated self- administered questionnaire consisting of 30 questions, divided into 3 categories covering the main aspects of asthma knowledge, clinical practice and guidelines adherence. The questionnaires, with a self-addressed stamped envelope for return, were mailed to 236 CPs and 300 GPs. Out of 536 questionnaires sent, 60 respondents (28 CPs and 32 GPs) completed the questionnaire. **Results**: There was no significant difference in knowledge (p=0.933) between the CPs and GPs (mean correct answers= 65.9% and 67.2% respectively). The percentages of correct answers of both groups to recent guidelines-derived questions were: 11% CPs and 9% for asthma classification, and 48% CPs and 44% GPs for guideline-based treatment. In terms of practice, the GPs had better management strategies than CPs as indicated by their choice of answers as 'always' or 'very often' to practice based on guidelines. A significantly higher number of GPs (71.9%) mentioned they follow guidelines compared to CPs (46.4%). **Conclusion**: Overall, the knowledge on asthma was moderately above average for both GPs and CPs. The results demonstrated that though most participants claimed they adhere to guidelines, but their knowledge was still lacking on most recent asthma guidelines.

PCP10 (000086)

Assessment of Blood Sampling Time of Gentamicin from Patients at Tertiary Care Hospital

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Gentamicin is an aminoglycoside antibiotic used to treat many types of infections, especially those caused by Gram-negative bacteria. Monitoring blood levels of gentamicin are important because it has a narrow therapeutic index. A retrospective study was conducted from January 2011 until July 2011 at HTAR, a tertiary care hospital to assess appropriateness of gentamicin use and monitoring. There were 30 patients who fulfilled the inclusion criteria. The majority of patients were aged between 18 – 65 years old, 23 males (77%) and 25 Malays (83%). The mean weight and creatinine clearance was 67.47 kg and 154.31 ml/min, respectively. Pneumonia was the highest indication for gentamicin use, 6 (20%); while sepsis was the lowest, 1 (3%). Eighty percent of patients received gentamicin for an appropriate indication while 20% had no clear indication noted in their records. Further assessment of TDM forms for completeness found 13 patients (54%) had completely filled forms while 11 patients (46%) forms were incompletely filled. Of the completed TDM forms, only 2 patients had appropriate pre and post sampling time and concentrations of trough and peak within the recommended therapeutic ranges. TDM forms for 10 out of the 13 patients recorded wrong sampling times. 80% of gentamicin use assessed in this study in HTAR had an appropriate indication. However, 46% of TDM forms were incompletely filled leading to potential wastage of sample and time. A greater involvement of pharmacists and nurses are needed to improve the use of gentamicin antibiotics.

PCP11 (000088)

Adherence to Iron Chelation Therapy in Transfusion-dependent Thalassaemia Patients in Sarawak: Preliminary Findings

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Adherence to iron chelation therapy (ICT) is vital for disease management and quality of life in transfusion-dependent thalassaemia patients. However, adherence to ICT in Sarawak is not much understood. This cross-sectional study examines the level of adherence to ICT and its influencing factors. Interview using a questionnaire with dichotomous scale was conducted on thalassaemia patients of 6 years and above in all

Sarawak government hospitals. To date, 69 patients were recruited via universal sampling method. Forty-one patients completed the survey prior to this abstract writing. Only 34% of patients reported no missed dose of ICT in the past 4 weeks before the survey. In terms of satisfaction with ICT, 56% and 37% who missed dose claimed that ICT administration is too frequent and very time-consuming, respectively. Almost 30% missed dose as they do not want to feel different from their friends. Pertaining to belief in ICT, 33% missed dose because they think that nothing will happen if they do not take ICT. As side effects of ICT are concerned, up to 48% missed dose for the drugs cause discomfort and pain. Only 15% missed dose due to lack of psychosocial support. Accessibility to ICT medications is not a reason of missing dose. Given a chance, 73% expressed preference over oral medication(s) to injections. These preliminary results showed that self-reported adherence to ICT is considerably low. The main reasons of missing dose appear to be dissatisfaction with the current ICT and side effects of ICT.

PCP12 (000089)

Health-Related Quality of Life in Transfusion-Dependent Thalassaemia Patients with Iron Chelation Therapy in Sarawak: A Preliminary Report

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Thalassaemia patients require life-long regular blood transfusion accompanied with iron chelation therapy (ICT). Therefore, patients' perception about their own health during the treatment is of paramount importance to ensure achievement of the treatment goals. This prospective study evaluates health-related quality of life (HRQoL) in transfusion-dependent thalassaemia patients with ICT in Sarawak government hospitals. Patients of 6 years and above were enrolled for 5 monthly follow-ups. During first clinic visit, MOS SF-36 Health Survey Questionnaire (Malaysia Version, 1.0 – 7/94) was administered via interview. To date, 51 eligible subjects have completed the survey. The mean age was 17 ± 8 years and 65% were male patients. Mean scores with SD for 8 health domains were 88.82 ± 9.47 (physical functioning), 70.59 ± 35.60 (role physical), 79.39 ± 21.35 (bodily pain), 64.22 ± 18.79 (general health), 69.61 ± 15.68 (vitality), 81.86 ± 17.56 (social functioning), 72.55 ± 36.94 (role-emotional) and 76.47 ± 11.94 (mental health). Compared to Malaysian general population of 18-29 years, these patients scored substantially lower in physical health components, particularly in the domain of role physical. In contrast, they demonstrated higher scores in vitality and mental health. This early result shows that Sarawak transfusion-dependent thalassaemia patients are yet to achieve quality of life as good as the general population if not better, despite the current treatments. However, stronger mental health component might be a possible factor that affects their willingness to receive medical treatments and adherence to ICT.

PCP13 (000092)

Barriers to Medication Adherence among Adult Asthmatics Attending Medication Therapy Adherence Clinic in a Tertiary Care Public Hospital

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Medication regimen for asthma care is predominantly vulnerable to adherence problems due to their duration, the use of multiple medications mostly delivered as inhalation and the periods of symptom remission. A prospective cross-sectional questionnaire-based study was conducted among adult asthmatics attending Medication Therapy Adherence Clinic of asthma (MTAC-asthma) in a tertiary care public hospital, Hospital Selayang, Selangor, Malaysia, to determine the medication adherence level and associated barriers. Post approval, from October until November 2011, questionnaires comprised of 30 items including socio-demographic, medication adherence measurement level (> 10 scores: good adherence) and 6 studied domain barriers toward medication adherence were directly disseminated to 45 recruited adult asthmatics (≥ 21 years old). Data were then recorded and descriptively analysed using IBM SPSS version 17.0. Majority of the respondents were between 36 to 50 years old, female (51.1%), Malay (64.4%), and completed diploma (33.3%) from any formal higher educational institution. About 55.6% of the respondents possessed good medication adherence. This study highlighted therapy regimen complexity, risks of medication side effects, and lack of general knowledge regarding medication adherence as barriers that contributed toward poor medication adherence level in 44.4% of the asthmatics (≤ 10 scores). Contrary, patient-prescriber trust, patients' cognitive functions and social supports from family and peers contributed to the good medication adherence. Effective communication between health professionals and asthmatics during asthma education is essential to enhance patients' medication adherence hence improve disease condition subsequently quality of life and care.

PCP14 (000093)

Outcome of the First Home Based Self Administration of Subcutaneous Methotrexate (HOSAM) Program in Malaysia

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This study aimed to assess the outcome of a home based self-administration of subcutaneous methotrexate (HOSAM) programme in Hospital Selayang. A retrospective review of the medical records of all paediatric rheumatology patients in Hospital Selayang who were offered the HOSAM programme was conducted. Data collected included patient characteristics and reported direct outcome measures namely correct injection techniques, correct handling of the drug and occurrence of spillage plus indirect measures via blood investigation results. Twenty five patients were offered and 16 (12

females, 4 males) enrolled in the HOSAM programme. Of the 16 patients, 12 had juvenile idiopathic arthritis, 2 juvenile dermatomyositis, 1 scleroderma and 1 Takayasu's disease. Mean duration on subcutaneous methotrexate (SQ MTX) was 38.4 months (0.7-90.3) with a mean of 3 (range 1-9) programme follow-up visits. Parents administered SQ MTX in 11 patients (mean age 9.8 years, range 3.6-18.5) whilst 5 patients self-administered (mean age 14.0 years, range 9.8-15.2). Of the 11 parents, 4 were homemakers and all had at least secondary school education. There were no adverse outcomes reported (n=15), with all reporting correct injection techniques, correct handling of drugs (including storage, transportation, and disposal of drug and used syringes) and no incidences of spillage. There were also no abnormal full blood counts or liver function tests which may indirectly indicate MTX toxicity potentially from wrong dosage. This study found that SQ MTX can be administered safely by a patient or parent at home in a pre-selected group of patients given appropriate education and support as demonstrated in our HOSAM program, which was the first in Malaysia

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PCP15 (000094)

Daily Clinical Dose Poorly Predicts Trough Serum Methadone Concentration (C_{trough}) in Patients Undergo Methadone Maintenance Therapy (MMT) with Good Adherence

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Methadone maintenance therapy (MMT) has been used in patients with opioid use disorder as one of the harm-reduction approaches to prevent the wide spread of HIV-related risks such as needle sharing behaviour and illicit drug use. With low costs calculated per patient, MMT has been put top priority on reducing opioid dependencies in Malaysia. However, the dosing strategy of this therapy, in certain circumstances was open to doubt. With the hypothesis of a personalized methadone therapy, methadone C_{trough} may possibly be a surrogate marker for such purpose. Accordingly, we conducted a 9-month prospective study to assess the relationship between C_{trough} and Dose (D) of methadone. After obtaining approval from the institutional ethics committee, 115 patients were recruited. Two ml of the trough blood samples were taken and centrifuged within 4 hours at 10x1000 rpm for 5 minutes. The resulting serum samples were kept at -20°C until analysis. The methadone concentrations were determined by using Methadone ELISA kit. Study subjects were requested to come for another 2 more follow- ups each at a 3-month interval. Blood samples were taken as previously prescribed. The initial correlation analysis reveals a significant positive correlation between methadone C_{trough} and daily clinical dose (D) in all follow-ups, with r values ranging between 0.403and 0.406 ($p < 0.005$). Further regression analysis reveals that the coefficient of determination, r^2 was poor with only 15-17% of the variability in C_{trough} can be explained by the changes in clinical doses ($p < 0.005$). Based on these results, we conclude that

daily clinical dose poorly predicts methadone C_{trough} for the purpose of dosing adjustment and monitoring of MMT.

PCP16 (000103)

Adherence of Inhaled Corticosteroid (ICS) in Asthmatic Adult in Hospital Sultanah Nur Zahirah (HSNZ)

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Regular use of either concurrent therapy (ICS and Short Acting Beta Agonist alone) or combination therapy (ICS with Long Acting Beta Agonist) can improve asthma symptoms and prevent exacerbations. Study objectives were to assess and compare adherence between asthmatic patients using combination and concurrent therapies, to investigate the relationship between the underuse of ICS and asthma control and to assess the factors of non-adherence of ICS. This cross sectional study was carried out via validated questionnaires in four different stations of pharmacy at Hospital Sultanah Nur Zahirah from April to May 2012. Inhalation technique was assessed. Other assessment tools included Modified Morisky Adherence Scale and Asthma Control Test (ACT). The data was analyzed using SPSS version 20. A total of 71 patients were included in this study. Asthmatic patients receiving combination therapy had higher adherence rate (n = 34, 26.5%) then those receiving concurrent therapy (n = 37, 18.9%). Highest percentage of ICS underuse (taking less puff (dose) or time (frequency) or both that presribed) was found in patient with asthma duration greater than 10 years (48%). A non parametric test using Mann-Whitney Test showed that there was significant difference of ICS underuse and duration of asthma p = 0.05. Significant difference was also found in inhalation technique between combination and concurrent therapy ($p = 0.03<0.05$), and between the ICS underuse and Modified Morisky Scale ($P < 0.05$). However, there was no significant difference of ICS underuse and ACT score ($p=0.932; > 0.05$). The most prominent reason for ICS underuse was forgetfulness (27.1%).

