The 4th UKM-TU Joint Research Symposium on Pharmaceutical Sciences

2019

Thursday, April 25

Online Proceeding

Lecture Room No. 2003 and 2007, 2nd Floor,
Health Sciences Central Auditorium and Laboratory Building

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MESSAGE FROM THE RECTOR, THAMMASAT UNIVERSITY

Dear all participants, colleagues, ladies and gentlemen:

I am so delighted to preside over this opening ceremony of The 4th UKM-TU Joint Research Symposium on Pharmaceutical Sciences organized every year and alternatively hosted by the Faculty of Pharmacy, Thammasat University and the Faculty of Pharmacy, Universiti Kebangsaan Malaysia. This is one of the activities under academic collaboration between the two institutes.

This research symposium is indeed a productive event where the participants from both institutes as well as others can share research knowledge and experience in the recent advances in Pharmaceutical Sciences. This would definitely bring about the promising joint research projects and publications between the two institutes. According to the vision of Thammasat University, "Leadership through World-Class Education and Research", concentration on research is one of our main strategies to be implemented. In 2019, Thammasat University ranks in the third place in Thailand by QS World University Rankings. Moreover, I am glad to know that the Faculty of Pharmacy, which has been established for only 7 years, could have visibility in QS World University Rankings by subject of Pharmacy and Pharmacology in 2019. Such successes would certainly come from both strong research activities and international collaborations. The Faculty of Pharmacy, Universiti Kebangsaan Malaysia is one of the world's leading institutes which have a close relationship with the Faculty of Pharmacy, Thammasat University since its establishment in 2013.

I would like to thank all over colleagues, students, and organizing committee members for all their contribution to this symposium. Many thanks to all our colleagues from the Faculty of Pharmacy, Universiti Kebangsaan Malaysia and distinguished guests. I wish you all a great time and the success of this symposium as expected.

G. Wi"U .

Associate Professor Gasinee Witoonchart

MESSAGE FROM THE DEAN, FACULTY OF PHARMACY, THAMMASAT UNIVERSITY

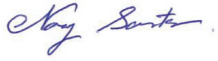
Dear all participants, colleagues, ladies and gentlemen:

On behalf of the Faculty of Pharmacy, Thammasat University, I would like to welcome all colleagues, graduate students, and participants from Universiti Kebangsaan Malaysia and others scientists for joining The 4th UKM-TU Joint Research Symposium on Pharmaceutical Sciences at Thammasat University. Particularly this year our Faculty of Pharmacy is almost reaching the 7 Anniversary on this coming April 30. The UKM-TU Joint Research Symposium on Pharmaceutical Sciences is one among many concrete activities of academic collaborations between TU and UKM since 2014.

For the past 7 years the Faculty has successfully accomplished in conducting researches such that the number of publications per faculty becomes the first rank among the Faculties in Health Science area of Thammasat University. This has recently resulted in the visibility in QS World Ranking Criteria by Subject of Pharmacy and Pharmacology at Thammasat University. Such issue brings about the pride and will power to all of our staff. I may say that such outcomes would be more or less the consequence of this platform in exchanging and sharing as well as encouraging our faculty of both institutes for their collaborative researches. This activity will not only pursue achievement in researches and publications, but also teaching and learning of Pharmacy Profession of both institutes as well. We have also successful exchanges of academic staff and Pharmacy students of two institutes for their clerkship trainings.

I would like to express my deep appreciation for the full support of research activities including this symposium from Thammasat University, and many thanks to the organizing committee. I do wish all of participants would enjoy and gain worthy knowledge and technology in Pharmaceutical Sciences from this symposium.

Best Regards,



Professor Dr. Narong Sarisuta

MESSAGE FROM THE DEAN, FACULTY OF PHARMACY, UNIVERSITI KEBANGSAAN MALAYSIA

Distinguished guests, delegates, fellow researchers and friends, greetings.

This year marks the 4th edition of the annual Thammasat University-Universiti Kebangsaan Malaysia Joint Research Symposium on Pharmaceutical Sciences. From the 1st edition held in 2016, I am extremely proud to see the symposium grows from strength to strength, showcasing the latest technologies and developments in pharmaceutical sciences from both our beloved institutions. It has indeed become a permanent fixture in the annual calendar of events for both TU and UKM, and a testament to the boundless commitment shown by members of both faculties.

In the ever expanding and borderless world of scientific exploration, the most important and significant discoveries are almost entirely built upon a strong foundation based on collaborations between many team of researchers working in tandem towards achieving the same goals. It is exactly this spirit of collaboration that we hope to instill by the gathering of minds; from researchers, scientists, to eager students, such as what we are witnessing by the organising of this event. Both our institutions have had the experience of working together for several years now, it is time to translate this into something tangible, and bring it into fruition in the form of joint research, supervision, grant applications and publications. I sincerely hope that we can continue discussing and exchange ideas, to strengthen the network we have built upon, and to forge new cooperation between those present today.

I would like to take this opportunity to congratulate and thank the organising committee, especially the Chairperson, Associate Professor Dr. Rathapon Asasutjarit and his team for a successful symposium. Our deepest appreciation also goes to the honorable Dean of the Faculty of Pharmacy, Thammasat University, Professor Dr. Narong Sarisuta, without whom all of these would not have materialised. On behalf of the Faculty of Pharmacy, UKM, I would like to thank Thammasat University, especially the Faculty of Pharmacy for the warm hospitality extended to our contingent. I wish all the delegates a fruitful symposium, and may this be the first step towards greater achievements in the future.

Best regards,

Associate Professor Dr. Jamia Azdina Jamal

MESSAGE FROM THE ORGANIZING CHAIRPERSON OF THE 4TH UKM-TU JOINT RESEARCH SYMPOSIUM ON PHARMACEUTICAL SCIENCES 2019

Dear all participants:

It is a pleasure to welcome you to the 4th UKM-TU Joint Research Symposium on Pharmaceutical Sciences, 2019 which is the second time organized by Faculty of Pharmacy, Thammasat University, Thailand.

In last 4 years, Faculty of Pharmacy, UKM, Malaysia and Faculty of Pharmacy, Thammasat University, Thailand have growing academic and research collaborations. We have exchange programmes for our academic staffs and researchers to gain experience in different work environment. This joint research symposium is one important part of our collaborations. It will enhance quality of our research and strengthen the collaboration between two faculties.

This joint research symposium is organized as a set of tracks in Pharmaceutics; Novel drug delivery systems; Drug discovery; Medicinal Chemistry; Natural products; Pharmacology; Pharmacokinetics; Clinical Pharmacy; Social Pharmacy; Pharmacy Administration and Pharmacy Study. We are honored to have Dr. Haliza Katas, Dr. Khairana Husain from Faculty of Pharmacy, UKM, Malaysia; Dr. Thanakorn Osotchan, Faculty of Science, Mahidol University, Thailand as our keynote speakers.

I would like to thank all researchers for the valuable works contributed to this symposium. I hope that all participants will take this great opportunity to interact with each other to share experience and make future collaboration on the subject of interests.

I would like to acknowledge our administrative staffs for their talents, dedication and time of many volunteers and strong support.

Hopefully, you will find the symposium both enjoyable and valuable.

Best Regards,

R. Asasutjarit

Associate Professor Rathapon Asasutjarit, Ph.D.

The 4th UKM-TU Joint Research Symposium on Pharmaceutical Sciences 2019 Program
Thursday 25 April 2019

TIME	ACTIVITY
OPENING CEREMONY: (Lecture Room No. 2007)	
08.00 - 08.45	Registration / Poster setup
08.45 - 09.30	**Welcoming Address** By Assoc. Prof. Dr. Rathapon Asasutjarit, Associate Dean for Research and Graduate Studies, Faculty of Pharmacy, Thammasat University Chairperson of the 4th UKM-TU Joint Research Symposium on Pharmaceutical Sciences
	Welcome Speech By - Prof. Dr. Narong Sarisuta, Dean, Faculty of Pharmacy, Thammasat University - Assoc. Prof. Dr. Jamia Azdina Jamal, Dean, Faculty of Pharmacy, Universiti Kebangsaan Malaysia
	Opening Remark By Assoc. Prof. Gasinee Witoonchart, Rector, Thammasat University
PLENARY SESSION : (Lecture Room No. 2007)	
09.30 - 10.15	**Plenary Lecture 1: Assoc. Prof. Dr. Haliza Katas, Faculty of Pharmacy, Universiti Kebangsaan Malaysia** *"Chitosan-based Multi-action Nanoparticles for Diabetic Wounds"*
10.15 - 11.00	**Plenary Lecture 2: Asst. Prof. Dr. Tanakorn Osotchan, Faculty of Science, Mahidol University** *"Applications of e-nose and e-tongue in pharmaceutical sciences"*
11.00 - 11.45	**Plenary Lecture 3: Assoc. Prof. Dr. Khairana Husain, Faculty of Pharmacy, Universiti Kebangsaan Malaysia** *"Chemical Constituents and the Anti-allergic activity of Selected Medicinal Plants in Malaysia"*
11.45 - 13.30	Lunch break / **Poster Session**

ORAL PRESENTATION BY INVITED SPEAKERS:		
TIME	**PHARMACEUTICS / NOVEL DRUG DELIVERY SYSTEMS / DRUG DISCOVERY / MEDICINAL CHEMISTRY / NATURAL PRODUCTS / PHARMACY PRACTICE** (Lecture Room No. 2007)	**PHARMACOLOGY / PHARMACOKINETICS / CLINICAL PHARMACY / SOCIAL PHARMACY / PHARMACY ADMINISTRATION / PHARMACY PRACTICE** (Lecture Room No. 2003)
13.30 - 13.45	**Special Lecture 1: Assoc. Prof. Dr. Endang Kumolosasi** (UKM) *"Silencing of Annexin A1 Induces Apoptosis Activity in Human Leukemic Cell Lines"*	**Special Lecture 1: Dr. Marhanis Salihah Omar** (UKM) *"Use of fall-increasing risk drugs in elderly"*
13.45 - 14.00	**Special Lecture 2: Assoc. Prof. Dr. Juriyati Jalil** (UKM) *"Phytochemical and biological studies of Cyathocalyx pruniferus (Annonaceae)"*	**Special Lecture 2: Dr. Farida Hanim Islahudin** (UKM) *"Plasmodium knowlesi management in Malaysia"*
14.00 - 14.15	**Special Lecture 3: Dr. Mazlina Mohd Said** (UKM) *"Rat foot pad analysis of standardized extract of Malaysian green tea (Camellia sinesis)"*	**Special Lecture 3: Dr. Noraida Mohd Shah** (UKM) *"Information support tool for Malaysian breast cancer patients on chemotherapy"*
14.15 - 14.30	**Special Lecture 4: Assoc. Prof. Dr. Ng Shiow Fern** (UKM) *"Pharmacy Students' Experience, Preference and Perceptions in Gaming and Game-Based Learning"*	**Special Lecture 4: Dr. Adliah Mhd Ali** (UKM) *"The Current Practice and Barriers on Value Added Services among Community Pharmacists"*
14.30 - 14.45	**Special Lecture 5: Assoc. Prof. Dr. Malina Jasamai** (UKM) *"Moringa oleifera extracts and their anti-hypertensive activities on rats"*	**Special Lecture 5: Dr. Ernieda Md. Hatah** (UKM) *"Factors that may influence medicine price setting in the private healthcare system in Malaysia"*
14.45 - 15.00	**Special Lecture 6: Dr. Shamin Mohd Saffian** (UKM) *"Methods for predicting warfarin dose requirements"*	**Special Lecture 6: Dr. Adyani Md Redzuan** (UKM) *"Complementary and Alternative Medicine (CAM) Usage Among Hypertensive Patients"*
15.00 - 15.15	Coffee Break (will be served in the lecture room no. 2007)	

ORAL PRESENTATION COMPETITION: (Lecture Room No. 2007)	
TIME	**PRESENTERS AND TITLE**
15.15 - 15.30	**Presenter 1: Nawarat Sooksai** *"Andrographolide-Loaded Nanoemulsion and Its Activity against Non-Melanoma Skin Cancer Cells"*
15.30 - 15.45	**Presenter 2: Kantsak Leerattanakul and Pheeraphong Adulheem** *"Optimization of production process of nanoemulsions containing alpha mangostin from mangosteen rinds by high pressure homogenization"*
15.45 - 16.00	**Presenter 3: Oranich Vera-Archakul and Chayaporn Sangamnarj** *"The Effect of Hydrophilic Polymers on Release Profiles of Metronidazole Films"*
16.00 - 16.15	**Presenter 4: Napasorn Ransibrahmanakul and Nontapat Sarovath** *"Determination of insecticidal activity and development of prototype product against American cockroach from Stemona collinsiae root extract"*
16.15 - 16.30	**Presenter 5: Pakawat Keetawattanakul and Nuntawan Loessaksrisakul** *"Factor Influencing Stroke Treatment Expenditure at Phramongkutklao Hospital"*
16.30 - 17.15	**Plenary Lecture 4: Asst. Prof. Dr. Kesinee Netsomboon, Faculty of Pharmacy, Thammasat University** **Good Research Award 2018, Faculty of Pharmacy, Thammasat University** *"Multifunctional adhesive polymers: Preactivated thiolated chitosan-EDTA conjugates"*
17.15 - 17.30	Awards Ceremony / Closing Ceremony

Note: 4.50 Credits of Continuing Pharmaceutical Education (CPE) for all pharmacists

PLENARY LECTURES' ABSTRACTS

Chitosan-based Multi-action Nanoparticles for Diabetic Wounds

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INTRODUCTION

Chitosan-based nanoparticles (CSNPs) have attracted great interests as versatile drug delivery vehicles due to their excellent properties including biocompatible and non-toxicity and biological effects such as anti-bacterial and anti-oxidant activities. CSNPs have also been extensively investigated as drug carriers for topical delivery. Thus, the ability of CSNPs to deliver active agents with different modes of actions were studied for the management of diabetic wounds. Curcumin (Cur) and Dicer-substrate small interfering RNA (DsiRNA) were used in this study due to anti-inflammatory and antioxidant activities of Cur and the ability of DsiRNA to inhibit expression of prostaglandin transporter (PGT) gene which resulted in vascularization and promotion of wound healing.

There has been also a remarkable surge in research to explore the antibacterial activity of CSNPs. Thus, the potential of CSNPs in combating bacterial infection has been explored by synthesizing derivatives with different azides and alkyne groups using click chemistry. Chitosan was also used as reducing and stabilizing agents in gold nanoparticles (AuNPs) production via green synthesis to enhance antibacterial potential of metal nanoparticles. Taken together, chitosan appears to be a useful biomaterial for the development of multi-action agent for diabetic wound treatment.