PCP17 (000110)

Antidiabetic Medications and Glycemic Control in Type 2 Diabetic Patients of Sub-urban Hospital of Malaysia

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Diabetes has become a highly prevalent health problem in Malaysia and uncontrolled diabetes may leads to complications. Extensive medication review is essential in view of multiple medications that the patients received. This study investigated patterns of antidiabetic treatment and attainment of glycemic control among individuals with type 2 diabetic patients of sub-urban hospital in Malaysia. A cross sectional descriptive study

was conducted retrospectively from the electronic database of the Hospital Sultan Abdul Halim, Sungai Petani. A standard data collection form was designed to collect information on the patients demographic data and drug utilization pattern for commonly prescribed antidiabetic drugs. Data was analysed by using SPSS version 14.0. Bon Ferroni test was applied to assess the significant difference between the groups. A total of 300 diabetic patients' medical data were taken into consideration for this study. Malay diabetic patient contributes to the highest percentage with 56.3% followed by Indian and Chinese with 31.3% and 11.3%, respectively. The most preferred drug for the monotherapy was found to be metformin with 57.7% prescriptions, followed by 33.7% with gliclazide and 9% with insulin therapy. The most common combination therapy given for the patients were found to be metformin and gliclazide followed by metformin and insulin. All the anti-diabetic drugs used had more or less the same outcome with no significance difference in FBS and HBA1c values. The FBS and HBA1c values (in mmol/L) for metformin, gliclazide, metformin+gliclazide, metformin+glibenclamide were 7.52, 7.68, 8.62, 7.56 and 7.33, 8.09, 8.27, 7.81, respectively. Most of the patients failed to attain the HbA1c target for glycemic control.

PCP18 (000111)

Unlicensed and Off-label Use of Medicines in Hospitalized Children in the Critical Care Units of Universiti Kebangsaan Malaysia Medical Center

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Unlicensed and off-label use of medicine in pediatrics has been a widespread phenomenon and the extent of such use has been quantified in many international studies. To date, the extent of this practice has not been reported in Malaysia. The objective of this study is to determine the extent of unlicensed and off-label use of medicine in hospitalized children in the critical care units of Universiti Kebangsaan Malaysia Medical Center. A prospective, observational exploratory study was conducted over an eight-week period on the medicines prescribed to all children admitted to the critical care units at this institution. Licensing and off-label status of all medicines prescribed were determined using the database prepared by the National Pharmaceutical Control Bureau and local drug compendium, MIMS Malaysia. A total of 194 patients were admitted to the units during the study period, 168 of whom received one or more prescriptions. Of the total 1295 prescriptions, 353 (27.3%) were unlicensed and 442 (34.1%) were off-label use. Based on the number of admissions who received one or more prescriptions, 44.0% received at least one unlicensed prescription and 82.1% received at least one off-label prescription. A multivariate logistic regression analysis showed that children below the age of two years, longer length of hospital stay and the more number of medicines prescribed were most likely to receive an unlicensed and/or off-label medicine. In conclusion, there is a high prevalence of unlicensed and off-label prescribing in children admitted to the critical care units of this institution.

PCP19 (000119)

Health Beliefs and Perception of Breast Cancer Patients in Relation to the Usage of Herbal Medicines

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Herbal medicine is widely used by cancer patients although its effect is not well-documented. Cancer patients are drawn to the benefits of herbal medicine based on anecdotal evidence. We aimed to investigate the health belief of cancer patient and predictors of their herb taking behaviour. This study was designed as a cross sectional survey. Breast cancer patients were recruited from a single centre via telephone interview. A structured questionnaire consists of the subject's general characteristic, herbal medicine usage and 7 constructs of health belief was administered to each subject. A total of 60 patients completed the questionnaire, response rate 92%. 67% of the patients reported using herbal medicine while on cancer treatment and 58% did not reveal it to their clinicians. Except for marital status, p = 0.040, no association was found between demographic characteristics and the use of herbal medicine, but significant differences were found in health belief scores between herbal medicine user and non-user in 3 out of 7 constructs, where herbal medicine users perceived greater benefits and personal modifying variables and less barrier to access of herbal medicine compared to non users, z = -3.51; -2.19; 3.57, p < 0.001; = 0.03; < 0.001, respectively. Logistic regression indicated patients' perceived benefit and perceived susceptibility/ vulnerability to breast cancer are predictive of herbal medicine use. This study confirmed that a substantial proportion of breast cancer patients in Malaysia utilize herbal medicine, often without informing their clinicians. Breast cancer patients' health belief provides insights into their herb taking behaviour.

PHARMACY PRACTICE & PHARMACY EDUCATION

PPP1 (000004)

Medication Errors in Intravenous Drug Preparation and Administration in Selayang Hospital

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Medications given via intravenous (IV) route provide rapid drug delivery to the body. It allows easy control of the amount of drug delivered as well as maintenance of drug levels. IV therapy is a complex process requiring proper drug preparation before administration to the patient. Therefore, errors occurring at any stage can cause harmful clinical outcomes, which may lead to morbidity and mortality. This was a prospective observational study to estimate the percentage of medication errors in preparing and administering IV medicines to the patients, and to determine associated factors and to identify strategies in reducing these errors. A total of 341 (97.7%) errors were identified

from 349 IV drug preparations and administrations. The most common errors were the vial tap was not swabbed during pre-preparation and injecting of bolus doses faster than the recommended administration rate. There was one incident of wrong drug attempted. Errors were significantly more likely to occur during administration time at 8.00 am and when bolus drugs were given. No significant associations were found between number of nurses in the ward or IV drugs to be prepared and administered with medication errors. Errors could be reduced with proper guidelines on IV procedures, more common use of IV infusion control devices and full concentration during the process. In conclusion, awareness among the nursing staff and training needs should be addressed to reduce the rate of medication errors. Standard IV procedures should be abided and this needs the cooperation and active participation of all healthcare professionals as well as the nursing staff.

PPP2 (000010)

Attitude of Pharmacy Personnel in Sarawak towards Cytotoxic Drug Reconstitution

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In Sarawak, delivery of cancer patient care faces geographical challenges. Some patients cannot afford high cost of traveling to obtain chemotherapy due to long distance from home to tertiary hospital. Therefore Sarawak State Health Department has planned to establish cytotoxic drugs reconstitution (CDR) services in district hospitals. Readiness of pharmacy staff to render the service determines success of this plan. We investigated their attitude towards CDR services and possible factors that influence their attitude. A 2-month cross-sectional survey was conducted in 66 Ministry of Health institutions in Sarawak using self-administered questionnaire (Cronbach's alpha, $\alpha = 0.544$). Questionnaires were posted to all pharmacists and pharmacy assistants ($N = 720$). 545 (79.6%) responded to this survey. 41% of respondents denied the fact that CDR is pharmacist's responsibility. 42% felt that working in CDR is stressful. 51% did not feel safe even with personal protective equipments. 75% thought that CDR poses higher occupational exposure risk to cytotoxic drugs compared with other pharmacy activities. More senior staff and pharmacy assistants showed less favourable attitude towards CDR services ($X^2 = 30.071$, $df = 2$, $p = 0.001$; $X^2 = 6.547$, $df = 2$, $p = 0.038$ respectively). This could be attributed to lack of awareness on safe handling of cytotoxic drugs. It is important to instil correct perception about handling cytotoxic drugs. Overall, pharmacy personnel lacks good attitude towards CDR. However, as we strive to cultivate good attitude towards CDR via training, we are optimistic for the success in making CDR services available at all district hospitals in the next five years.

PPP3 (000013)

Hospital Melaka: Cough and Cold Medicine Usage in Paediatric Patients

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The Food and Drug Administration (FDA) had issued a warning against safety usage of cough and cold medicine (CCM) in children under two years old. In fact, the rationale for using CCM in this group of patients has been repeatedly reviewed. This study aims to describe the usage of CCM among paediatric patients in Hospital Melaka. This is a descriptive study involving retrospective screening of outpatient prescriptions received from May to June 2011. A total of 36368 outpatient presciptions were screened. Out of this, 10.25% were for paediatric patients. 17.79% of this paediatrics' prescriptions contain CCM. A majority of the CCM was prescribed by the Emergency & Trauma Department (ETD), 45.40%, and to patients between 2-6 years old (40.61%) followed by 7-11 years old (39.82%) and less than 2 years old (13.57%). Chlorpheniramine (35.75%) and tripolidine (18.25%) were the most commonly used CCMs among paediatric patients. The usage of CCMs among paediatric patients in Hospital Melaka warrants further action. Approximately one out of every five paediatric patients was prescribed with a CCM, with a majority of them aged less than the recommended age which is six years old.

PPP4 (000019)

Adverse Drug Reaction Reported in Hospital Universiti Sains Malaysia (HUSM)

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Adverse drug reactions (ADRs) are a major health concern during medication therapy. Early detection of ADRs may prevent morbidity and mortality. The aim of this study was to evaluate the ADR reports submitted to the Research and Drug Information Unit, Department of Pharmacy, Hospital Universiti Sains Malaysia (HUSM). All ADR report forms received by the unit from January 2004 until June 2012 were retrospectively reviewed. For each of the ADR report, a causality assessment was made based on the Naranjo's algorithm. All data were analyzed descriptively. From 90 reports evaluated, the majority of the reports were received from doctors (67.8%) whilst pharmacists contributed the rest. Slightly more than half of the reports were reported to cause moderate reaction, followed by mild reaction (32%) and severe reaction (14.5%). At the time of reporting about two third of patients recovered. The causality assessment for about half of the ADR reports was categorized as "probable." Most of the reactions (60.9%) subsided after stopping the drug or reducing the drug dose. Most of the prescribers did not reintroduce the drug. Anti-infective agents, particularly cephalosporin group were recorded as the highest drug related to ADRs (34.4%). The most common organ-system affected was the skin (32.8%), followed by central nervous system (15.3%) and cardiovascular system (12.2%). This report should increase the awareness and encourage healthcare professional to report ADRs.

PPP5 (000034)

Ensuring Medication Adherence: The Role of HIV/AIDS Family Caregivers

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Adherence to combined antiretroviral therapy (ART) has been shown to be a determining factor in controlling viral replication and maintaining immunologic function as well as survival in HIV-positive individuals. This preliminary qualitative investigation intended to explore and describe the role of HIV/AIDS family caregivers in managing patients' medication. A convenient sample of family caregivers of HIV/AIDS patients was enrolled from Hospital Sultanah Nur Zahirah, Kuala Terengganu whereby semi-structured interviews were used to gather data. Results were transcribed and translated into English before being subjected to analysis using NVivo software. Twelve caregivers consented participation (age range = 18.0 - 81.0; female = 75.0%, mother/wife = 50.0%; married = 83.3%; ≤ primary school = 50.0%; self-employed = 66.7%). Currently, most patients had been prescribed with a combination of antiretroviral drugs for less than one year. One of the major findings was ensuring medication adherence; whereby working schedules had to be altered and constant reminders needed to be given to ensure patients continue to consume their medications. Interestingly, caregivers also attempted to seek traditional treatment in addition to conventional treatment for their family members. Several caregivers also mistakenly thought that the antiretroviral drugs were definite cures for their family member's HIV/AIDS problem. In conclusion, caregivers could play a pivotal role in promoting and improving patient adherence to antiretroviral medications.

PPP6 (000036)

Customer Satisfaction towards Retail Pharmacy Services in Sarawak

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Customer satisfaction serves as an indicator of health-care services quality and a predictor of patients' health-related behavior. This cross-sectional study evaluated the satisfaction level of customers towards retail pharmacy services in Sarawak. A survey using a self-administrated questionnaire adopted from a previous study was conducted at public areas of Sarawak with a total participation of 420 respondents. (Response rate 93%). Mean satisfaction score (±S.D.) of General Services, Intervention Services and Cognitive Services were 31.55 (±4.0), 29.62 (±5.2), 28.02 (±3.9) respectively. Results revealed that respondents were moderately satisfied (Prorated score ranging from 60-80%) with the services provided by retail pharmacies. Other findings included 55% of respondents were not satisfied with pricing of medication and less than half of respondents were satisfied with the medication information provided. Customers who visited pharmacy regularly and seek advice from pharmacist were reported to have significantly higher satisfaction

level towards intervention services. (t = 4.206, P = 0.003; t = 2.966, p = 0.003). Malay ethnic customers were found to have greater satisfaction level toward all three types of services provided ($p < 0.05$). Further studies are needed to examine aspects influencing satisfaction level in order to formulate effective strategies to provide a more holistic patient centered approach.

PPP7 (000040)

Factors Associated with Defaulted Patient in Methadone Maintenance Programme in Hospital Melaka

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Retaining patients in methadone maintenance programme is crucial. However there are defaulters in the programme. This study was aimed to identify factors associated with defaulting maintenance treatment, as part of ongoing evaluation and improvement in treatment policy. An unmatched case control study (1:2) was conducted among patients who undergone Methadone Maintenance Programme in Hospital Melaka from 1st January 2008 to 31st December 2010. Cases were classified as defaulter patients, while controls were those who are still active for more than 90 days during the study period. Both cases and controls were selected based on specified inclusion and exclusion criteria. Medical records of selected patients were retrospectively reviewed using a data collection form. A total of 175 patients were included in this study, which comprised of 60 cases and 115 controls. Factors associated with defaulting were distance from clinic to home [Adjusted OR 1.10, 95% CI (1.03, 1.17), p-value 0.004], living alone [Adjusted OR 5.23, 95% CI (1.36, 20.19), p-value 0.010], alcoholic [Adjusted OR 14.13, 95% CI (2.24, 89.33), p-value 0.005], history of abuse among family member [Adjusted OR 12.93, 95% CI (2.59, 64.56) p-value 0.002], number of individual counselling attended during treatment [Adjusted OR 0.56, 95% CI (0.36, 0.85), p-value 0.007] and those without take away dose privilege [Adjusted OR 31.16, 95% CI (2.27, 427.01), p-value 0.010]. Validity of the model was good (AUC-ROC= 0.94; overall correctly percentage (88.3%); and Hosmer-Lemeshow p-value = 0.084).This study suggest that retention rates would be significantly improved by a change in the treatment strategies.

PPP8 (000053)

A Survey on Public Attitudes and Knowledge of Contact Lens Use in Puncak Alam Selangor

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Issues of poor public knowledge and attitudes on contact lens use are of concern because of the reported complications such as infective keratitis and papillary conjunctivitis. This study was aimed to describe on public attitudes and knowledge on the use of contact lens. This survey utilized questionnaires by Tajunisah et al., 2008. Respondents were residents

of Puncak Alam, Selangor who were users of contact lens and age group of at least 15 years old. The respondents were divided into three groups of different educational level; secondary, intermediate and degree levels. The questionnaires comprised of three parts: demographic details, contact lens wear, and practice of hygiene and care of contact lens, knowledge of contact lens wear complications. The study was conducted from September to November 2011. Demographic data was descriptively described and non-parametric test was used to test for significance. A total of 84 respondents completed the questionnaires of which 95% of them were female and 76.2% were between 26 and 25 years old. The study showed 95.2% and 3.6% were students and professionals, respectively. The findings showed that respondents with higher education level had better understanding about the use, hygiene and care and complications towards lens use. However, no significance differences were found when knowledge and attitudes were compared among age, gender and occupations. The study revealed that most users did abide to instructions on contact lens use. Knowledge on lens use, hygiene and complications was more apparent in those with higher education level.

PPP9 (000054)

Methadone Maintenance Therapy Clinic in Malaysia: Out-of-pocket costs

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Out-of-pocket (OOP) payments may burden Methadone Maintenance Clinic patients. Since treatment is fully subsidized by the government, financial constraint might lead to patients being made to pay or be given incentive for inconvenience of therapy. This study thus evaluates the characteristic and commitment of methadone therapy in patients in terms of OOP cost, Willingness To Pay (WTP) and Willingness To Accept (WTA) concept. This was a survey utilizing the questionnaire by Borisova & Goodman (2003) on the OOP, WTP and WTA concept was conducted on patients at a government methadone clinic between 2th February 2010 and 1th April 2010. The subjects were selected by convenient sampling based on the predetermined set of inclusion and exclusion criteria. Their medical records from year 2009 – 2011 were also reviewed and recorded. Forty adult patient's records were selected, most were male (90%) and Malay (60%) was the predominant group. Patients were group into 3 income groups; ≤ RM 1000, ≥ RM 1000 - ≤ RM 2000 and ≥ RM 3000. The average OOP cost per month was RM 391.30 (s.d., RM 337.50) which is about 35% of employed patient's monthly income. The wide variation could be attributed by high inter-individual and significant differences between patients in terms of transport, times taken to clinic, cost per trip and weekly household income ($p = <0.05$). Patients with income of less than RM 1000 showed the highest tendency to pay for treatment, asked for the least money for inconvenience, and many are unwilling to accept any payments. These findings showed that WTP and WTA is less of a concern for patients in the low-income group. To conclude, OOP payment is not a treatment barrier for most of the Malaysian Methadone Maintenance Therapy patients although many are the urban poor category.

PPP10 (000061)

Pattern of Usage of Herbal Medicine among Hypertensive Patients in Hospital Seri Manjung

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There is a growing interest in herbal medicine among Malaysians and only a few related studies were carried out. Therefore, it is important to study the demographic data of hypertensive patients who used herbal medicine and to identify the factors contributing to its usage. A cross sectional survey involving face-to-face interview with hypertensive patients in Hospital Seri Manjung was conducted from February-March 2012. The calculated sample size was 377. Patients were randomly selected and questioned based on structured questionnaires and 364 respondents were included in the analysis. The study showed 103 (28.3%) respondents used herbal medicine whereby 52 (50.5%) were male and 51 (49.5%) were female. There were 3.5% more male herbal medicine users (p=0.458). However, 30.1% of the users belong to the age groups of 51-60 and 61-70 (p=0.686). About 54.4% of the users were those who completed secondary school (p=0.182). The same goes for income and HM use (p=0.769), whereby 60.4% of HM users perceived their health to be fair while 2.9% as very poor (p=0.769). About 48.5% and 47.6% of patients used HM for maintaining their general health and treating specific conditions, respectively. There were 21 patients (42.6%) claimed to use it for hypertension while 51.5% of the respondents were influenced by their friends. The demographic data of users were identified to be mostly male, of secondary school level education, belonging to the age groups of 51-60 and 61-70 and those who perceived their health to be fair. However, none of the factors significantly affect herbal medicine usage in our study.

PPP11 (000072)

Barriers to Practising Pharmaceutical Care in Malaysia: Views from Community Pharmacists

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With the increasing competition of community pharmacies and the recently proposed restructuring of national healthcare system ("1Care for 1Malaysia"), offering comprehensive pharmaceutical care services becomes the key point to the survival and development of community pharmacies in Malaysia. However, local community pharmacies have minimal focus on nondispensing-related pharmaceutical care services. Therefore, a pilot study was conducted to identify the perceived barriers to practising pharmaceutical care within community pharmacies. All community pharmacists (n=173) practising in the state of Penang, Malaysia were sent a questionnaire by mail, employing the modified Dillman Total Design Survey Method. The instrument contained questions to evaluate the community pharmacists' level of agreement using a 5-point Likert-type

response scale. Of the 173 community pharmacists, 94 returned the questionnaire (response rate=54.3%) following 4 contacts (3 mail-outs and a walk-in collection) with the respondents. Majority of the respondents were young (≤40years) (n=39, 83%), female (n=60, 63.8%) and self-employed (n=48, 51.1%) community pharmacists. The top 5 perceived barriers for implementation of pharmaceutical care were insufficient time (n=78, 82.9%), pharmacists' level of understanding of pharmaceutical care (n=70, 74.5%), lack of access to patient medical records (n=69, 73.4%), lack of reimbursement system (n=62, 66%) and lack of motivated personnel such as pharmacy assistants (n=60, 63.8%). In conclusion, a range of barriers need to be addressed before comprehensive pharmaceutical care can be integrated into community pharmacy practice in Malaysia. These barriers could be overcome through empowerment of community pharmacists by continuing professional development, revision of current pharmacy curriculum and availability of resources.

PPP12 (000083)

Unused Medicines among Older Adults in Universiti Kebangsaan Malaysia Medical Centre

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Older adults are the leading consumers of medicines. Nevertheless, the inclination among the seniors to have medicines underutilized may implicate significant loss of resources. To date, data from available studies were scarce to describe the wastage due to unused medicines among older adults in Malaysia. This preliminary study aimed to evaluate the extent of unused medicines among Malaysian veterans and its possible contributing factors. Sixty-four patients aged 60 years and above attending the Primary Care Clinic of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) were recruited by convenient sampling between April to June 2012. The subjects were surveyed to identify hoarding of unused medicines. The excessive medicines were collected from the consenting subjects for inspection and quantification. Only 22% of participants (n = 14) volunteered to return their unused medicines, while the others denied hoarding of excessive medicines or refused to have them surrendered. Thirty-seven types of medicines were collected totalling to 6,645 pills. Majority of the medicines returned (22 types) were drugs for cardiovascular diseases, particularly antihypertensive agents and lipid-lowering drugs. Total cost of medicines wastage computed was RM 2,406.67, with an average of RM 171.90 per patient. Non-adherence to prescribed medicines, discrepancies in supply of medications, and purposive hoarding of medications were the common reasons for accumulation of unused medicines among the participants. In conclusion, wastage due to unused medicines among elderly patients may be a hidden truth that needs to be addressed to prevent adversities of health and financial outcomes.

PPP13 (000084)

Beliefs and Adherence about Medicines among Psoriasis Patients in Government Hospitals

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Psoriasis is a chronic skin disease that affects an individual's quality of life. Beliefs about medicines have been identified as one of the contributor of patient's non-adherence. This study was to examine patients' beliefs in medicines and its relationship towards adherence among psoriasis patients.
A cross sectional survey was carried out among psoriasis patients at the dermatology outpatient clinic in Selayang and Serdang hospitals. Data were collected using patients' data form and validated "Beliefs about Medicines Questionnaires (BMQs)" and "Morisky Medication Adherence Scale-8 Questionnaires". Descriptive and parametric statistics were employed for data analysis. Multivariable logistic regression was used to determine predictors of self-reported medication adherence. A total of 146 psoriasis patients were involved which comprised of 47.9% (n = 70) male and 52.1% (n = 76) female. Most of the characteristics between the two hospitals are similar. Most of the patients (79.5%) had reported low medication adherence (MMAS < 2). The results from BMQs showed the mean of necessity score (mean ± S.D., 17.31 ± 4.191) slightly outweighs the concern score (Mean ± S.D., 15.90 ± 4.191). Forty five percent (45.0%) of patients had necessity scale outweighing concern score (43.1%). A positive correlation was found in necessity beliefs compared with other types of beliefs about medicines. Multivariate analysis has identified factors associated with low self-reported adherence are age, necessity beliefs and harm beliefs. The study showed that most of the psoriatic patients have poor adherence and medication beliefs which are correlated to their age, necessity and harm beliefs. Thus, improving their beliefs' about the prescribed medicines is critical so as to ensure patients' has no negative beliefs about medicines.