MATERIAL AND METHODS

Materials

Low molecular weight chitosan and Cur were obtained from Sigma-Aldrich. *Lignosus rhinocerotis* (Tiger milk mushroom) was a gift from Lignas Bio Synergy Plt.

Synthesis of chitosan derivatives

A series of chitosan derivatives was successfully synthesized by regioselective modification of chitosan via an azide-alkyne click reaction.

Preparation of Chitosan-based nanoparticles

Nanoparticles were fabricated by ionic gelation to form complexes of polyanionic penta-sodium tripolyphosphate (TPP) and cationic chitosan/derivatives.

Preparation of Cur/DsiRNA-loaded CSNPs

CSNPs were loaded with Cur and PGT DsiRNA during ionic gelation process and adsorption technique, respectively to produce multi-action formulation. The resultant nanoparticles were incorporated into Pluronic (PF-127) gel via cold method.

Preparation of Chitosan stabilized AuNPs

Chitosan was used as stabilizing agent in the biosynthesis of (AuNPs) using aqueous extracts of *Lignosus rhinocerotis* which later adsorbed with DsiRNA to provide antibacterial and wound healing effects.

Physicochemical characterization of chitosan-based nanoparticles

Particle size and zeta potential

Particle size and zeta potential of the nanoparticles were determined by dynamic light scattering (DLS) and electrophoresis technique, respectively (Zetasizer®, UK).

Drug loading and binding efficiencies

The amount of Cur and DsiRNA loaded in/onto CSNPs were determined by UV-spectrometer and the DsiRNA binding efficiency was determined by gel retardation assay.

Determination of biological effects of chitosan-based nanoparticles

In vitro antibacterial activity

The antibacterial activity of CSNPs and chitosan-stabilized AuNPs was determined by agar well diffusion and/or microdilution broth methods.

In vivo study

Wound healing efficacy of Cur/DsiRNA-loaded CSNPs was determined in diabetic induced female Albino Wistar rats using Streptozocin (Table 1). Animal study was approved by UKM Animal Ethics Committee (UKMAEC) (no. of approval FF/2017/HALIZA/29-MARCH/831-SEPT.-2017-DEC.-2017).

Table 1: Animal grouping classification

Group	Wound Treatment
Non-diabetic	
Group 1	Tegaderm only
Diabetic	
Group 2	Cur/DsiRNA CSNPs gel + Tegaderm
Group 3	Cur CSNPs gel + Tegaderm
Group 4	DsiRNA CSNPs gel +Tegaderm
Group 5	Blank CSNPs gel + Tegaderm
Group 6 (-ve)	Tegaderm
Group 7 (+ve)	Intrasite gel + Tegaderm

RESULTS AND DISCUSSION

Physical characteristics of chitosan-based nanoparticles

The particle size of CSNPs, Cur/DsiRNA loaded CSNPs and chitosan stabilized AuNPs were less than 500 nm. They were positively charged (>+30 mV) and able to load high percent of active agents.

Biological effects of chitosan-based nanoparticles

Antibacterial activity

Chitosan derivatives with triazole functionality and their nanoparticles showed significant enhancement in antibacterial activity in comparison to non-altered chitosan.

Chitosan-stabilized AuNPs displayed effective antibacterial activity against gram-negative (*Pseudomonas aeruginosa* and *Escherichia coli*) and gram-positive bacteria (*Staphylococcus aureus* and *Bacillus sp.*).

The present approach has provided numerous evidences that CSNPs destabilized and disrupted bacterial membrane leading to leakage of cellular components (Figure 1).

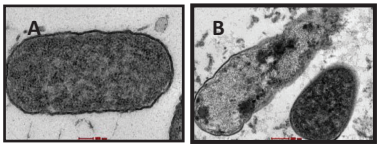

Figure 1: TEM images of bacteria that showing morphology of bacteria of (A) untreated and (B) treated *E. coli* with CSNPs

In vivo wound healing effects

Wound contraction for Cur/DsiRNA CSNPs treated group was faster than the vehicle and single ingredients groups as shown in Figure 2.

Semi-quantitative analysis of CD-31 positive endothelial cells revealed that the number of CD-31 was significantly higher on Day-3 for Cur/DsiRNA CSNPs treated group (Figure 3), indicating high angiogenesis than other groups.

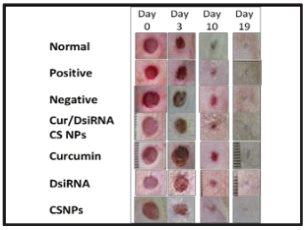

Figure 2: Representative photographs of wound contraction for different samples

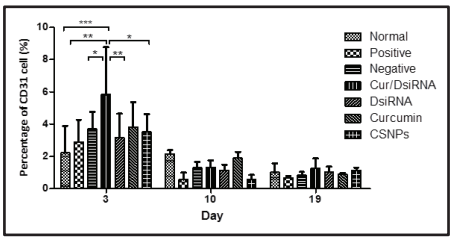

Figure 3: Semi-quantitative analysis of CD-31 positive endothelial cells for different samples, n = 3 (Right)

**p < 0.05, **p < 0.01 and ***p < 0.001 indicates significant difference when compared to other group(s) on the same day.*

CONCLUSION

These findings suggested that CSNPs efficiently deliver various active agents and exhibit antibacterial effect that would be a good candidate for nanomedicines in the future, particularly for treating diabetic wounds.

ACKNOWLEDGEMENT

This study was funded by Arus Perdana grant (AP-2017-008/3).

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Applications of e-nose and e-tongue in pharmaceutical sciences

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Electronic nose (e-nose) and electronic tongue (e-tongue) composed of non-specific gas and liquid sensor arrays sending electrical signals to processing unit for analyzing the group of data in order to classify the particular smell and taste, respectively. The e-nose and e-tongue try to mimic the human sensory systems however the knowledge on physical properties of smell and taste is still lack of full understanding and very depend on individual personal experience and the particular test condition. However, the analysis of these electronic data can be performed with non-supervision (statistics) or supervision (artificial intelligence) system. For medical application, e-nose has been applied to assist in diagnostic in some group of patients which can result in specially smell from their breath, sweat or urea. For pharmaceutical science, e-nose and especially e-tongue have offered an alternative approach for developing more pleasure drug in particular for chewable medicine. The bitterness is a crucial taste for drug development and the taste of quinine has been used for scaling the bitterness. The process of training e-tongue for marking the bitterness has been investigated in various situations including the suppression with sweetener.

Chemical Constituents and their Anti-allergic activity of Selected Medicinal Plants in Malaysia

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INTRODUCTION

Moringa oleifera and *Kopsia larutensis* is a well-known plant for its medicinal purpose such as antiinflammation, antioxidant, antimicrobial and anticancer but none has been reported on its anti-allergic properties. Allergic reaction cases increasing by years and the reactions can be mild as rashes and severe as anaphylaxis that can lead to death. Subsequent exposure of allergen will trigger mast cell degranulation which will release mediators that exhibit allergic symptoms such as bronchoconstriction, vasodilation and increased vascular permeability (Akdis & Agache, 2014). In this study, the anti-allergic activity of *M. oleifera* and *K. larutensis* and its isolated compounds will be evaluated using basophil cells in measuring the mast cell degranulation and its cytokines release upon early and late phase allergic reactions.

MATERIAL AND METHODS

Plant material

Plants material of *M. oleifera* and *K. larutesis* were obtained from Terengganu and Selangor, respectively. The specimen was deposited to the herbarium of Universiti Kebangsaan Malaysia (UKM), Bangi with voucher specimen number of UKMB40408 and UKMB5971**.**

Extraction and isolation

The dried samples of *M. oleifera* and *K. larutensis* were individually extracted by simple maceration method. Bioactive compounds for each plant were isolated from the active extracts using chromatographic techniques and the chemical structures were elucidated using various spectroscopic techniques such as ATR-FTIR, NMR and MS.

Preparation of RBL-2H3 cells for degranulation assessment

RBL-2H3 cells (JCRB, Japan) (2 x 10^5 / 400 µL) in enriched media (MEM containing 10% FBS and 1% penicillin-streptomycin) were seeded in 24 well plates. After two hours of incubation, the cells were sensitized with anti-DNP IgE (0.45 µg/mL, 100 µL) and incubated overnight until reaching 80% confluency.

Inhibitory effects on beta-hexosaminidase release

The protocol of the bioassay was conducted as reported (Shahari, Husain, Kumolosasi, & Rajab, 2017). The cells were washed twice with 500 µL Siraganian buffer (119mM NaCl, 5mM KCl, 5.6 mM glucose, 0.4 mM $MgCl_2$, 1mM $CaCl_2$, 25 mM piperazine-N, N'-bis (2-ethanesulfonic acid) (PIPES), 40 mM NaOH, 0.1% BSA, pH 7.2) and were reconstituted with 160 µL of Siraganian buffer. After 10 minutes of incubation, the cells were treated with 20 µL of test samples (7.81, 15.62, 31.25 µg/mL) and incubated for another 10 minutes before addition of 20 µL DNP-BSA (10mg/mL) allergen. After 30 minutes incubation, 50 µL of the supernatant was transferred to 96 well plate and added with substrate (1µM p-nitrophenyl-N-acetyl-β-D-glucosaminide in 0.1 M citrate buffer, pH 4.5) in 1:1 ration. The mixture was incubated for 1 hour and the reaction was stopped with addition of 200 µL stop solution (0.1M Na_2CO_3/ $NaHCO_3$, pH 10.0). The absorbance was measured at 405 nm using microplate reader. The percentage inhibition was measured using the equation below. (Test sample: (+) allergen, (+) test sample; control: (+) allergen, (-) test sample; normal: (-) allergen, (-) test sample; blank: (-) allergen, (+) test sample).

$$\text{Inhibition (\%)} = \left(1-\frac{\text{OD test sample - OD blank - OD normal}}{\text{OD control - OD normal}}\right) \times 100$$

Inhibitory effects on histamine

The protocol of the bioassays were conducted as reported (Itoh, Ohguchi, Iinuma, Nozawa, & Akao, 2008; Mastuda, Morikawa, Ueda, Managi, & Yoshikawa, 2002). The cells were washed twice with 500 µL enriched media and were reconstituted with 320 µL of enriched media. After 10 minutes of incubation, the cells were treated with 40 µL of test samples (7.81, 15.62, 31.25 µg/mL) before incubated for another 10 minutes. The cells were triggered with 40 µL DNP-BSA (10mg/mL) allergen. After 30 minutes of incubation, 50 µL of the supernatant was transferred to Histamine ELISA Kit (Elabscience, China).

Statistical analysis

The data obtained were reported as mean value ± standard error of mean (S.E.M) representing triplicate measurements. The IC_{50} values were measured with 95% confidence intervals and the significant of the data obtained were statistically analysed by Anova with p value < 0.05 using GraphPad Prism 5.

RESULTS AND DISCUSSION

M. oleifera and *K. larutensis* crude extracts and their isolated compounds were examined their anti-allergic activity upon early and late phase allergic reactions. Nine compounds were isolated from *M. oleifera* namely as (*E*)-2-hydroxyundec-7-en-3-one (**1**), 4-hydroxydodecan-5-one (**2**), 3,5,6-trihydroxy-2-(2,3,4,5,6-pentahydroxyphenyl)-4*H*-chromen-4-one (**3**), quercetin (**4**), kaempferol (**5**), β-sitosterol-3-*O*-glucoside (**6**), oleic acid (**7**), glucomoringin (**8**) and

stigmasterol (**9**). While only four indole alkaloids were isolated from *K. larutensis* identified as kopsilarutensinine (**10**), tetrahydroalstonine (**11**), (-)-eburnamine (**12**) and kopsinine (**13**).

Table 1: Table of IC_{50} and % inhibition of *M. oleifera* and *K. larutensis* values in inhibiting mediators release

IC_{50}	**β-hexosaminidase**	**Histamine**
M. oleifera leaves	7.17 ± 1.69**	11.66 ± 1.26
M. oleifera seed	10.68 ± 0.63	5.97 ± 0.84
M. oleifera pod	14.89 ± 1.25	7.43 ± 1.01
Compound (**1**)	15.24 ± 0.36	15.12 ± 2.53
Compound (**2**)	15.19 ± 2.92	16.28 ± 5.20
Compound (**3**)	6.20 ± 8.16	15.72 ± 0.74
Compound (**4**)	5.76 ± 2.17*	2.35 ± 8.42
Compound (**5**)	8.41 ± 1.79	13.44 ± 2.93
Compound (**6**)	14.38 ± 1.21	24.73 ± 7.29***
Compound (**7**)	15.18 ± 2.52	15.83 ± 10.48
Compound (**8**)	5.96 ± 0.87*	15.56 ± 10.64
Compound (**9**)	31.33 ± 1.92	15.80 ± 10.10
Ketotifen fumarate	15.86 ± 1.10	6.97 ± 0.00
Inhibition (%)	**β-hexosaminidase**	**Histamine**
K. larutensis barks	51.47 ± 5.8	48.12 ± 8.2 ***
K. larutensis leaves	51.99 ± 3.0	42.98 ± 8.5 ***
K. larutensis roots	50.94 ± 2.7	36.70 ± 5.2 ***
Compound (**10**)	56.78 ± 5.67	9.27 ± 0.01***
Compound (**11**)	60.59 ± 2.68*	23.92 ± 0.23**
Compound (**12**)	59.58 ± 4.11*	14.35 ±0.01***
Compound (**13**)	60.48 ± 6.62*	22.63 ± 0.05**
Ketotifen fumarate	41.80 1.0	45.22 10

Data are presented ± SEM (n=3) with significant value of *p<0.05, **p<0.01, ***p<0.001 compared to ketotifen fumarate

Allergic reactions were initiated by the binding of allergen on IgE-FcƐRI complex of mast cell that triggers degranulation. Mast cell degranulation releases mediators such as histamine, β-hexosaminidase, amines and proteases upon immediate response that lead to allergic reactions. In examining the anti-allergic properties of *M. oleifera* and *K. larutensis* and its isolated compounds, the concentration of β-hexosaminidase and histamine with and without the presence of the test samples were used as a marker of mast cell degranulation.