PPP14 (000107)

Self Medication Practice Assessment in Rural Area: Puncak Alam, Kuala Selangor

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Self medication is commonly practiced by individuals who prescribed medications to themselves without the guidance and supervision of medical practitioners. Self medication can actually serves as a useful behaviour to treat minor ailments but in certain cases can cause serious implications with the possibility of fatal consequences. This study was aimed to investigate the extent of self medication practice among the rural population

in the vicinity of Puncak Alam. Validated questionnaires were distributed to 200 over respondents in Puncak Alam who regularly has the habit to self medicate. Data collected was analyzed through SPSS version18. From the statistical analysis data, it was found that the three ailments most commonly treated through self medication were headache (77%); flu, fever, cough (58%); stomach ache (45%). How an individual perceived the seriousness of an ailment he or she experienced contributed largely to the practice of self medication. Many instances, particular ailments that may be considered serious and requires medical practitioner's attention is ignored and self medicated. 68.5% of the respondent perceived that their illnesses are not serious and could be resolved through self medication. Meanwhile, 62% of the respondents resort to self medication blaming cost as the major factor. Majority of the respondents (85%) claimed that they were satisfied with the results of their self medication. From these data obtained, we can see that self medication is becoming a norm with the rural population and it is essential that pharmacists understand the paramount importance of guided self medication to avoid any fatal implications.

PPP15 (000109)

Evaluating Knowledge, Attitude & Perception Regarding Halal Pharmaceuticals, Among Community Pharmacists in Malaysia

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This was a cross sectional, postal survey using a structure , self-administered questionnaires to evaluate the knowledge, attitude & perceptions (KAP) regarding "halalness" of pharmaceuticals, among community pharmacists across Malaysia, in April-June 2012. Questionnaires were sent to 542 systematic randomly selected pharmacists from a list of 1536 registered Pharmacies. A total of 175 responded to questionnaires with a response rate of 32%. Inclusion criteria were registered pharmacists with Malaysian Pharmacy Council. Study settings included randomly selected, community pharmacies in Malaysia. Data was analysed by using SPSS version 18. Results revealed that community pharmacists have a good knowledge and positive attitude and perceptions about "halalness" of pharmaceuticals. Mean knowledge score out of maximum possible 9 scores was 7.94 ± 1.42, mean attitude score out of maximum possible 45 scores was 36.65 ± 6.96 while mean perception score out of maximum possible 60 scores was 51.9 ± 6.07. Mean overall KAP score out of maximum possible 114 was 96.19 ± 12.33. There was a significant, positive, and good (0.5-0.75) correlation between knowledge and attitude ($r = 0.515$, $p<0.001$), excellent (>0.75) correlation between attitude and perception ($r = 0.753$, $p < 0.001$) and fair (0.25 - 0.5) correlation between knowledge and perceptions ($r = 0.458$, $p < 0.001$) This means that better the knowledge respondents have on halal pharmaceuticals, the better their perception & attitude is towards halal pharmaceuticals. P value of 0.05 or less was taken as statistically significant.

PPP16 (000125)

Pharmaceutical Care Provision: Are Community Pharmacists in Malaysia Ready?

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In line with the proposed restructuring of Malaysian healthcare system, greater emphasis on pharmaceutical care provision in community pharmacy will be targeted. Therefore, a cross-sectional survey was conducted to investigate the readiness of Malaysian community pharmacists to provide pharmaceutical care services. Special focus was on the attitudes and general understanding of pharmaceutical care concept by Malaysian community pharmacists. Data were collected with a postal questionnaire which was sent to all community pharmacists (n=173) practicing in the state of Penang, Malaysia. Of 173 community pharmacists, 94 returned the questionnaire (response rate=54.3%). Respondents were primarily younger (≤40years) (n=39, 83%), female (n=60, 63.8%) and self-employed (n=48, 51.1%) community pharmacists. This study demonstrated that community pharmacists in the state of Penang, Malaysia had a reasonable understanding of pharmaceutical care concept. In general, pharmaceutical care concept was better understood by employee pharmacists than the pharmacy owners (P=0.035). Over 90% of the respondents were aware of the pharmaceutical care practice in various settings, pharmacists' role and primary aim of pharmaceutical care concept. A high proportion of respondents (n=82, 87.2%) think that there is a need for continuing professional development on pharmaceutical care. 80.8 % (n=76) of them fully support pharmaceutical care concept and believed that pharmaceutical care requires major up-skilling of clinical knowledge. 41.5 % (n=39) had reserve about the other health professionals' support for pharmacists' pharmaceutical care role. In conclusion, Malaysian community pharmacists had expressed a willingness to implement pharmaceutical care practice but several actions are required to facilitate its implementation.

PPP17 (000127)

Factors Influencing the Role of Community and Hospital Pharmacists in Malaysia

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The professional roles of pharmacists have been cited as influential in guiding the career choices of pharmacy graduates in Malaysia. However, the leadership and the moral reasoning of the pharmacists themselves also influence their role as pharmacists. As such, the views of leaders of the profession would provide insights into identifying key factors which contributes towards the evolution of pharmacy practice in Malaysia. Semi structured tape recorded interviews were conducted with 3 senior hospital pharmacists and 2 senior community pharmacists to elucidate these factors. The participants were invited by the supervisor of the research project to be interviewed and were then interviewed by an undergraduate student with the supervisor. The interviews were coded

and transcribed. Qualitative research principles were used to identify and list the emerging themes which are considered to influence the role of pharmacist in Malaysia. The factors were identified and categorized into themes. All the information collected from the interviews pinpoints the factors which influence the role of hospital and community pharmacist. The factors then are categorized into 5 themes: Prescriber related factors; Patients related factors; Junior Pharmacist related factors; Malaysian health system issues; Pharmacy or hospital setting issues. Due to the different working background and experience of each participant, various factors were mentioned which influenced the role of pharmacists in different setting in Malaysia with a future prospect in rural pharmacy setting.

PPP18 (000020)

Study on the Impact of Colour Coded Syringe Labels (CCSL) for Emergency Drugs in Hospital Kuala Lumpur (EDHKL)

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Medication errors involving injectables is an on-going issue among healthcare teams in critical care areas such as Emergency Department (ED). Labeling of injectables is an integral part of drug preparation. Colour Coded Syringe Label (CCSL) utilises colour to differentiate classes of drugs, providing visual cues to reduce the risk of interclass errors and prevent accidental syringe swapping. This was a prospective observational study conducted at EDHKL for a period of 1 year (March 2011 till Febuary 2012). The objective of the study was to analyse the effect of CCSL in terms of user interface and compliance to labeling requirements. A total of 120 clinical staff from EDHKL participated in the study. Data collection was divided into 3 parts; (i) assessment of knowledge, experience and current practice methods of drug preparation prior to CCSL, (ii) compliance audit and (iii) identifying drawbacks and level of staff acceptance. 75.8% of respondents agreed that similar packaging of drugs contributed to medication errors in EDHKL. 71% of labelling procedures carried out were compliant to the requirements and procedures of CCSL usage protocol. 95% of clinical staff in EDHKL wanted the use of CCSL to continue due to various reasons such as convenience of use and quicker/timely drug preparation. CCSL was well accepted by the clinical staff in EDHKL, as reflected in the audit which showed a 71% compliance rate and the feedback questionnaire during the post introduction of CCSL. Suggestions for improvements of the CCSL was to provide separate labels for bolus and infusion drugs.

PPP19 (000041)

Economic Evaluation of Methadone Maintenance Therapy (MMT) and Long-Term Residential Treatment (LTRT) Program for Drug Abuse Patients in the State of Penang and Kedah, Malaysia

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MMT Programme was launched in Malaysia in 2005 as an alternative to LTRT for drug abuse patients. Both are fully funded by the government but little is known about which alternative is more efficient and should be preferred. The economic evaluation was based on data from cross-sectional HRQoL and retrospective cost studies involving 400 opiate-dependent patients. Consenting patients were interviewed to collect their socio-demographic data, drug consumption history, HRQoL status and opiate treatment evaluation using data collection forms and the EQ-5D, EQ-VAS, WHOQOL-BREF and OTI instruments. Cost data were collected using activity-based-costing and DATCAP instrument from the healthcare providers perspective. Mean EQ-5D score was significantly higher among MMT participants (mean = 0.78, SD = 0.19) compared to those in LTRT (mean = 0.71, SD = 0.23, $p < 0.05$). The capital cost for MMT program was MYR 26,035 and LTRT was MYR6,724,575. Monthly cost to provide MMT program for one patient was MYR 156, which was significantly lower ($P < 0.0001$) than LTRT program (MYR 1024). Very good fit regression model was produced with adjusted R^2 of 0.77 ($F_{10,174} = 62.462$, $p < 0.00005$). The results showed that after controlling for other factors, patients with severe pain had higher cost by 140%. The CER of MMT (MYR 2426/QALY) is dominant with lower cost and higher outcome compared to LTRT (MYR 18863/QALY). The calculated ICER was –MYR 413983/QALY. This study showed that MMT treatment for patients with substance use disorder resulted in better HRQoL. This analysis suggested that MMT is highly cost-effective compared to LTRT with the expected saving of MYR12419/patient/year. Sensitivity analyses conducted found that the results were robust to changes in the model parameters.

PPP20 (000090)

Perception of Public and Undergraduates towards Fear and Exclusion of People with Mental Illness

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A survey using self administered questionnaires was conducted to assess the perception level of fear and exclusion towards people with mental illness among public (P) and undergraduates (UG) in Shah Alam and Puncak Alam, Selangor, Malaysia. The study was conducted from July to September 2009. The questionnaire items were comprised of socio-demography and 8 negative attitudes with response using 5 Likert's scale ratings:

strongly agree to strongly disagree (Cronbach's alpha: 0.68). 463 questionnaire forms were disseminated to targeted population (age more than 18 years old). 400 questionnaires (n = 200 UG) were returned and completed (response rate: 82.0% UG; 91.0% P). Data were analysed using IBM SPSS version 14.0. Descriptive and inferential statistics such as independent student t-test were widely used to establish differences of perceptions between 2 study groups. A p-value of < 0.05 was considered as significant. Majority of respondents were in younger age of life (18 - 23 years old) with mean (±SD) age of 29.6 (±13.6) years old, female, single, Malay, Muslim, graduated and attending any formal higher educational institution, employed and had household monthly income of < RM 1500. There were significant differences between UG and P in items, locating mental health facilities in a residential area downgrades the neighbourhood (p = 0.008) and people with mental illness are a burden on society (p < 0.001) with both high level of disagreement (58.5% UG vs. 41.0% P; 37.0% UG vs. 45.0% P, respectively). Educational level, race and gender significantly influenced the positive perception level of fear and exclusion towards people with mental illness.