The results for the bioassays were tabulated in Table 1. In inhibiting the mast cell from degranulation, all three parts of *M. oleifera* inhibited the release of β-hexosaminidase and histamine with *M. oleifera* leaves (IC_{50}:7.17 ± 1.69 µg/mL) exhibited the higher significant activity compared to ketotifen fumarate (IC_{50} :15.86 ± 1.10 µg/mL). Similar to the activity of the crude extracts, all of the isolated compounds exhibited anti-allergic activity by stabilizing mast cell from degranulation with the flavonoids, compound (**3**) to (**5**) and a glucosinolate, compound (**8**) exhibited higher inhibition on the releases. The findings were similar with a study from Mastuda et al (2002) indicating that flavonoids exhibited anti-allergic properties. Among the isolated compounds, compound (**4**) and compound (**8**) exhibited higher significant activity than ketotifen fumarate in inhibiting β-hexosaminidase release by IC_{50} value of 5.76 ± 2.17 µg/mL and 5.96 ± 0.87 µg/mL respectively. In contrast, these two compounds exhibited similar activity with ketotifen fumarate in inhibiting histamine release.

While all the crude alkaloids from *K. larutensis* demonstrated inhibition of β-hexosaminidase release. Interestingly inhibitory activity of all sample from *K. larutensis* was higher than ketotifen fumarate (41.8 ± 1.0 %). Whereas *K. larutensis* leaves (52.0 ± 3.0 %) showed the most potent inhibitory activity. The crude alkaloids extract of stem-bark (48.1 ± 8.2 %) also showed optimal inhibition effect on histamine release as compared to others significantly. Besides that, all indole alkaloids isolated from *K. larutensis* still show significantly higher inhibition percentage than positive control. These results proved that among tested indole alkaloid compounds, compound (**11**) 60.6 ± 2.7%) possesses high potential to inhibit the degranulation process of mast cells. While all four indole alkaloid compounds tested showed lower histamine release inhibition percentage as compared to positive control significantly.

CONCLUSION

The study concludes that *M. oleifera* and *K. larutensis* has potential as anti-allergic drug with some of its isolated compounds as potential lead for the development of anti-allergic drug.

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Multifunctional adhesive polymers: Preactivated thiolated chitosan-EDTA conjugates

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AIM: The aim of this study was to synthesis preactivated thiolated chitosan-EDTA (Ch-EDTA-cys-2MNA) conjugates exhibiting in particular high mucoadhesive, cohesive and chelating properties.

METHODS: Thiol groups were coupled with chitosan by carbodiimide reaction and further preactivated by attachment with 2-mercaptonicotinic acid (2MNA) via disulfide bond formation. Determinations of primary amino and sulfhydryl groups were performed by TNBS and Ellman's tests, respectively. Cytotoxicity was screened by resazurin assay in Caco-2 cells. Mucoadhesive properties and bivalent cation binding capacity with Mg^{2+} and Ca^{2+} in comparison to chitosan-EDTA (Ch-EDTA) and thiolated Ch-EDTA (Ch-EDTA-cys) were evaluated.

RESULTS: Determination of 2MNA and total sulfhydryl groups indicated that 80% of thiol groups were preactivated. The results from cytotoxicity studies demonstrated that Ch-EDTA-cys and Ch-EDTA-cys-2MNA were not toxic to the cells at the polymer test concentration of 0.25% (w/v) while cell viability decreased by increasing the concentration of Ch-EDTA. Although EDTA molecule was modified by thiolation and preactivation, approximately 50% of chelating properties of the conjugates were maintained compared to Ch-EDTA. Ch-EDTA-cys-2MNA adhered on freshly excised porcine intestinal mucosa up to 6h while Ch-EDTA adhered for just 1h.

CONCLUSION: According to the combination of mucoadhesive and chelating properties of the conjugates synthesized in this study, Ch-EDTA-cys-2MNA might be useful for various mucosal drug delivery systems.

Keywords: Chelation; Cytotoxicity; Mucoadhesive properties; Mucosal drug delivery; Preactivation; Thiolation

INVITED SPEAKERS' ABSTRACTS

Silencing of Annexin A1 Induces Apoptosis Activity in Human Leukemic Cell Lines

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INTRODUCTION

Annexin A1, an endogenous glucocorticoid-regulated protein that was first discovered involves in inflammatory process. It has two domains, C-terminal domain for Ca^{2+} and membrane binding sites, N-terminal domain for proteolysis and phosphorylation that involves a broad range of biological processes in various cancer cells. ANXA1 activates a cascade of signaling pathways through association with formyl peptide receptors (FPRs). Solito et al., reported that treatment with exogenous ANXA1 on human neutrophils stimulated apoptosis [1]. Previous study showed the overexpression of ANXA1 induces apoptosis with caspase-3 activation in macrophages and bronchoalveolar cells [2-3]. Two major apoptosis pathway involves are extrinsic (through death ligand receptor) and intrinsic pathways (involve mitochondria) and both pathways involve the activation of caspases. The present study aims to explore the role of ANXA1 on apoptosis activity by transfection of small interfering RNA (siRNA) ANXA1 into leukemic cells using transfection reagent.

MATERIAL AND METHODS

Materials

The human leukemic U937, Jurkat and K562 cells (obtained from American Type Culture Collection, Manassas, VA, USA); RPMI 1640 medium, Iscove's Modified Dulbecco's medium (IMDM) supplemented with 2 mM L-glutamine, 10% heat-inactivated fetal bovine serum (FBS), 1% of 100 U/mL penicillin and 0.1 mg/ml streptomycin at 37℃ in 5% CO_2, 95% air humidified atmosphere.

Transfection with small interfering RNA (siRNA) of ANXA1

The leukemic cell lines were seeded at the density of $1.5x10^5$ cell/ml in a 6-well plate for 72 h. Jurkat, U937 and K562 was transiently transfected with ANXA1 siRNA 40nM, 80nM and 100nM respectively using INTERFERin transfection reagent (Polyplus-transfection Inc., New York, NY) according to manufacturer's protocol. Both transfection processes were done in serum and antibiotics free media. Cells incubated for 24h with FITC conjugated fluorescent oligonucleotide (Block-it, Invitrogen) were analyzed using fluorescence microscope to evaluate transfection efficiency.

Apoptosis assay

To assess the effect of knockdown ANXA1 on apoptosis rate, the Annexin V/propidium iodide (PI) staining was used. After 72h of transfection, cells were harvested and washed twice with cold PBS. The cell pellets were resuspended in 10µl of PI and FITC-labeled Annexin V solution for 10 min in room temperature and then the percentage of viable, apoptosis and necrosis cells was assessed using flow cytometer.

Western blotting

Protein expression level of ANXA1 after siRNA transfection, caspase-3, caspase-9, caspase-1, Bcl-2 and β-actin were examined using Western blot analysis. Cells were lysed with RIPA lysis buffer (MERCK) and total protein content was quantified using Bradford protein assay (Bio-Rad). Briefly, 20 µg of total protein were loaded onto 10% acrylamide gel and separated by SDS-PAGE. The separated proteins were then electrotransferred to PVDF membrane (MERCK). The membranes were blocked with 5% nonfat milk in TBST for 1h at room temperature and probed overnight with monoclonal antibodies against caspase-3, caspase-9, caspase-1, bcl-2 and β-actin (1:1000) from Cell Signaling Technology (Danvers, MA, USA). Proteins were visualized using the enhanced chemiluminescence (ECL) detection system (Amersham Biosciences, New Jersey) after 1 h incubation with secondary antibody HRP-conjugated anti-rabbit (1:5000) obtained from Cell Signaling Technology (Danvers, MA, USA). Band intensities were quantified using ChemiDoc MP System with Image Lab Software (Bio-Rad).

RESULTS AND DISCUSSION

Silencing of ANXA1 expression using siRNA

In this study ANXA1 expression was successfully knockdown in U937, Jurkat and K562 cells. Figure 1 showed that after 72h of transfection, the expression of ANXA1 protein was significantly decreased in all transfected cell lines compared to non-transfected cells. Different concentrations of ANXA1 siRNA with 40nM, 80nM and 100nM were used to knockdown ANXA1 expression in Jurkat (70%), U937 (63%) and K562 (69%) cells respectively using optimized transfection protocol.

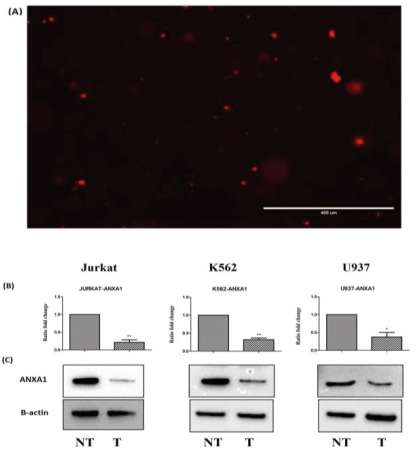

Figure 1: (A) The transfected cells were observed under fluorescence microscope (100xmag.). (B) Western blotting analysis showed ANXA1 protein expression was downregulated in transfected cell (T) compared to non-transfected cell (NT). (C) Quantification of ANXA1 protein expression (*p<0.05, **p<0.01). Data was presented in mean ± SEM in triplicate.

Previous study reported that ANXA1 is overexpressed in leukemia cells (Jurkat, K562 and U937) compared to peripheral blood mononuclear cell (PBMC) [4]. This finding indicated that knockdown of ANXA1 protein caused disruption in normal condition of leukemic cells and eventually might caused cell death.

Silencing of ANXA1 with siRNA induces apoptosis and necrosis

Figure 2 showed that the percentage of apoptosis was significantly increased in the transfected Jurkat (8.07 ± 0.79%), K562 (17.33 ± 1.95%) cells with p<0.05 for both cell lines and U937 (7.60 ± 1.41%) cells with p<0.01 as compared to its non-transfected cells. ANXA1 knockdown significantly increased (p<0.05) the percentage of necrotic cells in K562 (9.63 ± 0.97%) cells.

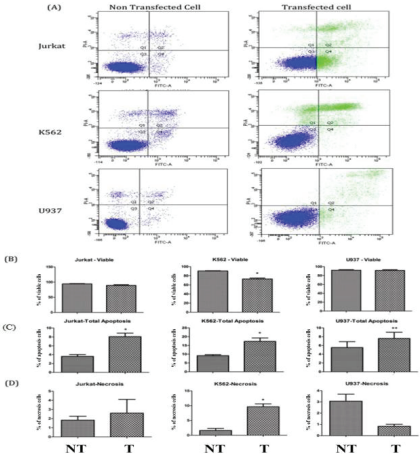

Figure 2: (A) A dot plot of the percentage of cell distribution after ANXA1 knockdown. Q1: Necrotic cells, Q2: Late apoptotic cells, Q3: Viable cells, Q4: Early apoptotic cells. (B) The effects of ANXA1 knockdown on cell viability, (C) apoptosis and (D) necrosis in Jurkat, K562 and U937 cells. T: transfected cells, NT: non-transfected cells. The value expressed as mean ±standard error mean (SEM); n=3, * (p<0.05), ** (p<0.01) compared with non-transfected cells.

Mechanism of apoptosis in non-transfected and transfected cells

Knockdown of ANXA1 significantly induced cell death and showed increased of procaspase-3 and procaspase-9 expression. transfected cells cause the initiator caspase, caspase-9 expression increased in U937 but decreased in K562 cells. Meanwhile, the effector caspase, procaspase-3 expression increased in Jurkat and decreased in U937 cells. However, no cleavage of caspases was observed. Bcl-2 expression showed upregulation in U937 but downregulated in Jurkat and K562 cells. Caspase-1, enzyme that involves in activation of pro-inflammatory cytokine, showed increased in expression after ANXA1 knockdown. Apoptosis is a process that regulated by certain caspases family and B-cell lymphoma 2 (Bcl-2) family [5].

CONCLUSION

In a conclusion, ANXA1 knockdown has the potential approach in treatment strategy of leukemia due to the ability of ANXA1 knockdown induces apoptosis in cancer cells. This unique characteristic of ANXA1 knockdown in inducing apoptosis through different mechanism for each cell line indeed convincing that this protein exhibits different effect based on cell-type behavior. These findings can contribute to further understanding of ANXA1 role in human leukemic cell lines.

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Phytochemical and biological studies of *Cyathocalyx pruniferus* (Annonaceae)

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INTRODUCTION

Cyathocalyx pruniferus belongs to the plant family Annonaceae, is a large monopodial tree which can grow up to 20-30 m depending upon its natural habitat. The *Cyathocalyx* species have been used in traditional medicine for treating wound healing and rheumatism (1). This study was carried out to isolate and identify the chemical constituents present in the leaves of *C. pruniferus* using chromatographic and spectroscopic techniques, as well as to determine their inhibitory effects on prostaglandin E_2 (PGE_2) production using radioimmunoassay (RIA). PGE_2 is a metabolite of arachidonic acid through the cyclooxygenase-2 (COX-2) pathway, which involved in inflammation.

MATERIAL AND METHODS

General

Liquid scintillation analyser (Tri-Carb 3110 TR Perkin Elmer, Waltham, MA, USA), mass spectrometer (HRESI-MS, Bruker MicroTOF-Q, Billerica, MA, USA), Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) Ion Trap Agilent Technologie 1200 series spectrometer (Santa Clara, California, USA), ^{1}H-NMR (600 MHz) and ^{13}C-NMR (150 MHz) spectrometer (Bruker Advance NMR, Billerica, MA, USA).

Plant materials

The leaves of *C. pruniferus* were collected from the Universiti Kebangsaan Malaysia (UKM) Bangi Forest Reserve, Selangor, Malaysia in December 2015. The voucher specimens (UKMB40412) was deposited at the Herbarium of the Faculty of Science and Technology, Universiti Kebangsaan Malaysia (UKM).

Extraction, isolation and structure elucidation of bioactive compounds

The dried and ground leaves of *C. pruniferus* (1.2 kg) were extracted with methanol using maceration technique (3 x 8L, 72 hours each). The extract was concentrated under reduced pressure using rotatory evaporator to yield crude methanol extract. The extract was further partitioned successively with hexane, ethyl acetate and acetone to give hexane (9.8 g), ethyl acetate (2.4 g) and acetone (37.7 g) fractions, respectively. Ten compounds were isolated from these fractions using various chromatographic techniques i.e. vacuum liquid chromatography, column chromatography, preparative thin layer chromatography. The structures of the compounds were elucidated using spectroscopic techniques (MS, 1D and 2D-NMR).

Preparation of sample for assay

Each sample (1 mg) was dissolves in 1 mL dimethyl sulfoxide (DMSO) and ethanol (1:1). DMSO and ethanol (1:1) was used as a negative control and indomethacin, a known cyclooxygenase inhibitor was used as a positive control.

Preparation of plasma from human blood

Blood (30 mL) was drawn from antecubital vein of healthy volunteer into polypropylene tube containing 10% (v/v) of 2% EDTA. The procedure was under approval of the Research Ethics Committee of the Universiti Kebangsaan Malaysia (NF-052-15). The blood (1 mL) was incubated at room temperature for 24 hours with 10 µL of compound and 10 µL of LPS. After incubation, the blood was centrifuged at 2600 x g for 15 min at 4ºC to separate plasma from the whole blood.

Radioimmunoassay for PGE_2

The radioimmunoassay was carried out according to the modified method as described previously (2) to determine the PGE_2 level in plasma after incubated with the compounds. The reaction mixtures consisting of 100 µL of plasma from sample or control solution, 100 µL of anti-PGE_2 and 100 µL of [^{3}H]-PGE_2 were incubated at 4ºC for 24 hours. The final concentration of sample in the reaction mixture was 10 µg/mL. After incubation, the mixtures were added with 200 µL of dextran charcoal and were incubated again for 10 min. After centrifuged at 3000 x g for 15 min at 4ºC, 3 mL of liquid scintillation cocktail was added to 300 µL of supernatant. The radioactivity was measured by liquid scintillation counter. The concentration of PGE_2 in each sample was determined by interpolation from the respective standard curve. Percentage inhibition of each sample was obtained by the following equation:

$$\% \text{ Inhibition} = \left\{ 1 - \frac{[\text{PGE}_2] \text{ in sample}}{[\text{PGE}_2] \text{ in control}} \right\} \times 100$$

Statistical analysis

All the experiments were performed in triplicates (n = 3) and data were expressed as means ± SD. The statistical

differences of values were determined by one-way ANOVA followed by Dunnett's post hoc test. $P<0.05$ was considered to be significant as compared to control. All analysis were performed using GraphPad Prism version 5.00.

RESULTS AND DISCUSSION

The crude methanol extract of *Cyathocalyx pruniferus* leaves was partitioned successively with hexane, ethyl acetate and acetone to give hexane (9.81 g), ethyl acetate (2.44 g) and acetone (37.67 g) fractions, respectively. The hexane fraction was further fractionated using vacuum liquid chromatography (VLC) on silica gel H and yielded several fractions. Fractions with same TLC profile were combined to give nine fractions. Further purification steps of the fractions were done using silica gel 60 or Sephadex LH-20 column chromatography (CC). Repeated CC of these fractions yielded four compounds. Meanwhile, six compounds were obtained from the acetone fraction. Structure elucidation of these compounds was carried out using spectroscopic techniques (MS, 1D and 2D-NMR). The compounds were identified as epicatechin (**1**), quercetin (**2**), chrysin (**3**), cyclopropane azulene (**4**), spathulenol (**5**), polycarpol (**6**), koetjapic acid (**7**), octaprenyl 1,4 hydroquinone (**8**), α-tocopherol (**9**) and β-sitosterol (**10**).

The compounds were then evaluated for their inhibitory activity on PGE_2 production in human blood induced by lipopolysaccharide (LPS) at concentration of 10 µg/mL (Table 1). Among the ten compounds, koetjapic acid (**7**) exhibited the highest inhibition of 78.13% with IC_{50} of 12.91 µM, followed by octaprenyl 1,4-hydroquinone (**8**) and quercetin (**2**) with IC_{50} of 12.67 and 13.89 µM, respectively. Meanwhile, the lowest inhibitory effect was showed by cyclopropane azulene (**4**) with 39.34% inhibition. The assay was determined based on indomethacin (positive control) having IC_{50} of 10.45 µM.

The results are consistent with the previous study conducted on LPS-induced human blood, where koetjapic acid (**7**) has shown significant PGE_2 inhibition with an IC_{50} value comparable to the control (3). Meanwhile, the derivatives of octaprenyl-1,4-hydroquinone (**8**) have shown significant PGE_2 and TNF-α inhibition in LPS-stimulated J774 cell (4), which is in agreement with our present study.

CONCLUSION

The results indicate that koetjapic acid (**7**), octaprenyl 1,4-hydroquinone (**8**) and quercetin (**2**) possess promising potent anti-inflammatory properties. Further studies are necessary to elucidate the mechanisms behind their anti-inflammatory effects.

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Table 1. Percentage inhibition and IC_{50} values of the isolated compounds of *C. pruniferus* in LPS-induced human whole blood.

Compound	Percentage inhibition (%) 10 µg/mL	IC_{50} (µM)
Epicatechin **(1)**	72.01 ± 1.90	14.43 ± 1.47**
Quercetin **(2)**	74.57 ± 0.71	13.89 ± 0.74***
Chrysin **(3)**	70.01 ± 0.59	14.33 ± 0.34**
Cyclopropane azulene **(4)**	39.34 ± 1.09	nd
Spathulenol **(5)**	71.01 ± 0.56	15.78 ± 1.89**
Polycarpol **(6)**	73.30 ± 2.22	17.01 ± 1.89*
Koetjapic acid **(7)**	78.13 ± 1.21	12.91 ± 0.81***
octaprenyl 1,4-hydroquinone **(8)**	77.45± 1.06	12.67 ± 1.48***
α-tocopherol **(9)**	47.09 ± 1.89	nd
β-sitosterol **(10)**	39.61 ± 3.01	nd
Indomethacin (Positive control)	88.91 ± 0.87	10.45 ± 1.01

Values are presented as mean ± SD (n = 3); *p<0.05, **p<0.01, ***p<0.001 as compared with control; nd = not determined

Rat foot pad analysis of standardized extract of Malaysian green tea (*Camellia sinesis*)

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INTRODUCTION

Sweating after a workout, playing sports, or in sauna, is an acceptable form of promoting well-being and social interaction. However, excessing sweating in normal life activities, is reflecting poor hygiene that leads to embarrassment and social barrier, especially when it is associated with foul odor. Hyperhidrosis is a skin disorder characterized by excessive sweating, which is affecting at least 3% of the population. Patients suffering from hyperhidrosis require continuous maintenance throughout life which leads to decreasing quality of life. Deodorants and antiperspirants make up one of the largest segments in the health and beauty industry with estimated sales volume of about US$18.9 billion in 2016. However, association of this class of products with cancer and Alzheimer`s disease increases the need to search for natural antiperspirant from natural resources. In this work, standardized Malaysian green teas (*Camellia sinesis*) will be screened for its antiperspirant activity using modified rat foot pad and antimicrobial assay.

MATERIAL AND METHODS

Preparation of Extract

C. sinensis leaves were obtained from two locations; Bharat Tea Plantations Sdn. Bhd. in Cameron Highlands (CH) and BOH Tea Plantation in Ladang Bukit Cheeding, (S). The powdered leaves were extracted using 80% ethanol as the solvent with a ratio 10ml: 1g. The mixture was then subjected to constant stirring under water bath of 60^{o}C for two hours. The mixture was then vacuum filtered using Whatman Filter Paper no. 1. The 80% ethanolic solvent was then evaporated using rotatory evaporator on a water bath 40^{o}C.

Standardization *C.sinensis* leaves' extract

Pharmacognostic evaluation through organoleptic and macroscopic examinations were performed as a preliminary identification of the plant. Chemical identification including colour test and heavy metal limit were determined. Physico chemical properties (ash content, loss on drying and extractive values) were identified. Fingerprint chromatographic analysis including thin-layer chromatography (TLC) and spectroscopic analysis using Fourier-transform infrared spectroscopy (FTIR) were also performed. The quantitation of catechin was also determined using Ultra-Violet (UV) spectrophotometry assay

Antiperspirant animal model.

30 male Sprague-Dawley rats weighing 200-250 g were used in this study.

Toxicity study

A 14 days in vivo toxicity test was done where the rats were injected subcutaneously on their foot pad on first day and observed for the subsequent 13 days to note for any toxic reaction.

Rat foot pad model

The rats were randomly divided into three groups (n=6) where each group representing 50 mg/kg, 100 mg/kg and 150 mg/kg dose of *C. sinensis* extract, respectively, with 25% AlCl as positive control and WFI as negative control. The antiperspirant efficacy of the *C. sinensis* extract was determined by the number of dark spots stains that appeared after sweat stimulation via heat stress (starch -iodine test). All the rats were injected on the first day for the first cycle and fifth day for the second cycle. Starch-iodine test was performed on the first, second, fifth and sixth day.

RESULTS AND DISCUSSION

The tea leaves from both locations showed consistent macroscopic characteristic as well as chemical identification. Ethanolic extraction of both Cameron Highlands and Selangor tea leaves yielded 17.98% and 19.23% respectively. TLC fingerprint for both tea leaves extract showed consistency and was compared with standard, catechin. FTIR analysis for both tea leaves extract revealed the functional groups of O-H, C=O, C=C, C-H and C-O. UV spectrophotometry quantified the efficiency of CH and S extract which are 53.5% and 53.25% respectively.

Antiperspirant analysis

There was no sign of toxicity observed in any of the rats and thus, the extract was deemed to be safe. The starch-iodine

purple spots appeared only after the heat stress, and were carefully quantified with the aid of a magnifying glass. Figure 1 showed that the antiperspirant effect of *C.sinesis* increased with higher extract concentration post rat food pad injection while there were no significant differences in number of spots between the three dose groups of *C. sinensis* after topical application.

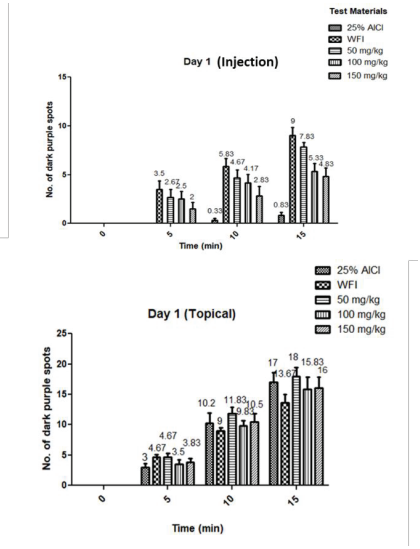

Figure 1. Number of dark spots that appeared on Day 1 post footpad injection (upper) and topical application (bottom)

CONCLUSION

Standardized *C. sinensis* extract has a potential in inhibiting sweating. The antiperspirant activity was better observed when injected subcutaneously on the foot pad compared to topical application. A dosage up to 150 mg/kg showed no acute toxicity effect in rats.

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Pharmacy Students' Experience, Preference and Perceptions in Gaming and Game-Based Learning

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INTRODUCTION

Due to the shift towards experiential and interactive learning, technology has been assimilated in higher education. Pharmacy students nowadays are technologically savvy and they prefer highly interactive and experiential learning offered by digital technologies. Using serious games (SG) in pharmacy education is a promising approach that fits well with the learning styles of these students. Due to limited studies regarding serious games in pharmacy education, this study was conducted to investigate pharmacy students' experience, preference and perceptions in gaming and game-based learning (GBL).

METHODS

Study Design and Population

A cross-sectional survey study was conducted from August 2018 to November 2018 among pharmacy students. Self-administered survey questionnaires were distributed face-to-face. Participants were given an information sheet to read, and their written consent was obtained prior to administration of survey questionnaires. The study population was pharmacy students from six universities in Malaysia (Table 1). The ethics approval to conduct this study was obtained from the UKM Research Ethics Committee with the reference number of JEP-2018-382. Ethics approval from each universities were also obtained prior to study.

Inclusion & Exclusion Criteria

The inclusion criteria of the participants were Malaysians and pharmacy students from Year 1 to Year 4 of study at the aforementioned universities. The exclusion criteria of the participants were pharmacy students that were not willing to give their consent to participate in the study.

Pilot Study

A pilot study was conducted and the questionnaire was pre-tested on 20 pharmacy students. The pilot study was conducted to test the validity and reliability of the questionnaire and also to estimate time for the completion of the questionnaire. The Cronbach's alpha reliability coefficient test obtained was 0.890.

Sampling Method

Stratified sampling was used as the probability sampling technique. With stratified sampling, the researcher divided the population of pharmacy students into separate subgroups according to their respective universities. The sample was taken randomly from each subgroup.

Sample Size

Krejcie and Morgan formula was used to calculate sample size. Total average pharmacy students population in UKM, UM, UiTM, Taylor's University, UCSI university and CUCMS = 2271. Therefore, from the equation, sample size was 328.

Table 1. Study population and sample size obtained

Name of University	Sample Size
Universiti Kebangsaan Malaysia (UKM)	43
Universiti Malaya (UM)	26
Universiti Teknologi MARA (UiTM)	105
UCSI University	58
Taylor's University	22
Cyberjaya University College of Medical Sciences (CUCMS)	79
Total	328

Data Collection Tool

The questionnaire was divided into three sections, namely Section A, B and C. Section A consisted of demographic information of the respondents. Section B investigated the experience and habits of pharmacy students in gaming and gamification. Section C was further divided into two parts. Section C (i) consisted of statements regarding the perceptions of game-based learning in pharmacy students. Section C (ii) consisted of questions regarding the preferences of gamification aspects among pharmacy students regarding game genre, game style and game reward system.

All the data analysis was performed using the Statistical Package for Social Sciences (SPSS) Version 23. The data about demographic information, experience, preference and perceptions of students were illustrated by using descriptive statistics. Inferential statistics were used to analyse the relationship between demographic characteristics and experience with perceptions of pharmacy students about

game-based learning. Normality of the subscales under perceptions, which were learning opportunities and preferences, were checked using Kolmogorov-Smirnov Test. Mann-Whitney and Kruskal-Wallis tests were used to analyse the difference in the score of the perceptions of pharmacy students about game-based learning based on different categorical groups. Bonferroni post hoc procedure was applied if significant differences were found using Kruskal-Wallis test. Spearman's correlation test was used to analyse the relationship between continuous variables and the score of the perceptions. Statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSION

Users Smartphone Background information

Out of 328 pharmacy students participated in this study, almost all of them possessed smartphone (n=326, 99.4%). Android (n=217, 66.2%) was the most common type of mobile operating system, followed by iOS (n=106, 32.3%).

Gaming Experience among Pharmacy Students

Majority (n=276, 84.1%) of the pharmacy students experienced in playing video games with at least 1 year of experience. Among these students, over a quarter of them (n=97, 35.1%) had more than 9 years of experience in playing video games. Most of them (n=249, 90.3%) played less than 3 hours for each gaming session. The pharmacy students had more experience in gaming with at least 3 years of experience, however they spent less time for each gaming session, which was less than 1 hour for each gaming session (n=129, 46.7%).