PPP21 (000095)

The Outcome of Continuous Assessments on Undergraduate Pharmacy Students' Performance

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Mid semester examination (MSE) was abolished and replaced by continuous assessments (CA) in Kulliyyah of Pharmacy, International Islamic University Malaysia in 2010. The overall score of CA and MSE contribute 40% of the total score. This study examined the outcome of CA on the students' academic performance in Medical Biochemistry. We studied the impact of CA on overall students' performance before and after curriculum changes. A retrospective desktop study was done by using the records of students' performance. Total 373 students from two different groups were included. Group I consisted of 175 students who had taken the MSE under the old curriculum whereas Group II consisted of 198 students. Both groups received the same structure of questions for the end semester exam (ESE). The comparative analyses of scoring in CA versus MSE and cross analysis of final grading in accordance with academic years were done. Group II achieved better results with CA (27.91±3.28) than group I (23.91± 3.41) with MSE [p <0.05]. The ESE result in group II (67.84±7.2) was significantly higher than that of group I (61.56±8.52) [p<0.05]. A total of 8 students (4.6%) from Group I failed but no failure from Group II. Thus, CA assists the students in improving their grades at the ESE. This CA is not favoured by the students as they have to work hard to meet the commitments but it has more credibility than MSE in evaluating students' study progress. In conclusion, the new system of assessment of CA is more applicable and beneficial to the students than the MSE.

PHARMACEUTICAL CHEMISTRY / PHARMACOLOGY / TRADITIONAL & COMPLEMENTARY MEDICINE

PPM1 (000033)

Betulinic Acid Inhibits Toll-like Receptor-4 (TLR4) Dimerisation and Its Molecular Interactions

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Betulinic acid is commonly known for its health benefits to mankind. It is also reported to suppress immune response by down regulating the pro-inflammatory cytokines makes it to be a potential molecule for further investigation. However its specific target in immune system remains to be identified. One of the recently characterised proteins that play a key role in autoimmune disorders is Toll-like receptor-4 (TLR-4). Homodimerisation of TLR-4/MD-2 complexes which are stimulated by pathogens will result in life threatening immune responses. Therefore, in this study we evaluated the effect of betulinic acid on TLR-4/MD-2 homodimerisation and its molecular interactions with TLR-4. HEK-293 cells transfected with TLR-4/MD-2; lipopolysaccharide (LPSEc) from Escherichia coli, a known agonist of TLR-4 were used to evaluate the effect of betulinic acid on homodimerisation. The effect of betulinic acid on homodimerisation in the presence of LPSEc was determined. The results revealed that betulinic acid is preventing homodimerisation. To further understand the molecular interactions between betulinic acid and TLR-4/MD-2, we have performed molecular docking studies. The majority of the interactions between betulinic acid and TLR-4/MD-2 are through MD-2, a unique protein that only associate with TLR-4 but not with other toll-like receptors. These results are suggesting that betulinic acid might be selective towards TLR-4 compared to other TLRs. This suggests that betulinic acid could specifically prevent TLR-4 over-activation through disturbing the homodimerisation of TLR-4/MD-2 complexes and thus able to prevent life threatening immune responses in autoimmune disorders.

PPM2 (000079)

Novel 1,4-Benzothiazine Derivatives as Antimicrobial Agents: Synthesis, Characterization and Evaluation

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Despite the increase in microbial infections, therapeutic options are very limited and are often unsatisfactory because of high toxicity and an inability to eradicate infections. The chemistry of heterocyclic compounds has been an interesting field for the development of new medicinal compounds. Different classes of benzothiazine compounds possess an

extensive spectrum of pharmacological activities such as analgesic, anti-inflammatory, anticonvulsant, antiulcer, anticancer, antibacterial and antifungal. In this study, a series of novel 1,4-benzothiazine derivatives were synthesized and evaluated for their antibacterial and antifungal properties. Oxidative cyclization of 2-amino thiophenol with ethyl chloroacetate yielded 1,4-benzothiazine-3-(2*H*)-one which was refluxed with hydrazine hydrate in methanol to form 3-hydrazino benzothiazine and finally refluxed with different ketones to form 3-substituted benzylideno hydrazino benzothiazines. The synthesized compounds were confirmed by melting point and TLC and their structures were established by various analytical techniques such as IR and ^{1}HNMR spectral studies. All the newly synthesized compounds exhibited moderate to good antibacterial and antifungal activities.

PPM3 (000120)

Chemical Composition and Antimicrobial Activity of *Eucalyptus Camaldulensis* Dehnh Essential Oil from Malaysia

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Eucalyptus are important plants containing essential oil widely used in cosmetic, pharmaceutical and food industries. Chemical composition and biological activity of essential oils are determined by a number of genetic factors, climate, time of harvesting, the plant age and others. Although they are native to Australia and Tasmania, Eucalyptus species have been cultivated worldwide and yet have not been commonly grown in Malaysia. The objectives of this study were to investigate the chemical and biological activity of *E. camaldulensis* grown in Malaysia. An investigation of the oil constituents of the fresh, crushed leaves of *E. camaldulensis* Dehnh grown in University of Malaya compound, was carried out. The oil was extracted by hydrodistillation and the chemical composition was analyzed by GC-MS. The essential oil yield was 1.33% dried weight, a relatively higher content of essential oil. Majority of the oil components were identified. The oil was highly rich in monoterpenes. Four major compounds were dominated in the oil. Terpinene is the main component of the essential oil. Its relative content was 63.8% followed by o-Cymene, Terpinen-4-ol and Terpinolene (22.5%, 9.5% and 1.3%, respectively). However, other Eucalyptus oil components such as 1,8-cineole, ±-pinene and ±-phellandrene were found to be in very low concentrations in the oil (0.71%, 0.44% and 0.02%). Antibacterial screening tests against different bacterial species revealed that the oil has potent inhibitive effects. The results showed that these valuable oils can be produced commercially in Malaysia environment.

PPM4 (000123)

Energies Evaluation in the Binding of the Monoclonal Antibody 1A1D-2 Complexed with Domain III of the Viral Envelope Glycoprotein E of DENV

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Dengue is endemic and has a high fatality rate. Reported cases of illness have been increasing over the past years in tropical regions. Even though there are a few vaccines being currently evaluated, development of an antibody as a treatment would also be a good treatment option. Antibody 1A1D-2 has been reported as having a neutralizing effect on DENV type 1, 2 and 3. In this study, computational assisted modeling was carried out to investigate the importance of specific residues in the binding site of the monoclonal antibody 1A1D-2 complexed with domain III of the viral envelope glycoprotein E of DENV 2 using the Discovery Studio 2.5. The interaction energy was found to be relatively low (negative), indicating a stable system and thus a likely binding interaction. The interaction energy of the heavy chain of the antibody was found to be lower than the light chain by about ~170 kcal/mol with CHARMM force field. Besides, examining the interactions of the residues in the heavy chain and the light chain with the fragment complex under 3Å indicated that more amino acid residues are involved in binding with the heavy chain which implies a vital role of the heavy chain upon binding. Specific residues located in the complementary determining regions (CDRs) and their interaction energies with the viral envelope glycoprotein E were identified.

PPM5 (000067)

Molecular Characterization of the K-ras Protein in Lung Cancer

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Computational experimental strategies of modeling and docking are becoming pivotal in the new drug screening process. The methods are fast and reliable enough to identify possible hits for old and emerging diseases. K-ras protein mutations at codon 12 and 13 have been implicated to play a critical role in development and progression in non small cell lung cancer (NSCLC). The purpose of this study was to analyse the key mutations occurring in the K-ras protein by developing models of the mutated K-ras protein using Modeller. RMSD values from the Swiss PDB viewer, DOPE score generated by Modeller, and Ramachandran plots obtained from PROCHECK were used to assess the predicted models of mutated K-ras protein in its active and inactive forms. Docking was performed with Autodock Vina 4.2 on a reported crystal structure of the K-ras protein

(4dsn.pdb) with reported potentially active compounds from Malaysian herbs. Phytol, hexadecane, hexadecanoic acid and pheophorbide found in *T. flagelliforme* were selected for docking studies. The selected ligands were found to have a high binding affinity for the SOS pocket, an important binding site on the K-ras protein.

PPM6 (000076)

Anti *Helicobacter pylori* Activity of *Hibiscus vitifolius* in Ulcerated Albino Rats

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The root of *Hibiscus vitifolius* (Malvaceae) is traditionally used for the treatment of ulcer and different type of microbial infections. The study was designed to evaluate anti *Helicobacter pylori* activity of *H. vitifolius* roots extracts in ulcerated rats. On the basis of phytochemical screening of various extracts of *H. vitifolius*, methanol extract (ME) was selected to assess anti *Helicobacter pylori* since it was found to be rich in phytoconstituents. The extract showed no sign of acute toxicity up to a dose level of 2000 mg/kg b.wt. All male Wistar rats were divided into five groups (n=6). Group-I served as normal control whereas group-II induced with acetic acid and inoculated with *H. pylori*. Group-III and IV induced with acetic acid and inoculated with *H. pylori* and treated with ME at a dose of 200 and 400 mg/kg b.wt., respectively. Group–V served as standard and received combination of Amoxicillin (50 mg/kg b.wt.), Clarithromycin (25 mg/kg b.wt.) and Omeprazole (20 mg/kg b.wt.) orally. After 14 days treatment, the blood was collected and the stomachs were removed. Administration of ME (400 mg/kg b.wt.) in ulcerated rats showed the significant ($p<0.001$) reduction in ulcerated area. The level of IL-1ß was significantly ($p<0.01$) decreased and the level of IL-10 was significantly ($p<0.01$) increased when compared with H. pylori induced ulcerated rats. The biochemical observations were supported by histopathological examination of stomach sections. These findings conclude that methanol extract of *H. vitifolius* possesses significant anti *Helicobacter pylori* activity and supports its traditional claim.

PPM7 (000078)

Analgesic and Antipyretic Activity of *Manihot esculenta* crantz Extracts

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The study was carried out to investigate the analgesic and antipyretic activities of leaves and tubers extracts of the plant *Manihot esculenta* crantz. The antipyretic activity was determined using brewer's yeast induced pyrexia method while analgesic activity was carried out by two different models such as hot plate and tail immersion methods in Swiss albino rats. Dried powdered plant materials were subjected to successive solvent maceration with acetone, methanol and water. The phytochemical studies revealed the presence of alkaloids, glycosides, flavonoids, phenolic compounds, saponins, steroids and

carbohydrates in all the three extracts. The extracts at a dose of 200 mg/kg body weight were subjected to analgesic and antipyretic activities. The methanol extract of the leaves and tubers showed a significant ($p<0.001$) analgesic activity which was compared with standard drug, diclofenac sodium 10 mg/kg. The antipyretic activity of the methanol extracts of *M. esculenta* also significantly ($p<0.001$) reduced the elevated body temperature in albino rats which was well compared with paracetamol 150 mg/kg. This findings support the ethnomedical use of *Manihot esculenta* crantz in the treatment of pain and fever.

PPM8 (000113)

Involvement of Opioidergic and Serotonergic Pathways in the Analgesic Activity of *Cissus quadrangularis* L. (Patah Tulang) Stem Extract in Mice

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Cissus quadrangularis L. (Vitaceae) is an edible plant, indigenous to Asia and Africa. It exhibited good fracture healing property and analgesic effect in rodents. Our previous study indicated that the chloroform extract of stem had potent analgesic activity in hot plate experiment than the methanolic extract. Hence, in this study, the mechanism of analgesic activity of chloroform extract of stem of *C. quadrangularis* was explored in hot plate experiment in mice. The powdered stem of *C. quadrangularis* was extracted with chloroform and the extract was dried to semisolid residue. The residue was suspended in 10% tween 20 in normal saline and administered (300 mg/kg, i.p. at 0 min) to albino mice after pretreatment with naloxone (opioid antagonist, 1 mg/kg, i.p. at -15 min), p-chlorophenylalanine methyl ester (pCPA, inhibitor of serotonin synthesis) (100 mg/kg, i.p. once daily for three days) and phentolamine (alpha blocker, 20 mg/kg, i.p. at -15 min). Morphine sulphate (3 mg/kg, i.p. at 0 min) was administered after pretreatment with naloxone (1 mg/kg, i.p. at -15 min). The response time in seconds was measured at -15, 0, 15, 30, 45, 60, 75 and 90 minutes in hot plate test. The data were analysed by one-way ANOVA followed by Dunnett's test. Analgesic activity was observed significantly ($p < 0.05$) in the group pretreated with phentolamine but not in the groups pretreated with naloxone and pCPA. These results suggest that the analgesic activity of *C. quadrangularis* in mice might involve opioidergic and serotonergic pathways.