Gaming Preference and Habits

In terms of gaming platform, pharmacy students usually played video games using mobile phone (n=231, 70%). The top reasons for playing video games among pharmacy students were to relieve boredom (n=224, 68.3%) and to relieve stress (n=182, 55.5%). Game genres that were popular among pharmacy students were adventure games (n=139, 42.4%), action games (n=138, 42.1%) and strategy games (n=133, 40.5%).

Pharmacy Students' Experience in Playing SG

Majority of the students (n=252, 76.8%) have never played SG before. Only 76 (23.2%) out of 328 of the students reported playing SG before.

Perceptions of Pharmacy Students regarding GBL

More the 50% of the pharmacy students agreed or strongly agreed that playing pharmacy-related GBL will motivate them in learning (67.4%), allow to experiment with knowledge (79.7%) and offer opportunity to take control over learning process (52.5%). 70.2% of respondents also agreed or strongly agreed that pharmacy related SG will allow them to think critically.

Preferences of Gamification Aspects in Pharmacy-Related SG among Pharmacy Students

Both role playing and strategy showed the highest percentage of 53% (n=174), followed by simulation (n=159, 48.5%) and puzzle (n=148, 45.1%). The most popular game reward systems for pharmacy-related SG was score (n=204, 62.6%). Majority of the students (n=279, 85.1%) did not prefer advertisement while playing pharmacy-related SG. Also, majority of the pharmacy students (n=250, 76.5%) were also unlikely to spend money to achieve the highest ranking in pharmacy-related SG. Over half of the pharmacy students (n=175, 53.4%) would like to share their high scores after SG ends. Over three quarters of the pharmacy students (n=292, 89.3%) would like to see the results of the assessment after playing pharmacy-related SG.

CONCLUSION

In conclusion, pharmacy students showed positive perceptions regarding the implementation of GBL. Pharmacy students played video games intermittently for short duration for each gaming session to seek entertainment and escape from stress for a temporary period. Preference for serious games is strategy and role playing game. This study drives the need to develop a pharmacy-based GBL for the integration of pharmacy knowledge and real-world application for pharmacy education.

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Moringa oleifera extracts and their anti-hypertensive activities on rats

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INTRODUCTION

Moringa oleifera is high in nutritional values and most of the plant parts have been used traditionally in the Southeast Asia for various ailments including as cardiac circulatory tonic and diuretic (1,2). Although the anti-hypertensive activities of *M. oleifera* have been reported previously (3), the mechanism of action on how the blood lowering effect is achieved has not been fully explored and little is known about the effect of these plant parts on non-hypertensive individuals. In this work, hypotensive effect of different *M. oleifera* ethanolic and aqueous extracts were evaluated on spontaneously hypertensive (SHR) and normotensive (NT) rats. Diuretic and angiotensin converting enzyme (ACE) activities of these extracts were also investigated.

MATERIAL AND METHODS

Materials

SHRs were purchased from the Animal Unit, University Malaya and Sprague Dawley rats were purchased from the Animal Unit, Universiti Kebangsaan Malaysia. Positive controls for the *in vivo* study were clinically used drugs (perindopril 5 mg, Coversyl®, Servier; ibersatan 150 mg, Aprovel®, Sanofi Aventis; hydrochlorothiazide 12.5 mg, Hydrochlorothiazide®, Royce Pharma).

Preparation of plant parts

M. oleifera plant parts (leaves, twigs, stems, roots, pods and seeds) were obtained from a farm in Kuala Trengganu. They were authenticated and deposited in the UKM Herbarium with a voucher specimen of HF-133. The plant parts were cut into small pieces, dried, ground and stored at room temperature (29ºC) until further use. Water extraction was carried out by boiling the plant materials (0.1 kg) in distilled water (0.15 L) for 6 hr (4) while ethanol extraction was carried out by maceration process. Tragacanth suspension was prepared by dissolving 3 g tragacanth powder in 300 mL distilled water prior to the preparation of test samples and controls. Next, plant part extracts (4.9 g), perindopril [positive control (PC1)] (9.8 mg), ibersatan [positive control (PC2)] (98 mg) and hydrochlorothiazide [positive control (PC)] (29.4 mg) were dissolved in 35 mL of 1% tragacanth prior to be fed to rats.

Determination of systolic and diastolic BP

Blood pressure (BP) lowering effects of *M. oleifera* plant part extracts were investigated using 60 male adult SHRs weighing between 200-300 g. They were randomly divided into 12 groups with 5 rats in each group. Each group of rats were fed with controls and plant part extracts. Five NT rats were also used in this study. Systolic and diastolic BP were measured prior to the administration of extracts and controls on day 1 and on day 15 post treatments.

Evaluation of the diuretic activity

Diuretic activity was determined on day 14 of the study. Rats were deprived of food but not water for 18 hr prior to urine collection. Groups receiving extracts and negative control were fed as usual and a group receiving positive control was fed with hydrochlorothiazide. After the administration of extracts and controls, rats were placed individually in metabolic cages and cumulative urine output was determined at hourly intervals for 5 hr.

ACE inhibition assay

ACE inhibitory activity of extracts was determined using a method described by Agboola et al. (5) with some modifications. Briefly, 80 µL aliquot of positive control and extracts (4, 8, 10, 20, 40, 60 and 80 µg/mL) were dissolved in 0.1 M borate buffer containing 0.3 M NaCl (pH 8.3) and mixed with 20 µL ACE solution (0.1 U/mL). The mixture was incubated at 37ºC for 10 min. Next, 200 µL of 5.0mM hippuryl-histidyl-leucine substrate was added and the enzyme-substrate mixture was incubated further for 30 min at 37ºC. The hippuric acid produced was extracted by adding 1.7 mL ethyl acetate to the mixture. The residue was dissolved in 1 mL distilled water and the absorbance was determined on a UV-visible spectrophotometer at 228 nm.

RESULTS AND DISCUSSION

In this study, systolic and diastolic BP (Figure 1) of SHRs treated with ethanolic leaf extract (ELE), aqueous leaf extract (ALE), ethanolic root extract (ERE), ethanolic twig extract (ETE), ethanolic pod extract (EPE) and ethanolic stem extract (EEE) were significantly lower after 14 days of treatment ($p<0.05$- $p<0.001$) when compared with the negative control. However, for ethanolic seed extract (ESE)

and aqueous pod extract (APE), the BP lowering effect was only observed in systolic ($p<0.01$- $p<0.001$) and not diastolic. Among the extracts studied, only aqueous stem extract (AEE) was devoid of BP lowering activity when compared with the negative control. Nevertheless, none of these extracts showed significant BP lowering effects when compared with the positive controls (perindopril and ibersatan) therefore it can be concluded that their BP lowering effects are comparable to that of positive controls.

On day 14, urine output of SHRs treated with ELE was comparable to that of hydrochlorothiazide as no significant difference was observed between them. A similar pattern of diuresis was reported with *M. oleifera* root, leaf and flower aqueous extracts (4). However, in this present study, diuretic activity of aqueous root extract was not significant when compared with the negative control.

In the ACE inhibitory assay, ELE, ALE and EPE showed significant inhibition with the latter having the highest level of inhibition (>50%) at 80 µg/mL. Half inhibitory concentration (IC_{50}) of these active extracts were determined and presented in Table 1. IC_{50} values of the three active extracts were significantly different when compared with lisinopril. This denotes that these extracts were effective in inhibiting ACE activity but were not as effective as lisinopril.

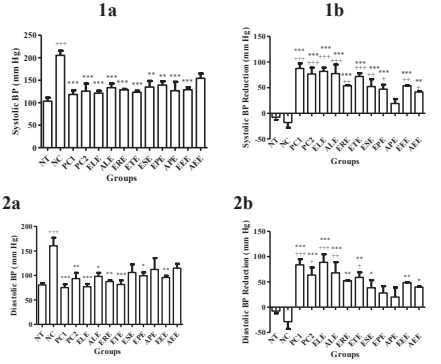

Figure 1: Systolic BP (1a), systolic BP reduction (1b), diastolic BP (2a) and diastolic BP reduction (2b) in SHRs after 14 days of treatment with M. oleifera plant part extracts

Table 2
IC_{50} (µg/mL) values of lisinopril and plant extracts in ACE inhibitory activity

Substance	IC50 (µg/mL)
lisinopril	10.93±1.00
ELE	58.65±1.55***
ALE	71.35±1.00***
EPE	54.04±1.00***

CONCLUSION

Most of the studied plant extracts reduced systolic and diastolic BP in SHRs but had no significant effect on NT rats and diuresis was observed in SHRs treated with ELE. Some of the plant parts (ELE, ALE and EPE) also showed good inhibition (>50%) of the ACE activity and this might contribute to the hypotensive effect observed.

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Methods for predicting warfarin dose requirements

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INTRODUCTION

Warfarin has been the mainstay oral anticoagulant therapy for the past several decades and remains widely used for the treatment and prevention of thromboembolic diseases. It is a difficult drug to dose accurately and safely with daily maintenance doses differing by upwards of 15-fold between patients. Dosing is further complicated by a narrow therapeutic range and several well-documented drug interactions. Since warfarin was used clinically in the 1950's, there has been a large body of literature exploring different strategies to aid in dosing decisions [1]. This study aims to review and summarize the literature on methods for predicting warfarin dose requirements.

METHODS

Identifying published warfarin dosing methods

Medline (1946 to January 2019) to identify all studies that evaluated the predictive performance of algorithms designed to predict the maintenance dose of warfarin. The Medline MeSH terms included: "warfarin," "algorithm*," "regression analysis," "statistical models," "Bayes theorem," "Dose-Response Relationship, Drug or dose response," "international normalized ratio," "pharmacogenetics," "machine learning," and keywords "dose predict*," "regression," and "dose calculation" were used. The search was limited to articles published in English and human studies. Key review publications were also identified and mined for further relevant studies. In addition, the reference lists from the identified studies were further examined for further.

RESULTS AND DISCUSSION

Warfarin dosing methods can be broadly categorized based on the clinical information required to predict the warfarin dose, namely (i) methods based only on INR response data (e.g. dosing nomograms [2]), (ii) methods based only on patient characteristics (e.g. pharmacogenetic algorithms [3]), (iii) methods based on both patient characteristics and INR response data (e.g. several specific warfarin dosing algorithms [4]), and (iv) methods based on Bayesian forecasting (e.g. Bayesian dosing tool described by Xue et al 2016 [5]). More recently, several new methods using machine learning techniques utilizing patient characteristic and INR response data have been developed [6]. It was found that there is evidence to suggest that some published warfarin dosing algorithms developed using linear regression techniques will produce biased maintenance dose predictions in patients who require higher than average doses [7].

CONCLUSION

There has been progression of methods used to aid in predicting the dose requirements of warfarin in the literature. This remains an area that is actively researched. Despite the long clinical use and experience of warfarin in clinical practice, predicting the dose requirements is still challenging. The performance of current dosing methods in predicting warfarin dose still fall short often for patients who are at the extrema of dosing requirements.

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Use of fall-increasing risk drugs among elderly

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INTRODUCTION

Falls are the principal cause of injury and hospitalization among older people aged 65 years or above, with residents of long-term care facilities accounted up to 50% in experiencing recurrent falls. Fall-risk medication has been a well-known modifiable risk factor in causing falls. Nevertheless, the prevalence of prescribed medications among older people still considerably high even though with the evidence of drug-related falls Thereby, this study aimed to determine the prevalence of drugs causing falls and the fall risk status among older people.

MATERIAL AND METHODS

Study design and instruments

A cross-sectional study was conducted among residents in 27 long term care facilities including nursing homes, residential care homes and elderly care centers in Malaysia from March 2018 until November 2018. Residents were recruited in this study based on the following criteria: older people aged 65 years and above, staying at a long-term care facility for at least 3 months and were not bed-ridden. Those who failed to provide informed consent and did not complete the questionnaire were excluded from the study.

Study tools

The FRAIL questionnaire was utilized to identify the frailty status among older people in the nursing home. The total frailty score was categorized into three levels of frail status, including robust (0), pre-frail (1-2) and frail (3-5). The prevalence of drugs causing falls among older people in the nursing home were determined using an established and validated list developed Milos et al. (2014). Each medication was assigned with unique WHO Anatomic Therapeutics Chemical (ATC) classification codes regardless of the dosage or number of drugs taken for the individual resident. The assigned ATC codes were further categorized into specific group of fall-risk increasing drugs (FRIDs) or orthostatic drugs (ODs).

All data analysis was performed using Statistical Package for Social Science (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Demographic characteristics, frailty status, presence of at least one medication that may cause fall (FRIDs) and items of fall risk questionnaire were analyzed using descriptive analysis. Chi-square analysis was performed to determine the association of fall risk status with demographic characteristics, frailty status and presence of at least one FRIDs. Univariate and multivariate logistic regression were performed to identify the predictive factors for the high fall risk among older people living in nursing home

RESULTS AND DISCUSSION

In this study, 212 participants were recruited. The age group distributions of participants were almost similar, with 70-74 years (n=49, 23.1%) and 75-79 years (n=47%, 22.2%) accounted for the most. More than half of the participants were classified as pre-frail (n=122, 57.5%). A total of 145 (68.4%) of the participants were taking at least one FRIDs or ODs, with 95 (65.5%) of them presented at a higher risk of falling. Overall, length of stayed in facilities ($p=0.031$), frailty status ($p<0.001$) and number of drugs in total ($p=0.010$) and as needed ($p=0.025$) were significantly associated with an increased risk of falls. In particular, pre-frail (n=104, 85.2%) and frail (n=13, 92.9%) status mainly predisposed residents to a higher risk of falling. The five most commonly prescribed drugs in FRID list were quetiapine (n=6), fluvoxamine (n=5), risperidone (n=5), tramadol (n=4) and haloperidol (n=4). In contrast, the most commonly prescribed drug groups in the ODs list were discovered to be C08 (n=97, 34.3%) and renin-angiotensin system inhibitors (C09) (n=59, 20.8%).

When evaluating specific FRIDs or ODs in causing falls, only beta-blocking agents (C07) and renin-angiotensin system inhibitors (C09) were associated with a greater risk of falling. Despite the association between antihypertensive agents and falls via orthostatic hypotension has long been implicated, the relationship with class-specific adverse effects remained unclear. No specific antihypertensive agent was associated with an increased risk of falls, in which previous studies have shown mixed results involving participants at different phases of treatment, such as initiation and continuation phases

The risk of falls also appeared to be significantly increased with the use of renin-angiotensin system inhibitors (C09). However, conflicting findings were shown in most of the studies, whereby no association was found with the precipitation of falls.This current study showed that residents who took a greater amount of medications, particularly with ‘’as needed’’ medications, including for both non-FRID and non-OD were presented at a significantly higher risk in falling. Previous studies have reported the effects of multiple medications in precipitating falls, however only with the

Table 1: Association of respondent's characteristics with fall risk status (N=212)

Variable/characteristics	Frequency, n (%)	Fall risk status		p-value
		High risk of falling (N=137)	Low risk of falling (N=75)	
Age (years), n (%)				
65-69	44 (20.8)	24 (54.5)	20 (45.5)	0.274[a]
70-74	49 (23.1)	30 (61.2)	19 (38.8)	
75-79	47 (22.2)	30 (63.8)	17 (36.2)	
80-84	37 (17.5)	26 (70.3)	11 (29.7)	
85 or above	35 (16.5)	27 (77.1)	8 (22.9)	
Gender, n (%)				
Male	83 (39.2)	49 (59.0)	34 (41.0)	0.172[a]
Female	129 (60.8)	88 (68.2)	41 (31.8)	
Frailty status, n (%)				
Robust	76 (35.8)	20 (26.3)	56 (73.7)	<0.001[a*]
Pre-frail	122 (57.5)	104 (85.2)	18 (14.8)	
Frail	14 (6.6)	13 (92.9)	1 (7.1)	
Taking ≥ 1 FRIDs or ODs, n (%)				
Yes	145 (68.4)	95 (65.5)	50 (34.5)	0.689[a]
No	67 (31.6)	42 (62.7)	25 (37.3)	

presence of at least one FRIDs However, the current study showed no association between the use of FRIDs and ODs, for both continuous and as needed use in the development of falls after taking into account the contribution of other covariates. This may indirectly signify the presence of other potential fall risk-increasing drugs. In this study, only frailty status was found to be independently associated with an increased risk of falling. A similar finding was observed in an explanatory study conducted under home care, in which frail older people are subjected to double or triple folds of fall risk as compared to those who are non-frail. Frail older people also have proven to be significantly associated with recurrent falls and fractures. Most studies have also demonstrated that frail older people are subjected to the loss of muscle mass, which is one of the major components of frailty syndrome that predispose to higher fall risk.

CONCLUSION

The present study showed that majority of older people were taking at least one FRIDs. Frailty status was found to be the only independent factor significantly associated with heighted fall risks, with frail older people presented with a higher fall risk compared with those who were non-frail.

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Plasmodium knowlesi management in Malaysia

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INTRODUCTION

Malaria has caused severe public health problems and economic burden worldwide. Approximately 3.2 billion people remain at risk of malaria, with an estimated 214 million cases and 438 000 deaths in 2015 (1). The fifth and most recent malaria parasite infection is caused by the *Plasmodium knowlesi* parasite. *Plasmodium knowlesi* is now being recognized as a common malaria infection in Southeast Asia including Malaysia (1). Reports of an increase in the incidence of *P. knowlesi* malaria cases in Hospital Kuala Lipis, Malaysia has been observed. The delay in parenteral anti-malarial treatment due to misdiagnosis of *P. knowlesi* has been identified to affect the clinical outcome of management (2). However, current treatment of early definitive *P. knowlesi* is largely based on oral antimalarials. Therefore, this work aims to identify factors that affect clinical management of early definitive *P. knowlesi* infection.

MATERIAL AND METHODS

Study design

This study is a cross-sectional, retrospective study carried out at Hospital Kuala Lipis, Pahang from January 2012 to December 2016.

Study criteria

Patients aged 18 years and above, diagnosed with early definitive *P. knowlesi* malaria were eligible and enrolled into the study. The exclusion criteria were those with incomplete medical records, discharged at their own risk, pregnant or lactating mothers and any known allergies towards antimalarial medications. Patients were selected using non-random purposive sampling based on a name list from the medical record unit.

Sample size

The sample size was calculated as 10 x the number of factors studied (3). Seven factors were identified which were gender, age, nationality, drug treatment, body temperature, first blood film malaria parasite (BFMP) reading and presence of complication. Approximately 70 subjects were needed to identify association between study factors and clinical outcome.

Data collection

Patient's medical history, physical examinations and laboratory investigations were recorded on a standard case record form. The indicator used to determine clinical outcome was number of days to achieve BFMP clearance. BFMP clearance was defined as the time to achieve zero or negative parasite count on blood films (4).

Ethical approval

This research was registered with the National Medical Research Register and approved by the Medical Research Ethical Committee, Ministry of Health, Malaysia (ID NMRR-13-865-17379).

Statistical analyses

All continuous variables in the study were expressed as mean and standard deviation (SD). All categorical data was presented as frequency and percentage. Univariate and multivariate linear regression analysis were conducted to identify factors affecting clinical outcome.

All variables tested in the univariate analysis were included in the multiple linear regression analysis regardless of their level of significance in the univariate analysis. A confidence interval of 95% was utilized. A p-value of less than 0.05 was regarded as statistically significant.

RESULTS AND DISCUSSION

Demographic data

A total of 125 patients were diagnosed with *P. knowlesi* over the past five years from 2012 to 2016. 53 case notes were incomplete. The remaining 72 cases were included in the study. Table 1 demonstrates the characteristics of the study population.

The average age of infected patients was 37.4±14.6 years, with males constituting a large portion (n=56, 77.8%) of malaria cases, a scenario frequently seen in other work (2, 4, 5). The influx of migrant workers (2) also contribute to a significant number of malaria cases reported by foreigners (n=30, 41.6%) from Bangladesh, Myanmar and Indonesia. Most of these (n=44, 61.1%) worked in the plantation industry such as rubber tappers, palm oil plantations and farmers, similarly observed in other studies (2, 4, 5).

Clinical data

A total of 56 (77.8%) patients received artemisinin-based treatment (artemeter-lumafentrine or artesunate-doxycycline), whilst 16 (22.2%) patients received non-artemisinin-based treatment (chloroquine-doxycycline, quinine-fansidar). The frequent use of artemisinin-based treatment is due to first-line arteminisin recommendations since 2013 (1, 4). With the use of antimalarials, the average length of hospitalization for *P. knowlesi* was 5.89±1.0 days. The average time to achieve BFMP clearance was 4.14±1.0 days. Both length of hospitalization and BFMP clearance was similar to previous work (5).

Table 1: Characteristic of the study population (n=72)

Variables	Values	
Gender, n (%)		
Male	56	(77.8)
Female	16	(22.2)
Age, mean (SD)	37.39	(14.6)
Nationality, n (%)		
Malaysian	42	(58.4)
Non Malaysian	30	(41.6)
Drug treatment, n (%)		
Artemisinin	56	(77.8)
Non-artemisinin	16	(22.2)
Body temperature, mean (SD)	38.69	(0.75)
BFMP count /uL, mean (SD)	11161	(19548.1)
Presence of complication, n (%)		
Yes	16	(22.2)
No	56	(78.8)

Factors that affect BFMP clearance

The risk of severe disease in P. knowlesi increases in older patients that are misdiagnosed (2). Interestingly, the current work clearly demonstrated that an increase in age also increased the time to BFMP clearance in patients with early definitive P. knowlesi. Specifically, based on the multiple linear regression model obtained in the current work, an increase in age by 1 year increased the time to BFMP clearance by 0.32 times (Adjusted B: 0.32; 95% CI: 0.004-0.007; p-value=0.016). This model explained 6.4% of the variation within a population (adjusted R^2=0.064).

CONCLUSION

P. knowlesi is a common malaria infection in Malaysia. Despite this, very few clinical studies are performed on *P. knowlesi* patients due to its very recent emergence. The current work demonstrates that parasite clearance of *P. knowlesi* infection is dependent on age. Closer monitoring of older patients is warranted to ensure optimal outcome. Further nation-wide studies are warranted to facilitate efforts to improve surveillance of this emerging parasite.

ACKNOWLEDGEMENT

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Information support tool for Malaysian breast cancer patients on chemotherapy

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INTRODUCTION

Breast cancer is the most common cancer among women in Malaysia.[1] Chemotherapy is one of the main treatment for breast cancer, however, misconceptions on chemotherapy continue to persist.[2] As such, development of an information support tool on chemotherapy for breast cancer patients in Malaysia would be of paramount importance. The aim of this study was to develop and validate an information support tool in the form of booklet and web-based in Malay and English for breast cancer patients on chemotherapy.

MATERIAL AND METHODS

Study design
Semi-structured interviews were conducted on breast cancer patients attending the Universiti Kebangsaan Malaysia Medical Centre (UKMMC) and National Cancer Society of Malaysia (NCSM) to figure out patients' personal experiences, information needs and side effects after completion of chemotherapy. Findings from this qualitative study were also incorporated into the tool. The study involved 5 phases :-

Phase 1: Literature review

Pubmed, Science Direct and EBSCOhost were the databases used to find scientific literature. Keywords such as "chemotherapy", "breast cancer", "side effects", and "complementary treatment for breast cancer" were used.

Phase 2: Development of tool (first draft)

Findings from qualitative interview and extensive literature review were used to develop the tool based on the International Patient Decision Aid Standards (IPDAS) Collaboration.[3]

Phase 3: Content validity by panel experts

This was performed by three experts: a consultant surgeon, an oncologist and a pharmacist.

Phase 4: Pilot testing

Patients with breast cancer attending UKMMC and NCSM were invited to assist in the pilot test of the tool.

Phase 5: Tool finalization

The tool undergone several amendments based on experts' recommendations and patients' opinions. Forward and backward translations were conducted to translate the English version to Malay language. The final tool was developed in the form of booklet (A5 size) and webpage (https://www.wix.com).

RESULTS AND DISCUSSION

Phase 1: Literature review

From the literature, 92 papers were screened but only 32 papers provided relevant information.

Phase 2: Development of tool (first draft)

Six main themes obtained from the interview: know-nothing of chemotherapy; fear of chemotherapy; patients' beliefs in alternative treatments; symptom management; staying healthy after chemotherapy; concerns of patients after chemotherapy.[4] Content included general information about breast cancer, incidence statistics in Malaysia, stages, chemotherapy, side effects from chemotherapy and the use of complementary and alternative medicines.

Phase 3: Content validity by panel experts

Suggestions were incorporated in the tool (e.g. list of chemotherapy side effects and use of complementary and alternative medicines). The panel experts suggested to only include complementary and alternative medicines concerning physical activities, diet, spiritual beliefs and healthy lifestyle in the tool. This is because there is lack of evidence on the efficacy and safety of herbal therapy in patients with breast cancer.[5,6]

Phase 4: Pilot testing

Nineteen patients (86.4%) found that the tool increased their knowledge on chemotherapy for breast cancer. Majority of the patients (n = 21, 95.5%) felt that the tool was easy to follow and would recommend it to other women with breast cancer on chemotherapy. Decision aids improved decision-related outcomes for many breast cancer treatment decisions including chemotherapy.[7]

Phase 5: Tool finalization

See Figures 1 and 2.

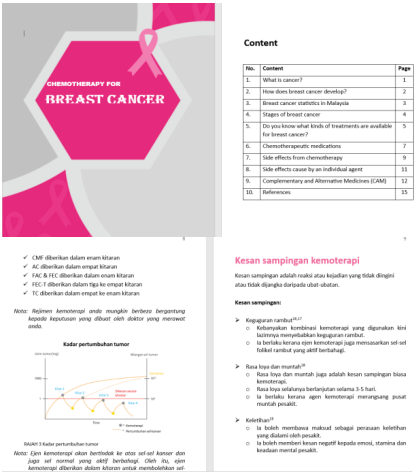

Figure 1: Selected pages of information support tool in booklet

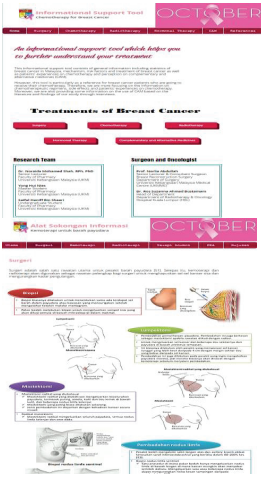

Figure 2: Screenshots of information support tool in webpage

CONCLUSION

The tool entitled Chemotherapy for Breast Cancer was successfully developed and had undergone content validity by experts. The tool will be a useful and reliable source of information for breast cancer patients undergoing chemotherapy and can be utilized by healthcare practitioners during treatment consultations.

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The Current Practice and Barriers on Value Added Services among Community Pharmacists

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INTRODUCTION

Pharmacy Value Added Services (PVAS) is defined as pharmacy activities to improve the delivery of pharmaceutical care to the patients. Extending community pharmacists' role could benefit patients by improving the quality of care, optimization of drug therapy and a reduction in long term healthcare costs (Sadek et al. 2016). Optional services in section 4 of the National Pharmacy Benchmarking Guideline 2016 includes Home Medication Review (HMR), Medication Therapy Adherence Clinic (MTAC), Certified Smoking Cessation Service Provider (CSCSP), weight management or health screening services (Chua et al. 2013; Pharmaceutical Services Division 2016). Therefore, this study was conducted to evaluate the current practice and barriers on value added services among community pharmacists.

METHODS

A cross-sectional survey was conducted from June 2018 until November 2018. The questionnaires were distributed to community pharmacists working in Kuala Lumpur areas such as Bukit Bintang, Setiawangsa, Wangsa Maju, Batu, Kepong, Segambut, Lembah Pantai, Seputeh, Bandar Tun Razak and Cheras. Respondents who are fully registered pharmacists under Pharmacy Board of Malaysia and have been working in the Malaysian community pharmacy setting for at least one year were included in this study.

RESULTS AND DISCUSSION

During a period of four months, 160 questionnaires were distributed and 139 questionnaires were filled and returned, giving a response rate of 86.9%.

Demographic characteristics of community pharmacists in Kuala Lumpur

Around 41.7% respondents were men and 58.3% were women. The highest percentage of respondents were Chinese (84.9%) followed by Indian (7.9%) and Malay (6.5%). Almost three quarter of the respondents (70.5%) were employees while 33 respondents (23.7%) were pharmacist and store manager. Only 5.8% of the respondents owned the community pharmacy. Most respondents (46.8%) have been practicing as a community pharmacist for 2 to 5 years whereas 23% had been practicing for 6 to 10 years.