PPM9 (000115)

Investigation of Gastro-Protective Activity of Schiff Bases Complexes and their Mechanisms

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Schiff bases have regularly been used as chelating ligands in organization chemistry. Schiff base with donors (N, O, S, etc) have formation similarities with neutral biological systems and because of presence of amine group are utilized in elucidating the mechanism of conversion of racemisation reaction in biological system. They show biological activities including antibacterial, antifungal anti-diabetic antitumor, anti-proliferative anticancer herbicidal and anti-inflammatory activities. Therefore, this study was conducted to investigate the gastro-protective activity of some Schiff bases compounds and their mechanisms of the compounds for treatment. The compounds were tested on SD rat for anti-ulcer activity by using ethanol inducing ulcer. The study showed all the Schiff bases metal complex possessed very good activity as a gastro protective agent and even better than the drug control (omeprazole). The immunochemistry assays showed that the PGE2 (Prostaglandin) interfere to protect the stomach from ethanol to induce ulcer by producing more mucus compare to ulcer control (Ethanol group). The biochemistry assays (anti-oxidant enzymes) showed that for all the compounds, the oxidative stress donor (MDA) reduced sharply compared to ulcer control. Catalase enzyme the first defensive anti-oxidant enzyme against oxidative stress donor was increased for compounds LPSVoSo4, CdGH and LPACdCl2 but there were no changes of catalase level for compounds LPACdSCN and LPSDphSnCl2. However nitric oxide (NO) assay showed opposite result compared to catalase assay except for compound CdGH which the NO level was high. Superoxide dismutase was increased for all compounds which was one of the line for protecting the tissue and cells from superoxide.

PPM10 (000121)

Anti-leukemia Effect of Thymoquinone Isolated from *Nigella sativa*

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Nigella sativa is an annual flowering plant with pale blue to white flowers and a large fruit. It has various synonyms names such as Black cumin, Black caraway, Black onion seed, Black seed, Fennel flower, Roman coriander and Kalonji. It has been used in different countries in Asia, Middle East and Africa as traditional herb against inflammation, asthma, cough, influenza and cancer. There were numerous studied on the anti-cancer properties of thymoquinone (TQ) on different cell lines and in animal model. But the effect of this compound on lymphoblastyoid leukemia is not established yet. This study aimed to evaluate the anti-leukemic effect of thymoquinone (TQ) isolated from this plant using CEMss cells as an in vitro model. The results showed that treatment with TQ inhibited the cell growth in CEMss significantly. The mode of cell death was confirmed by DNA laddering as well as AO/PI fluorescent staining and Annexin V flow cytometric staining. The cell death was closely associated with the cell cycle arrest at G0/G1 phase. In addition the expression of Bax, Bcl2 and HSP 70 proteins were observed by western blotting. The caspase 3, 8 and 9 were significantly elevated by the treatment. The results obtained from the present study had clearly showed that the TQ has the potential to be developed as anti-leukemic agent. The mode of cell death was found to be via apoptosis.

PPM11 (000009)

Study on Antidiabetic Plants Cocktail Containing *Andrographis paniculata, Cinnamomum burmannii* and *Tinospora crispa*

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The present study was aimed to investigate antidiabetic potential of the mixture *of Andrgraphis paniculata*, *Cinnamomum burmannii* and *Tinospora crispa* (ACT) in the *in vitro and in vivo* studies. In *in vitro* method, the effect of ACT on lipid accumulation of 3T3-L1 adipocytes was analyzed by using Oil Red O staining. 2-Deoxy-D-[^{3}H] glucose was used to measure glucose uptake activity. In the *in vivo* study, a set dose of ACT (500, 125 and 75 mg/kg b.w., respectively) were administered to both normal and streptozotocin induced diabetic male Sprague-Dawley rats. The blood glucose levels were measured at 0, 3, 7, and 10 days after oral administration of ACT. Result of cell based study showed that ACT induced triglyceride accumulation in 3T3-L1 cells at relatively small concentration in a dose-dependent manner. In addition, 2-deoxy-D-[^{3}H] glucose uptake activities were significantly different at dose 50 µg/mL ($P < 0.05$ compared to basal). Gene expression analysis using quantitative RT-PCR showed that adipocytes-treated with ACT significantly increased the expression levels of PPARγ which regulate the adipogenesis process and its target gene GLUT4 that involve in glucose uptake when compared to the basal. The result of *in vivo* study demonstrated, ACT exhibited blood glucose lowering effects in streptozotocin induced diabetic rats. Taken together, the *in vitro* and *in vivo* results indicate that mixture of ACT possesses antihyperglycemic activity.

PPM12 (000027)

***In Vitro* Effect of Various Herbal Active Constituents on Cytochrome P450 2E1**

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Cytochrome P450 (CYP) enzymes are responsible for metabolism of various internal or external substances including a great number of clinically used medications. CYP2E1 is a member of this mixed-function oxidase system which has been widely studied because of its metabolism of ethanol, activation of procarinogens, and its clear relevance to alcoholism, diabetes, and other maladies. Herbal medicines are often consumed in combination with conventional drugs, which raises the potential of drug-herb interactions. In this study, nine known active constituents (eurycoumanone from *Eurycoma longifolia*; andrographolide from *Andrographis paniculata*; asiaticoside, asiatic acid and madecassic acid from *Centella asiatica*; eupatorin, sinensetin, caffeic acid and rosmarinic acid from *Orthosiphon stamineus*) were examined with regard to their effects on CYP2E1 activity *in vitro*. Fluorescence-based enzyme assay was established and 7-methoxy-4-(trifluoromethyl)-coumarin (7-MFC) was selected as a CYP2E1 substrate. The herbal compounds were investigated at various concentrations (ranging from 0 to 250 µM). The results indicate that no significant effects were observed for all compounds investigated except for madecassic acid and eupatorin (IC_{50} values of 13.7 and 100.0 µM respectively). Inhibition by these two compounds was considered only moderate as the IC_{50} values were much higher than the typical concentrations observed for the two compounds in blood circulation. Thus, clinically significant interactions due to co-administering any of the nine substances and CYP2E1 substrates are unlikely if similar results were acquired from *in vivo* assays.

PPM13 (000060)

Analgesic Activity of *Cissus quadrangularis* (Patah Tulang) Stem Extracts in Mice

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Cissus quadrangularis L. (Vitaceae) is an edible plant, indigenous to Asia and Africa. It is reported to have bone fracture healing property and analgesic effect in rodents. However, the previous study on analgesic effect used only alcoholic extract and hot plate test. Hence, the present study was designed to expand the study on analgesic activity by including tail flick test and using two successively extracted extracts. The powdered dried stem of *C. quadrangularis* was successively extracted with chloroform and methanol. The dried extracts were suspended in 10% tween 80 in normal saline and administered (i.p.) to separate groups of albino mice at the doses of 75, 150 and 300 mg/kg. Morphine sulphate (3 mg/kg, i.p.) was used as the positive control. In both tests, the response time in seconds was measured at -15, 0, 15, 30, 45, 60, 75 and 90 minutes. The data were analysed by one-way ANOVA followed by Dunnett's test as the post hoc test. The yield of chloroform extract was 1.87% w/w and that of methanol extract was 4.23% w/w. Chloroform extract showed significant ($p < 0.05$) analgesic effect at the doses of 75, 150 and 300 mg/kg in hot plate and tail flick tests. Methanol extract showed significant ($p < 0.05$) analgesic effect at the dose of 300 mg/kg in hot plate and at the doses of 150 and 300 mg/kg in tail flick tests. The present study indicates that chloroform extract is more potent than methanol extract in inducing analgesic effect in mice.

PPM14 (000066)

Antibacterial Activity of Methanolic Extract of *Clinacanthus nutans* (Sabah Snake Grass) Leaf

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Clinacanthus nutans (Acanthaceae) is a medicinal herb traditionally used against skin and gastrointestinal infections. *C. nutans* exhibited several bioactivities including antibacterial effects against *P. acnes* and *S. epidermidis*. Our present study aimed at exploring the antibacterial effect of methanolic leaf extract of *C. nutans* against *Propionibacterium acnes*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus cereus* and *Escherichia coli*. The powdered dried leaf was extracted with methanol. The dried extract was reconstituted in 10% DMSO v/v and tested at the concentrations of 0.1, 0.2, 0.39, 0.78, 1.56, 3.15, 6.25 and 12.5 mg/mL in a 96-well microplate by microdilution method. Absorbance was taken with ELISA plate reader at 630 nm. Data were analysed by one-way ANOVA followed by Tukey's multiple comparison test as the *post hoc* test. Erythromycin and chloramphenicol were used as the positive controls. Methanolic leaf extract of *C. nutans* showed significant ($p < 0.05$) antimicrobial activity against *S. aureus*, *S. epidermidis* and *E. coli*. Methanolic leaf extract of *C. nutans* did not show any significant activity against *P. acnes* and *B. cereus* at the concentrations employed in the study. *S. epidermidis* showed high susceptibility amongst all the three susceptible organisms. The ineffectiveness of methanolic leaf extract of *C. nutans* against *P. acnes* is different from previous reports and needs further exploration. Further studies are required to identify the bioactive compounds from *C. nutans* and their antibacterial mechanism of action.

PPM15 (000075)

Hepatoprotective Activity of *Swietenia macrophylla* Fractions in CCl_4 Intoxicated Rats

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The fruit of *Swietenia macrophylla* King (Meliaceae) also called "Sky Fruit" and it is traditionally claimed by Orang Asli, Sarawak, Malaysia for the treatment of diabetes and jaundice. In a previous study, methanol extract of *S. macrophylla* reported a significant ($P<0.05$) hepatoprotective activity at a dose of 400 mg/kg b.wt. The aim of the present study was to evaluate the hepatoprotective effect of n-butanol, ethylacetate and n-hexane fractions of *S. macrophylla* in CCl4-induced hepatotoxic albino rats. The fractions showed no signs of acute toxicity up to a dose level of 1000 mg/kg b.wt. The ethyl acetate fraction at an oral dose of 200 mg/kg b.wt. exhibited a significant ($P < 0.001$) protective effect as shown by lowering serum levels of glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase, total cholesterol and total bilirubin and increasing the levels of total protein and albumin levels as compared to silymarin (100

mg/kg b.wt.). These biochemical observations were supported by histopathological examination of liver sections. The phytochemical nature of the ethyl acetate fraction reveals the presence of carbohydrates, amino acids, alkaloids, steroids, phenolic compounds, flavonoids and glycosides. Thus, it could be concluded that ethyl acetate fraction possesses significant hepatoprotective property which may be due to the presence of flavonoids and phenolic compounds.

PPM16 (000104)

Analgesic Effect of *Ruta graveolens* in Albino Mice and Rats

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Aim of the present study was to investigate the analgesic effect of *Ruta graveolens* by using thermal and chemical induced pain; and to confirm the traditional medicinal use of the plant as analgesic and anti-inflammatory agent. The antinociceptive and anti-inflammatory effects of orally administered alcoholic extract of *Ruta graveolens* (whole plant) was studied with hot plate (thermally induced pain) method in albino rats and mice, with acetic acid (chemically induced pain) in albino mice and with paw formaldehyde induced edema in albino mice. The Ruta graveolens alcoholic extract treated animals showed significant increase in hot plate reaction time, complete protection of animals against acetic acid writhing and a significant decrease in paw edema compared to control animals (n = 6). These results confirm the traditional use of *Ruta graveolens* for painful and inflammatory conditions. It is therefore concluded that the *Ruta graveolens* contains compound(s) which may act as both non-opioid (aspirin like) and opioid (morphine like) analgesics and have nonsteroidal anti-inflammatory drugs like action.