Community pharmacists' current practice

Around 31.7% respondents were occasionally involved and 30.2% were frequently involved in the prescription screening. Community pharmacists in Kuala Lumpur has not been actively involved in prescription screening due to the absence of dispensing separation. General practitioners in the private clinics do not issue prescriptions to patients unless upon request as they practice both prescribing and dispensing of medication (Shafie et al. 2012). However, it was noted that 43.9% of the respondents were never involved in medication compounding and a quarter of the respondents (25.9%) did not provide medication compounding service. The provision of extemporaneous preparation and medication compounding services has been reduced substantially due to the increase in readily available pre-packed products compared to a nationwide study conducted in 2008 (Chua et al. 2008). This is in contrast with counselling and advisory services in which majority of the respondents (91.3%) were very frequently involved. Health screening services are some of the common services provided in the community pharmacies. About half (48.9%) of the community pharmacists were frequently involved in providing hypertension health screening service. This is similar with diabetes health screening with half (52.5%) of the respondents were also frequently involved.

Regarding optional services carried out in the community pharmacy, more than a third of the respondents (28.8%) were never involved in medication review service, one third of the respondents (25.2%) rarely involved in this service, while only 16.5% of the respondents were occasionally involved in providing this service. Medication Therapy Adherence Clinic (MTAC) service was one of the optional services in which most of the respondents were not actively involved in conducting. Only 27.3% respondents were never involved in MTAC service, 18% were rarely involved and 23% respondents were occasionally involved. Smoking cessation service was not a popular service with 32.4% respondents were occasionally involved, 20.9% respondents were rarely involved and 20.1% respondents were never involved in providing this service. Lastly, around 39.6% respondents were occasionally involved in providing weight management services, 20.9% were rarely involved while 20.1% were frequently involved in providing this service.

Barriers in the current pharmacy practice situation which affect the provision of pharmacy value added services (PVAS)

Most of the respondents (75.6%) strongly agreed and agreed that they face shortage of time for pharmacist to handle customers. The value was found to be statistically significant with respect to race and years of practicing as a community pharmacist ($p<0.05$). Respondents expressed mixed opinion

regarding salary, almost half of the respondents (48.2%) did not agree nor disagree that the salary level was inappropriate for pharmacists. However, more than a quarter (27.4%) of the respondents felt that the salary level was appropriate for the pharmacists, while close to a quarter of the respondents (23.8%) felt that the salary was inappropriate for pharmacists. The value was found to be statistically significant with respect to gender ($p<0.05$). More than half (55.4%) of the respondents strongly agreed and agreed that they were unappreciated financially for the pharmacy value added services that they offered. However, slightly more than a quarter (30.9%) of the respondents were neutral regarding this matter. The value was found to be statistically significant with respect to pharmacists previous working experience after becoming fully registered pharmacists ($p<0.05$).

Community pharmacists' traits which affect the provision of pharmacy value added services (PVAS)

This section explain the traits of community pharmacists which affect the delivery of PVAS. More than half (51.8%) of the respondents strongly disagreed and disagreed that they lack appropriate knowledge to provide value added services. The difference was seen between pharmacies with more middle-aged customers ($p<0.05$). However, close to half (47.5%) of the respondents agreed that pharmacists lack of confidence to conduct PVAS while more than a quarter (36.7%) of the respondents neither disagree nor agree regarding this matter. The value was found to be statistically significant with respect to pharmacists who worked in the government hospitals ($p<0.05$) after becoming fully registered pharmacists. Among the respondents, about 38.2% of them refused to acknowledge that their lack of interpersonal and management skills became a barrier to conduct PVAS. While a quarter of them (25.1%) strongly agreed and agreed that their lack of interpersonal and management skills were found to be barriers in providing value added services. More than half (66.9%) of the respondents strongly disagreed and disagreed that providing PVAS were not felt to be part of their job.

External barriers faced in providing pharmacy value added services (PVAS)

Almost half of the respondents (47.5%) strongly agreed and agreed that other healthcare professionals underestimated them. Respondents had mixed opinion when asked whether the customers felt the pharmacist roles are not important as 39.6% strongly agreed and agreed. However, 34.5% of the respondents strongly disagreed and disagreed regarding this matter. The survey showed that more than half (57.6%) of the respondents strongly agreed and agreed that the rising pressure on pharmacists to generate sales hindered PVAS provision. However, more than a quarter of the respondents (28.8%) felt neutral about this barrier. The value was found to be statistically significant with respect to pharmacists' previous working experience after becoming fully registered pharmacists ($p<0.05$). Among the respondents, majority of them (61.2%) strongly agreed and agreed that pharmacy practice in Kuala Lumpur has turned to be business-focused. The value was found to be statistically significant with respect to race, years of practicing as a community pharmacist, average prescription filled per month, pharmacist who worked as community pharmacist after becoming fully registered pharmacist, pharmacies with high socioeconomic status customers and customers who are of older age ($p<0.05$).

CONCLUSION

Prior to this study, the current practice on PVAS among community pharmacists in Kuala Lumpur are not clearly understood. The respondents in this study showed that PVAS in the community pharmacy setting is still low. Some of the barriers faced by the community pharmacists are related to the current pharmacy practice situation, community pharmacists' traits and external factors barriers when providing PVAS.

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Factors that may influence medicine price setting in the private healthcare system in Malaysia

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INTRODUCTION

Medicine pricing strategy is unique to the Malaysia healthcare system as it consists of two main providers that are separate and independent of each other. The government-funded public sector that is financed through taxation and country's general revenue, contain medicine price through several approaches [1]. While the medicine prices in the private healthcare sectors that is financed through private health insurance and out-of-pocket money, are solely determined by market forces and competition. Up to date, the government has not yet implemented any control over the medicine price in the private healthcare sectors. Although in 2011 pharmaceutical industries are encouraged to declare their wholesale and recommended retail medicine price (RRP) to the government as part to increase the price transparency to public (RRP are published for consumer guide in medicine purchasing), this practice was merely voluntary and did not include any price containment strategy. Because of that medicine prices in the private healthcare sector in Malaysia are reported to be variable and highly markup [2]. Nevertheless little is known how the medicine price is set in the private healthcare sector in Malaysia. Thus, this study aims to investigate factors that may influence the high medicine retail price in the private healthcare setting in Malaysia.

METHODOLOGY

The current study investigated PSD medicine price databases from 2011 to 2015 that consisted of 1) wholesale and RRP prices of controlled and over the counter (OTC) medicines declared by pharmaceutical companies and 2) consumer wholesale and retail medicine prices (sampled by the PSD through the Medicine Price Monitoring Survey (MPMS) either at institutional counters, from medicine invoices, or both) and 3) the International Reference Prices (IRP) database that provides information on median buyer prices. For all medicines, the unit drug prices were calculated by dividing the drug pack selling price by the number of tablets, capsules, vials or doses contained.

The IRP was converted from the United States Dollar (USD) to local currency according to the Bank Negara exchange rate of the year of study as following: USD 1 to RM 3.00 (2011), RM 3.17 (2012), RM 3.19 (2012), RM 3.18 (2014), and RM 3.96 (2015). The median price ratio (MPR) of medicine within the same therapeutic group was then calculated using the following formula:

$$\text{MPR} = \frac{\text{Median retail price of medicines}}{\text{International Reference Price (IPR)}}$$

MPR of 1 indicates that the consumer price is equivalent to the IRP and an MPR cut-off point of ≤ 2.5 was commonly considered an acceptable consumer medicine price set up [16]. Factors that may influence the MPR of > 2.5 were investigated using binary logistic regression (BLR) with backward likelihood-ratio analysis. Variable with a p-value of < 0.05 were considered as significant. Prior to this evaluation, a univariate analysis was conducted to determine the variables to be included in the final model analysis, and only those with a $p < 0.25$ were included.

RESULTS AND DISCUSSION

A total of 2527 medicine prices data were analyzed. The majority of the medicines (n = 2325, 92%) had MPR > 2.5. Medicines used for chronic diseases, manufactured locally and sold in East Malaysia were more likely to have MPR > 2.5 ($p<.05$). While generic medicines, rural areas and medicines in other than tablet forms were less likely to have MPR > 2.5 ($p < .05$). An increase in RM 0.01 of the medicine RRP declared to PSD for a single dosage unit increased the chances of a retail medicine exhibiting MPR > 2.5 to 52% and a RM 0.01 reduction in the retail wholesale price increased the chances of medicines having MPR > 2.5 to 72%.

The declared price that is published in the PSD website can be considered as reliable medicine pricing information for consumers. Accurate medicine prices information will provide consumers with options, thus, allowing for more efficient and effective procurements [3]. The latter may empower consumers and spark real competition in the marker in which long-run reduced medicine retail price [3]. Nevertheless, the number of pharmaceutical companies that declared their medicine prices to the PSD was still inadequate. To increase the pharmaceutical industries practice of medicine price transparency, the government may want to implement the price disclosure as part of the pharmaceutical pricing regulations such as occurs in the South Africa, Vietnam, and some European countries [19].

The medicine price disparity between urban and rural area may frame on issue related to market segmentation.

Variables	MPR		Univariate analysis (n=2527)			Multivariate analysis (n=2527)		
	MPR ≤ 2.5 (n=202), n (%)[a]	MPR > 2.5 (n=2325), n (%)[a]	Crude OR (95% CI)	Wald's χ2 (df)	P-value	Adj. OR (95% CI)	Wald's χ2 (df)	P-value
Indication:								
Acute	99 (11.3)	774 (88.7)	1.00			1.00		
Chronic	103 (6.2)	1551 (93.8)	1.93 (1.44, 2.57)	19.76 (1)	< 0.001	2.05 (1.46, 2.70)	16.84 (1)	< 0.001
Type of medicine:								
Original	32 (3.6)	851 (96.4)	1.00			1.00		
Generic	170 (10.3)	1474 (89.7)	0.33 (0.22, 0.48)	32.22 (1)	< 0.001	0.24 (0.15, 0.37)	39.81 (1)	< 0.001
Manufacturer:								
Import	149 (8.8)	1542 (91.3)	1.00			1.00		
Local	53 (6.3)	783 (93.7)	1.43 (1.03, 1.98)	4.61 (1)	0.032	3.86 (2.61,5.71)	45.88 (1)	< 0.001
Region:								
Peninsular	161 (8.7)	1686 (91.3)	1.00			1.00		
East Malaysia	41 (6.0)	639 (94.0)	1.49 (1.04, 2.12)	4.83 (1)	0.028	1.84 (1.26, 2.68)	10.32 (1)	< 0.001
Type of Facility:								
Community Pharmacy	179 (8.3)	1984 (91.3)	1.00					
Private Hospital	23(6.3)	341 (93.7)	1.34 (0.85, 2.09)	1.61 (1)	0.200	-	-	NS
Location:								
Urban	152(7.1)	1975 (92.9)	1.00			1.00		
Rural	50(12.5)	350 (87.5)	0.54 (0.38, 0.76)	12.77 (1)	< 0.001	0.48 (0.34, 0.69)	15.86 (1)	< 0.001
Form:								
Tablet	161(6.9)	2181 (93.1)	1.00			1.00		
Other form	41(22.2)	144 (77.8)	0.26 (0.18, 0.38)	47.95 (1)	< 0.001	0.20 (0.13, 0.32)	51.53 (1)	< 0.001
PSD Wholesale	5.94 [d]	15.70 [e]	1.58 (1.27, 1.96)	17.29 (1)	< 0.001	-	-	NS
PSD RRP	8.60 [d]	20.84 [e]	1.47 (1.25, 1.74)	20.96 (1)	< 0.001	1.52 (1.17, 1.98)	10.03 (1)	< 0.001
MPMS Wholesale	5.21 [d]	11.96 [e]	1.36 (1.09, 1.69)	7.17 (1)	0.001	0.72 (0.55, 0.93)	6.10 (1)	0.013

Notes: [a] The percentage is reported by column, adding up to 100% based on available information; [d] Median price over IRP; [e] IQR of price over IRP.
Abbreviations: MPR, median price range; OR, odds ratio; CI, Confidence interval; NS, Non-significant; PSD, Pharmaceutical Service Division; RRP, Recommended Retail Price; MPMS, Medicine Price Monitoring Survey.

Table 1: Factors that influence Medicine's Median Price Ratio (MPR) of > 2.5 in private healthcare sectors in Malaysia

Although segmentation of the market can be welfare-enhancing, as suppliers able to disaggregate the demand into segments of potential customers and charge according to willingness-to-pay, it also may result in price discrimination which enables the providers to charge the price that is more than what consumer is willing to pay [5]. Local manufacturers were also found to have a higher likelihood of MPR > 2.5 than the foreign manufacturers. Although foreign manufacturers able to offer low-cost and large-volume import, supporting local manufacturers maybe a systemic approach to improve access to medicine.

CONCLUSION

The declared medicine prices would serve as a useful reference for consumers, however, the government of Malaysia still in needs to identify strategies to increase the medicine price transparency practice of the pharmaceutical industry. This may include regulatory policy enforcing price declaration and medicine price control mechanism in the private healthcare settings.

ACKNOWLEDGEMENT

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Complementary and Alternative Medicine (CAM) Usage Among Hypertensive Patients

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INTRODUCTION

The increasing popularity and use of complementary and alternative medicine (CAM) in both developed and developing countries, including Malaysia, have raised significant public health policy issues. Based on World Health Organization (WHO), about two-thirds and 50-80% of the population of developed and developing countries, used CAM, respectively. Association of Southeast Asian Nations (ASEAN) has found that Malaysia has the highest percentage in usage of CAM which is 55.6%, followed by older adults in Singapore (42.7%), Philippines (6.3%), Cambodia (5.4%), Vietnam (3.5%), Thailand (2.6%) and Indonesia (2.0%). The prevalence of CAM use of patients in biomedical health facilities is generally high. It has been used in cancer patient, medical patients, patients with chronic conditions, diabetic patients, asthmatic patients, HIV patients and hypertensive patients (Kearney et al. 2005)

METHODOLOGY

Study design

The current study was conducted as cross-sectional, self-administered survey among the Malaysian hypertensive patients regarding usage of Complementary and Alternative Medicines (CAM). Data collection was done between September to November 2018.

Study population

Subjects who are diagnosed with hypertension, aged 18 years old and above, Malaysian citizen, and able to understand English or Malay language were included in this research. Subjects who cannot read, illiterate or unable to give consent or those who have cognitive impairment such as Alzheimer's disease or dementia were excluded in this research.The sample size is calculated by using the 10 cases per variable calculation based on 10 factors affecting CAM usage as reported by previous literatures. Using convenient sampling, the hypertensive patients who fulfilled the inclusion criteria and agreed to participate were invited to participate in the study. Survey questionnaires were distributed via face-to-face in Universiti Kebangsaan Malaysia Medical Centre (UKMMC).