PPM17 (000128)

Antidiabetic Effect of Steroidal Compound Isolated from *Melothria maderaspata*

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Melothria maderaspata were successively extracted using different solvents in an increasing order of polarity. The methanol fraction of *M. maderaspatana* was concentrated and the residual amount of methanol was removed *in vacuo*. The residue was washed with diethyl ether, hexane, chloroform and the finally dissolved in methanol. The methanol solution was filtered and the filtrate was poured into excess of diethyl ether whereby a light brown color mass was precipitated. The precipitate was separated by filtration and purified by repeating of dissolution in methanol and precipitation with diethyl ether. The isolation of the reported compound was done by following appropriate chromatography and spectral methods and interpreted efficiently. The spectral data (UV, IR, MS, NMR proton and carbon) and their interpretation led us to the conclusion that the

isolated chemical constituent was found to be a steroidal lactone that contain a cyclopentanoperhydrophenanthrene ring system with a total of 28 carbons in the whole structure. The molecular formula of this compound obtained from Mass spectra revealed its' molecular weight to be 457.89 and molecular formula $C_{28}H_{38}O_5$. The compound showed a marked positive activity in enhancing oral glucose tolerance of normal and diabetic animals.

PPM18 (000130)

Effects of Hopea Extracts on Human Colorectal Cancer Cell Proliferation via Induction of Apoptosis

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Hopea is one of the largest genus belongs to the family of Dipterocarpaceae, which consisting of over 100 species. However, there are limited studies had been performed on biological activities of *Hopea ponga* and *Hopea odorata*. Therefore, this study was undertaken to determine the antiproliferative activities of *Hopea ponga* and *Hopea odorata* (leaves and stem bark) on human colorectal cancer cell lines, HT29. In this study, a total of 16 extracts from four different extraction solvents (hexane, ethylacetate, methanol and water) were tested for their antiproliferative activities via 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The potency of the extracts of *Hopea ponga* and *Hopea odorata* were compared using IC_{50} value, the concentration with 50% inhibition of cancer cells proliferation. Ethyl acetate extracts for both leaves and stem bark of *Hopea ponga* and *Hopea odorata* shown good antiproliferative activities on HT29 cells. The IC_{50} of ethyl acetate extracts of leaves and stem bark of *Hopea ponga* were 20.11 ± 2.53 μg/ml and 20.21 ± 10.95 μg/ml respectively. While IC_{50} of ethyl acetate extract of *Hopea odorata* stem bark was 13.13 ± 4.20 μg/ml which exhibits strongest antiproliferative activity on HT29 cells among 16 extracts. The mode of colorectal cancer cell death was found to be apoptosis. Therefore these extracts exhibit good antiproliferative activities which might be potential cytotoxic agents against human colorectal cancer. Hence further studies will be warranted to determine the underlying antiproliferative and apoptosis pathway.

PPM19 (000131)

Inhibition of Human Estrogen Dependent Breast Carcinoma Proliferation by *Hopea odorata* and *Hopea ponga*

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Hopea is one of the main genus of Dipterocarpaceae and it is widely distributed from mainland of South-East Asia toward Peninsular Malaysia. *Hopea* is locally known as *merawan hitam* or *pengarawan*. *Hopea* genus has been reported to have anticancer activity, antimicrobial activity and antioxidant. However, there are limited studies of *Hopea odorata* and *Hopea ponga* on estrogen dependent breast cancer. Hence, the aim of

this study was to determine the anti-proliferative activities of the leaves and stem bark of *Hopea odorata* and *Hopea ponga* extracts (hexane, ethyl acetate, methanol and water) on estrogen receptor dependent breast cancer cells (MCF-7). Anti-proliferative activities were determined using the MTT assay. The extracts were first prepared by soxhlet extraction using solvents with different polarity. The potency of each extracts of *H. odorata* and *H. ponga* were compared using the IC_{50}, the concentration with 50% growth inhibition. Hexane extract from leaves of *H. odorata* and the ethyl acetate extract from the leaves of *H.ponga* exhibited the most potent inhibition on cell proliferation, with IC_{50} were 83.775 ± 3.061 µg/mL and 27.713 ± 13.159 µg/mL respectively. The extracts were also found to be selective toward cancerous cells and sparing the non-cancerous cells. Apart from that, the apoptosis induction activities by these extracts were confirmed through fluorescence microscopic examination and apoptosis kit. In conclusion, ethyl acetate extract from leaves of *H. ponga* exhibits the most potent antiproliferative activity against human estrogen dependent cancer.

PPM20 (000132)

In Vitro Cytotoxic Effects of *Hopea odorata* and *Hopea ponga* on Estrogen Independent Breast Cancer

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Estrogen receptor (ER) negative breast cancers are generally unresponsive to conventional anticancer therapy and have poorer prognosis as compared to ER-positive breast cancers. In recent years, natural products are widely explored in the search of new anticancer agents. *Hopea*, locally known as *merawan hitam*, belongs to the family of Dipterocarpaceae which contains a variety of resveratrol oligomers. Resveratrol oligomers were reported to have antiproliferative effect on cancer cells. Where no reported traditional use of *Hopea ponga* is available, resins of *Hopea odorata* stem bark was reported to have medicinal properties in treating sores and wounds. However, no scientific evidence was published on evaluation of antiproliferative activity of leaves and stem bark of *H. odorata* and *H. ponga* tested on human breast cancer. Therefore, antiproliferative effects of extracts (hexane, ethyl acetate, methanol, water) from leaves and stem bark of *H. odorata* and *H. ponga* on the ER-negative breast cancer cells (MDA-MB-231) were investigated using cell viability test. The antiproliferative activities of the plant extracts were compared using IC_{50} value, 50% inhibitory concentration. Among the 16 extracts tested, hexane extract of *H. odorata* leaves and ethyl acetate extract of *H. ponga* leaves had the most potent antiproliferative activities, with the IC_{50} of 64.68 ± 12.8µg/mL and 18.82 ± 1.48µg/mL respectively. Apoptosis induction effect was confirmed under microscopic observation and apoptotic assay kit. In conclusion, extracts of *H. odorata* and *H. ponga* do exert antiproliferative activities on ER negative breast cancer which may be a potential agent in treating ER-negative human breast cancer.

PPM21 (000133)

Antiproliferative Property of *Hopea odorata* and *Hopea ponga* Extracts on Human Cervical Cancer Cells

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Hopea, the main genus of Dipterocarpaceae, is widely distributed in the South East Asia. Active constituents are found in Dipterocarpaceae such as vaticanol G, hemlesyanol C, ascorbic acid, hopheaphenol etc. Dipterocarpaceae exhibits some biological activity for instance antibacterial, anticancer, antihepatotoxic and anti-HIV. There is limited literature on the antiproliferative activity of stem barks of *Hopea odorata* on human cervical cancer and there is no any scientific report on the antiproliferative activity of *Hopea ponga* on human cervical cancer. Thus, the aim of this study was to determine the antiproliferative activities of hexane, ethyl acetate, methanol and water extracts of leaves and stem bark of *Hopea odorata* and *Hopea ponga* on human cervical (HeLa) cancer cell line through in vitro cytotoxic (MTT) assay. The extracts of *Hopea odorata* and *Hopea ponga* was prepared by sequential extraction with hexane, ethyl acetate, methanol and water in a soxhlet extractor. The IC_{50} (concentration required to inhibit 50% of cell growth) is used to compare the potency of different extracts of *Hopea odorata* and *Hopea ponga*. In *Hopea odorata*, the most potent extracts was hexane extract of leaves (IC_{50}:102.94 ± 1.83 µg/mL), while in H*opea ponga*, the most potent extracts was ethyl acetate extract of leaves (IC_{50}: 32.37 ± 1.94 µg/mL). Methanol and water extracts from stem barks of *Hopea odorata* and *Hopea ponga* was found to have IC_{50} more than 250 µg/mL. Apoptosis is confirmed through microscopic examination and commercial available apoptosis kit. In conclusion, ethyl acetate extract of leaves show the most potent result and further investigations are required to be done.

PPM22 (000134)

Antiproliferative Activity of *Hopea ponga* and *Hopea odorata* Leaves and Stem Bark on Leukemia Cancer Cell Lines (CEMss)

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Hopea genus is widely distributed in the tropical rain forest such as Malaysia. Scientific reports had shown that it produces resveratrol oligomer that exhibits variety of biological activities, such as antibacterial, anti-inflammatory, anticancer and antioxidant. *Hopea odorata* showed significant cytotoxicity activities against a few cancer cell lines, however leukemic cell line is yet to be studied. Since *Hopea ponga* reported to have antioxidant and antibacterial effect, it is promising that it may also exhibits cytotoxicity activities. Therefore, the objective of this study was to determine the antiproliferative activities of *Hopea ponga* and *Hopea odorata* (stems and leaves) extracts on CEMss cancer cell lines through MTT assay. The extracts were prepared by sequential extraction using soxhlet extractor extracted with hexane, ethyl acetate, methanol and water which followed by drying step using the rotary evaporator. Antiproliferative activities by ethyl acetate

extracts of the *Hopea ponga* leaves was found to be the most potent extract in the dose response curve on CEMss which exhibited IC_{50} of 9.184 µg/mL. Apoptosis of the CEM_{SS} was examined through microscope and Cell Death Detection ELISAPLUS (Roche, Germany) kit. Further investigations are required for the determination of mechanism of action of the particular extracts in human. Thus, it can be concluded that ethyl acetate extracts of the *Hopea ponga* leaves is the most potent extract in this study which could be the potential candidate in against leukemia.

PPM23 (000135)

The Cytotoxic Activities of *Hopea odorata* and *Hopea ponga* Extracts on Human Ovarian Cancer Cells

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Hopea genus belonging to the Dipterocarpaceae family is widely distributed throughout Peninsular Malaysia. They are known to produce a wide range of resveratrol oligomers which have shown to have anticancer activities. The aim of this study is to determine the antiproliferative activities of *Hopea odorata* (*H. odorata*) (stem bark and leaves) and *Hopea ponga* (*H. ponga*) (stem bark and leaves) extracts (hexane, ethyl acetate, methanol and water) on the ovarian cancer cell lines (CaOV3) using viability studies of cells in culture. National Cancer Registry reported ovarian cancer as the fourth most common cancer in women in Malaysia. Although chemotherapy is the preferred treatment modality, chemoresistance severely limits treatment success with evidence suggesting the deregulation in key apoptotic pathways as a factor. However, there is still no reported study on the cytotoxic activities of *H. odorata* and *H. ponga* extracts on human ovarian cancer cells. Potency of different extracts was compared using IC_{50}, which represents the concentration of extracts required for 50% of cells inhibition. The results demonstrated that for *H. odorata*, the most potent extract against CaOV3 cells was hexane extract of *H. odorata* leaves with IC_{50} of 50.14 µg/mL while ethyl acetate extract of *H. ponga* leaves was found to be most potent at IC_{50} of 130.44 µg/mL. Apoptosis was found to be the mechanism of cancer cells death by observing under fluorescence microscope and confirmed using an apoptosis induction kit. Thus, hexane extract of *H. odorata* leaves has a potential in the treatment of human ovarian cancer.

PHARMACEUTICAL TECHNOLOGY

PPT1 (000006)

Preparation of Carvedilol Spherical Crystals Having Solid Dispersion Structure by the Emulsion Solvent Diffusion Method and Evaluation of Its *in vitro* Characteristics

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Spherical crystallization (SC) is a promising alternative for improving micromeritic properties and dissolution rate of active pharmaceutical ingredients. In the present work, spherical agglomerates of carvedilol (CAR) were prepared by emulsion solvent diffusion (ESD) method using methanol, water and dichloromethane as good solvent, poor solvent and bridging liquid respectively. Agglomerates were prepared using Poloxamer F68 and F127 as hydrophilic polymers. The agglomerates were characterized by fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD) and scanning electron microscopy (SEM), and were evaluated for flowability, solubility and drug release. CAR agglomerates exhibited significantly improved micromeritic properties, solubility as well as dissolution behaviors in comparison with pure CAR crystals. Differential scanning calorimetric and powder X-ray diffraction studies confirm that the formulation process altered the crystalline nature of carvedilol.

PPT2 (000022)

Comparative Evaluation of Different Spreadability Techniques on Extemporaneously Prepared *Cocos nucifera* Topical Dosage Forms

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The rheological properties of topical preparations influence the performance of drug delivery systems. The spreadability is an important parameter for uniform and convenient application of topical preparation in relation to patient compliance. The therapeutic efficiency of a formulation also depends on its spreading value. Keeping the significance of spreadability in mind, the objective of the present study was to prepare *Cocos nucifera* topical dosage forms using two different dermatological bases by fusion technique and to carry out a comparative evaluation of the spreadability of these extemporaneously prepared formulations using two different techniques [Method I and Method II]. The spreadability results of the formulations obtained with method I and method II ranged from 0.43 to 12.09 g.cm/sec and 18.67 to 25.33 mm, respectively. The results exhibited difference in spreadability results indicating the lack of reproducibility of the methods employed and the necessity for standardization for routine assessment of spreadability parameter for semi-solid preparations. The studies also demonstrated the suitability of carbopol gel base as a suitable dermatological base for use in a *Cocos nucifera* topical

formulation as it possessed good spreadability characteristics thereby providing assurance for better therapeutic efficacy.

PPT3 (000048)

Erosion and Dissolution Performance of Intermediate Molecular Weight HPMC Controlled Release Polymers

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Dissolution and erosion of intermediate molecular weight (MW) HPMC grades (BenecelTM HPMC K250 PH PRM, K750 PH PRM, and K1500 PH PRM) were evaluated against equivalent viscosity HPMC blends of different MW HPMC. Formulations with 25% drug, glipizide and carbamazepine (insoluble) and theophylline (soluble), 30% polymer, and 44.5% micro crystalline cellulose were wet granulated with water. Tablets of 400 mg weight were compressed after drying, milling and lubrication with addition of 0.5% magnesium stearate. Dissolution, erosion and swelling studies were carried out in USP apparatus I (phosphate buffer pH 6.8 for carbamazepine and theophylline; pH 7.5 with 0.1% polysorbate 80 for glipizide). The time to 50% drug release, t50% for low soluble glipizide and carbamazepine (n=3) of HPMC K750 was 9.5-11 hrs and 8-10 hrs, respectively with standard deviations (SD) < 5%. Tablets of 750 cps HPMC blend had slower and more variable drug release with t50% of 10-15 hrs and 7-12 hrs, respectively with SD of up to 10%. In contrast, t50% for soluble theophylline was 5.5-6.5 hrs with SD < 5% for both HPMC K750 and the 750 cps HPMC blend. Similar trends were observed with HPMC K1500 and HPMC K250. Erosion and swelling profiles for low soluble glipizide and carbamazepine with new intermediate MW grades were less variable (8% SD) compared to equivalent viscosity HPMC blends (18% SD). Less variability of erosion and swelling profiles was observed with soluble theophylline with both the intermediate MW HPMC grades and similar viscosity blends. Both average MW and MW distribution are important for matrix erosion and swelling. Bimodally distributed blends results in slower release and more variability than the unimodal custom HPMC grades. MW distribution is of less importance for soluble drugs.

PPT4 (000049)

Aqueous Solubility Enhancement of Ketoconazole Using Solid Dispersion and Complexation Technique

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Dissolution is the rate limiting step for drugs with poor aqueous solubility which in turn affects their therapeutic activity. Ketoconazole is a poorly water soluble drug which is classified as class II drug under biopharmaceutics classification scheme. Keeping this fact in mind, the aim of the present study was designed to prepare inclusion complexes and

solid dispersions of ketoconazole (KET) in order to enhance its dissolution. The phase solubility studies were carried out by the method described by Higuchi and Connors. The solid dispersions of MCC and soluble starch were prepared using solvent evaporation method, whereas inclusion complexes with β-cyclodextrin (β-CD) were prepared by co-evaporation method. The prepared formulations were evaluated for percentage yield, drug content, thermal characteristics, X-Ray diffraction pattern, SEM analysis and in-vitro drug release. The solubility of ketoconazole at 25 °C was found to be 15.972 µg/ml. The stability constant value was found to be 883.9 M^{-1} which indicated the stability of KET-βCD complexes at 1:1 molar ratio. Inclusion complexes at 1:3 molar ratios showed fastest dissolution rate (83.60 % after 120 minutes) in distilled water. Solid dispersion of ketoconazole with MCC and soluble starch showed better dissolution at 1:10 weight ratio (74.49 % and 63.62 % respectively). The studies showed that solubility and dissolution rate of ketoconazole were distinctively increased in the prepared binary mixtures compared to pure ketoconazole. The order of increase in dissolution rate with different carriers was β-CD > MCC > soluble starch. Increase in solubility and dissolution rate was ascribed due to the conversion of crystalline form into partially amorphous form and reduction in particle size with surface adsorption of drug onto carrier as shown by PXRD pattern and SEM analysis. The study concluded that addition of carriers such as β-CD and MCC to ketoconazole was able to improve its dissolution rate.

PPT5 (000069)

Formulation and Evaluation of Gastroretentive Matrix Tablets of Metformin Hydrochloride with Xanthan and Tamarind Gum

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Gastroretentive floating drug delivery systems (GRFDDS) were often designed to prolong the gastric residence time of drugs with absorption window in the upper parts of gastrointestinal tract to improve their bioavailability. GRFDDS offer continuous input of drug at its site of absorption due to their ability to float on gastric contents over prolonged period of time. The aim of the present study was to develop optimal gastroretentive drug delivery system for Metformin HCl. Metformin HCl, an antidiabetic drug, with absorption window in the stomach, has oral bioavailability of around 50 %, probably due to its poor absorption from lower gastrointestinal tract. The present study was to formulate Metformin HCl matrix tablets with natural release retardants like xanthan and tamarind gum (Tamarind Kernel Powder). The gastroretentive matrix tablets of Metformin HCl were prepared using xanthan and tamarind gum in different ratios, sodium bicarbonate was used as gas generating agent for buoyancy. Four formulations, TKP 2, TKP 3, TKP 4 and TKP 5 were prepared using tamarind gum:xanthan in the ratios of 4:1, 3:2, 2:3, 1:4, whereas TKP 1 and TKP 6 were prepared using only tamarind gum and xanthan respectively. The matrix tablets were prepared by wet granulation method with 1 % w/v xanthan as binder solution and evaluated for pharmacopoeial requirements. All the prepared formulations exhibited good tablet characteristics with a floating lag time of < 1 min. The drug release profiles of the matrix tablets indicated the inability of tamarind gum to control the release when used alone. However, TKP 3 has short floating lag time (< 30 sec), and was found to have an optimum release of 99.29% in 10 h. The

dissolution data was fitted to popular mathematical models to assess the mechanism of drug release, TKP 3 showed predominant zero order release (r = 0.9518) and Higuchi diffusion (r = 0.9930). It is concluded therefore that TKP 3 with tamarind gum and xanthan (3:2) has optimum Metformin HCl release in 10 h.

PPT6 (000073)

Formulation and *In-vitro* Evaluation of Matrix Type Transdermal Patches of Captopril

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Captopril is an angiotensin converting enzyme (ACE) inhibitor and there is a need for an alternative to the oral route due to its reduced oral absorption and short elimination half-life. This study was aimed to design and evaluate matrix-type transdermal patches of captopril. Polymers used were hydroxypropyl methylcellulose (HPMC) and polyethylene glycol (PEG) 400. Menthol and aloe vera were used as permeation enhancers. Matrix type transdermal patches of captopril were prepared by moulding technique. Eight formulations (F1-F8) were prepared by varying the ratios of polymers and enhancers. The FTIR results showed no abnormal peaks and thus it was concluded that no incompatibility between the drug and polymers. Skin irritation was studied by modified Draize test and the results showed no noticeable irritation on rabbit skin, indicating the skin compatibility of drug as well as polymer matrix. The uniformity of drug content was evidenced by low S.D values (± 0.012 to ± 0.057). High folding endurance (>280) revealed that the prepared films were having good flexibility. The weight of the patches was uniform and thickness varied from 0.0533 to 0.1267 mm. *In vitro* permeation through excised rat skin was carried out using modified Franz diffusion cell and the results showed that film (F6) containing HPMC and PEG 400 (1:1) with menthol as a permeation enhancer demonstrated the highest drug release (90.04%) at 24 hours ($p < 0.05$). In conclusion the developed captopril transdermal patches showed good *in-vitro* drug release. However, further *in-vivo* studies are required to explore these findings.

PPT7 (000099)

Effect of Polymer Concentration on Plasticity of Hot Air-Dried Guluronate- and Mannuronate-Rich Alginate Films

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The present study investigates the plasticity of hot air-dried guluronate-rich (MG) and mannuronate-rich (MC) alginate films prepared from 2 and 4 % (w/w) alginate solutions, which contained the same amount of polymer, keeping the content of solid polymer in all films at 0.4 g through hot-air drying at 60 ˚C for the use as transdermal drug delivery system. These films were subjected to thermomechanical, differential scanning calorimetry, fourier transform infrared, moisture content, viscosity and polymer molecular weight analysis. It was found that the film plasticity increased when diluted alginate solution and MC were employed in film preparation. This was due to a decrease in polymer-polymer interaction at high strength domains of the matrix involving C-H, O-H, C-O and/or C=O moiety of the alginate, attributing to plasticization effect of water and ease of molecular rearrangement of the MC.

PPT8 (000126)

People Perception towards Impact of Good Manufacturing Practice Implementation in Malaysia

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Improving the actual performance of the Pharmaceutical Good Manufacturing Practice (GMP) to ensure quality, safety and efficacy of medicines is an important task for health systems. Health policy makers have the responsibility for the care of the people whose perception plays a crucial role in the evaluation of health policies and systems. Therefore, this study was intended to assess the perception of the general public concerning the quality and affordability of Malaysian manufactured medicines. Questionnaires were designed following Likert scale method, validated and reliability test was conducted. As many as 600 questionnaires were distributed either personally, by post or email within three states in Malaysia through random sampling methodology. Out of which 550 were returned, 544 (90.6%) were usable. The age of the respondents was between 20 to 60 years. They were either educated or uneducated. The results were analysed using (SPSS) software version 16. The results indicate that the majority (65.1%) are satisfied with the quality of manufactured medicines in Malaysia. Further, 66% of the respondents are contented with the price. Some (45%) prefer the locally manufactured medicines than imported ones and only few (2.6%) have complained about it. However, there has been concern about the escalating prices and hence, the need for proper price regulation as ascertained by majority (88.9%). The study found that product brand name does not significantly influence acceptance of use although of the perception that medicine quality is directly proportional to the price. This study also suggests that the acceptability and use of generic medicines increase affordability in addition to the positive impact of GMP implementation in Malaysia on the medicine quality.