Study instruments

A structured questionnaire was developed by the researchers based on the literature review of previous studies (Ali-Shtayeh et al. 2013; Bishop et al. 2005; Siew-Mooi et al. 2013) and input from experts in the area. The questionnaire was prepared in both English and Malay languages. The questionnaire consisted of four sections: section A, B, C and D. Details about each section of the questionnaire are as the following:

- Section A was aimed to gather respondents' background information
- Section B investigated the respondent's hypertensive status.
- Section C assessed the pattern of Complementary and Alternative Medicine usage
- Section D evaluated the patient's belief toward Complementary and Alternative Medicine.

Data analysis

All data collected from the completed questionnaires were analyzed using Statistical Package for the Social Sciences (SPSS) software version 21.0.

Ethical approval

Ethics approval for this study was obtained from the Research Ethics Committee of The National University of Malaysia with a registration number UKM PPI/111/8/JEP-2018-383.

RESULTS AND DISCUSSION

Demographic characteristics

A total of 135 subjects were included in this study. There were 75 (55.6%) males and 60 (44.4%) females in this study. Most of the respondents were between the age of 50 to 59 (n=47, 34.8%). Majority of the respondents were Malay (n=66, 48.9%), followed by Chinese (n=54, 40.0%) and Indian (n=15, 11.1%). A total of 48.9% (n=66) respondents were Muslim, followed by 32.6% (n=44) Buddhist, 11.1% (n=15) Hinduism and 7.4% (n=10) Christian. Our findings suggested that knowing the current blood pressure reading and beliefs in natural treatment, were the two significant independent predictors of CAM use in our studied population. Similar finding was found in other studies that

showed CAM use is associated with the belief in natural treatments where they are safer, no side effects and more effective than orthodox medicines (O'callaghan & Jordan 2003).

Types of CAM	Frequency	Percentage (%)
Herbal products		
Bitter Gourd	18	21.7
Garlic	20	24.1
Orthosiphon aristatus / Misai kucing	1	1.2
Honey	13	15.7
Lemon Juice	20	24.1
Green Tea	18	21.7
Alternative medical systems		
Acupuncture	6	7.2
Energy therapies		
Qi Gong	4	4.8
Tai Chi	3	3.6
Manipulative and body-based systems		
Massage	9	10.8
Reflexology	1	1.2
Exercise	56	67.5
Mind-body interventions		
Yoga	1	1.2
Prayer	12	14.5

Table 1 – Types of CAM being used

Types of CAM used by patients with hypertension

Table 1 shows the types of CAM used among hypertensive patients in this study. Of the 135 study participants, 83 (61.5%) patients had experience in using some form of CAM. The most popular CAM used in hypertensive patients in PPUKM was exercise (n=56, 67.5%). More than half of the patients with hypertension used herbal products (n=52, 62.7%). The specific herbal used either alone or in combination with other CAM and their frequencies among the 83 CAM users were as follows: garlic (n=20, 24.1%), lemon juice (n=20, 24.1%), bitter gourd (n=18, 21.7%), green tea (n=18, 21.7%), honey (n=13, 15.7%) and Misai Kucing (n=1, 1.2%). The high level of CAM use indicates the patients' preference towards an integrative approach to HTN management. The variations in the prevalence of CAM use across different countries might be due to the variations in sociocultural background, accessibility of modern medical practice, and perceptions on the importance of CAM.

Patterns and reasons of use of CAM by patients with hypertension

Majority of the respondents (n=47, 56.6%) reported that they want to try a new alternative treatment to improve their blood pressure control and overall well-being. Some of them (n=29, 34.9%) started to use CAM when they heard the good examples from others who claimed that their health status had been improved after the used of CAM. One (1.2%) respondents believed that the modern medicine gives more adverse effects which then encourage him/her to use CAM in hypertension treatment and there were 7 (8.4%) respondents used CAM due to the religious beliefs. Friends or family member were the most important source (n=69, 83.1%) of influence on hypertensive patients to use CAM.

CONCLUSION

In conclusion, this present study reported a high percentage of CAM use (61.5%) among patients with hypertension. Health care providers should be open to discuss the use of CAM with their patients as it will lead to better health outcome. They should be more aware of CAM usage and able to counsel patients regarding the potential of herb-drug interactions.

ACKNOWLEGMENT

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ORAL PRESENTATION COMPETITION

No.	Presenters	Title
1	Nawarat Sooksai	Andrographolide-Loaded Nanoemulsion and Its Activity against Non-Melanoma Skin Cancer Cells
2	Kantsak Leerattanakul and Pheeraphong Adulheem	Optimization of production process of nanoemulsions containing alpha mangostin from mangosteen rinds by high pressure homogenization
3	Oranich Vera-Archakul and Chayaporn Sangamnarj	The Effect of Hydrophilic Polymers on Release Profiles of Metronidazole Films
4	Napasorn Ransibrahmanakul and Nontapat Sarovath	Determination of insecticidal activity and development of prototype product against American cockroach from *Stemona collinsiae* root extract
5	Pakawat Keetawattanakul and Nuntawan Loessaksrisakul	Factor Influencing Stroke Treatment Expenditure at Phramongkutklao Hospital

Presenter 1

Andrographolide-Loaded Nanoemulsion and Its Activity against Non-Melanoma Skin Cancer Cells

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Andrographolide (AG) is a diterpenoid lactone found in *Andrographis paniculata* leaves and stems. It has excellent activity against various cancer cells, for example, skin cancer cells. The skin cancer is the most common malignancy in the Caucasian population. However, application of AG for skin cancer treatment in clinical trials is limited due to its poor water solubility. To overcome this problem, the oil in water AG-loaded nanoemulsion (NE) (AG-NE) would be prepared. The objectives of this study were to investigate physicochemical properties of AG-NE and to determine its activity against non-melanoma skin cancer cells. NE containing AG (0.1%w/w), which was dissolved in a mixture of various oils, i.e. coconut oil, sesame oil, jojoba oil, □-tocopherol including a mixture of Tween 80 and Span 80 (5:1) (10% w/w) as an emulsifier and NE base (NE without AG) were formulated and prepared using high-pressure homogenization technique. Both NE base and AG-NE were investigated their physical stability after preparation by centrifugation and observed the appearance of phase separation. Their droplet size, zeta potential and FTIR spectra were determined. Cytotoxicity of AG and AG-NE to non-melanoma skin cancer cells (A-431 cells) and normal skin fibroblast cells (HFF-1 cells) were investigated. The apoptosis induction of A-431 cells by AG and AG-NE was estimated using flow cytometry technique. The results showed that NE base and AG-NE had droplet size in a nanometer range. They had low viscosity with the flow behavior consistent with the Newtonian liquids. Although their zeta potential values were slightly low, they showed good physical stability against centrifugal force. AG and AG-NE were not toxic to HFF-1 cells, but they could induce apoptosis of A-431 cells with IC_{50} of 25.83 μg/ml and 58.32 mg/ml, respectively. Therefore, AG-NE has become possible to use for further investigation of its efficacy and safety in animal models and clinical trials.

Keywords: Andrographolide, Nanoemulsion, Non-melanoma skin cancer, Apoptosis

Presenter 2

Optimization of production process of nanoemulsions containing alpha mangostin from mangosteen rinds by high pressure homogenization

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This study was aimed to investigate the effect of production parameters on physicochemical properties of nanoemulsion (NE) containing alpha-mangostin (AMG) (AMG-NE) and to determine anti-inflammatory activities and skin toxicity of the obtained AMG-NE in cell lines. Blank NEs (NEs without AMG) were prepared by high-pressure homogenization technique with varying in 3 production parameters, i.e. pressures, numbers of homogenization cycle and temperatures following the face-centered central composite design. They were observed the effect of these parameters on their droplet size and polydispersity index (PDI). The optimized production parameters were used for investigation of production scale-up on droplet size and PDI of AMG-NEs. A representative AMG-NE was determined its anti-inflammatory activity and skin toxicity in murine macrophage (RAW 264.7) cells and human skin fibroblast (HFF) cells, respectively. The results showed that the pressure, the number of homogenization cycle and the temperature significantly affected droplet size and PDI of Blank NEs. After addition of AMG to the optimized Blank NE, the obtained AMG-NE had comparable droplet size and PDI to those of Blank NE. However, an increase in batch size of AMG-NE production by using optimized production parameters caused changes in particle size and PDI but they were still within acceptable criteria. AMG-NE showed anti-inflammatory activity with IC50 of 7.908 μg/ml. In addition, HFF cells could tolerate AMG-NE at various concentrations with %cell viability more than 70%. These suggested that AMG-NE could be prepared for large scale by using the optimized production parameters. Furthermore, AMG-NE had anti-inflammatory activity without toxicity to human skin cells. AMG-NE thus had a potential for using in further investigation of the efficacy and safety in animal models and clinical studies.

Keywords: Production, Nanoemulsions, Alpha-mangostin, High-pressure homogenizer, scale-up

Presenter 3

The Effect of Hydrophilic Polymers on Release Profiles of Metronidazole Films

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Thin film is one of the promising drug delivery systems that has drawn immense interest in recent years and has become an alternative delivery system for local treatment of periodontitis. The objective of this study was to determine the effects of type and concentration of hydrophilic polymers, i.e. hydroxypropyl methylcellulose (HPMC), sodium carboxymethyl cellulose (SCMC), hydroxyethyl cellulose (HEC) and polyethylene glycol MW6000 (PEG) on the release profiles of metronidazole films. The films were prepared by hot melt extrusion in total of 20 formulations. Each formulation contained 10 %w/w metronidazole as an active drug. In addition, 5 %w/w glyceryl monostearate and polycaprolactone 70 – 82 %w/w were used as a plasticizer and a polymer matrix, respectively. The hydrophilic polymers were varied from 3, 6, 9, 12 and 15 %w/w. The physiochemical properties of the films i.e. weight variation, thickness variation, content uniformity and drug release were investigated. As a result, the obtained films were thin round white glossy sheets with 6 mm in diameter. An average weight was 6.06 ± 1.01 mg, an average thickness was 317.87 ± 3.15 □m and an average drug content was 97.42 ± 6.39 %. The drug release study showed that the films could release metronidazole over 48 hours continuously. The films containing SCMC had rapid drug release rate while the films containing HEC had the slowest drug release rate. Moreover, an increasing of polymer concentration affected in slower drug release rate. The release coefficient of the film was closed to 0.5, indicating that the release mechanism of this films followed Fickian diffusion. This result shows that diffusion is the primary mechanism of drug release.

Keywords: metronidazole, films, hydrophilic polymer, drug release mechanism

Presenter 4

Determination of insecticidal activity and development of prototype product against American cockroach from *Stemona collinsiae* root extract

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Stemona collinsiae root have been used in pesticide and vector control for long time. However, the insecticide activity against American cockroach (*Periplaneta americana*) have not been studied. In this study, the insecticidal activity using bait method and repellent activity were tested. Hexane, dichloromethane, ethanol and water crude extract were prepared using reflux extraction method and extractants as hexane, dichloromethane, ethanol and purified water were used. Temperature of the extraction was controlled not more than 70 ^{0}C. The four crude extracts at concentration of 10 mg/cockroach were used for bait method. Ethanol crude extract showed the highest mortality rate as 96.56% corrected mortality while hexane, dichloromethane and purified water crude extracts presented at 3.45%, 68.97% and 44.83% corrected mortality, respectively. Ethanol crude extract at range of concentration $6.25x10^{-3}$- 0.1 g extract/g fructose showed percent of corrected mortality in range 20.69-96.56% and LC_{50} was 0.0233 ± 0.0000 g extract/g fructose. For the repellent test, concentration of dichloromethane crude extract in range 1-10% w/w in cream base could repel American cockroach calculating as 100% repellent activity and this activity had maintained for more than 2 hours.

Conclusion, ethanol and dichloromethane crude extracts showed insecticidal activity via oral administration and repellent activity, respectively. Thus, dichloromethane crude extract at concentration 4% w/w was prepared as active ingredient in repellent cream. Repellent cream could repel American cockroach having duration of repellent activity more than 2 hours with 90% repellent activity

Keywords: Americana cockroaches, insecticidal activity , *Stemona collinsiae, Periplaneta americana*

Presenter 5

Factor Influencing Stroke Treatment Expenditure at Phramongkutklao Hospital

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Introduction: Stroke is one of a major global health problem. In Thailand, the mortality rate of stroke patients has been increasing every year. Information on factors affecting cost of medical care is necessary for hospital financial status management but the studies in Thailand are still limited.

Purpose: The aim of this study is to determine the factors influencing stroke hospitalization cost at Phramongkutklao Hospital.

Method: A retrospective analytical study was conducted among stroke inpatients who were admitted during the financial year 2017 at Phramongkutklao hospital, identified by ICD-10. The data was collected form Electronic database & Electronic medical records. Multiple regression analysis was used to determine the association between the hospitalization costs and factors that influenced the costs in term of a correlation coefficient. All statistical test were performed using SPSS version 24.0. The methodology was approved by the ethical committee of Institutional Review Board Royal Thai Army Medical department (IRBRTA).

Results: Among 272 in-patients with stroke, the proportion with ischemic stroke, hemorrhagic stroke, transient ischemic attack were 53.3%, 41.5%, and 5.2%, respectively. While the average cost: 136,643 ± 211,005 THB; the median 52,854 THB, the interquartile range 120,233 THB. 57% of the patients were male and their mean age was 69.2 ± 14.2 years, the mean length of stay (LOS) was 25.6 ± 40.2 days. Multiple regression analysis among 13 independent factors revealed that, female patients, had surgery, had a nosocomial infection, use of ventilator, and prolonged LOS had significant positive correlation with stroke hospital costs. (R-square = 0.788)

Conclusions: Surgery, use of ventilator, nosocomial infection, and LOS are the factors related to the stroke treatment cost which the hospital can control the use of resources efficiently.

Keywords: Stroke, factor, hospital cost, inpatients, diagnosis related groups (DRGs)

POSTER PRESENTATION COMPETITION

Pharmaceutical Technology (PT)

Poster No.	Presenters	Title
PT 1	Nawarat Sooksai	Andrographolide-Loaded Nanoemulsion and Its Activity against Non-Melanoma Skin Cancer Cells
PT 2	Rangsima Jarusuwanwong	Development of ganciclovir-loaded liposomes incorporated ion-sensitive in situ gels for ophthalmic applications
PT 3	Kantsak Leerattanakul and Pheeraphong Adulheem	Optimization of production process of nanoemulsions containing alpha mangostin from mangosteen rinds by high pressure homogenization
PT 4	Oranich Vera-Archakul and Chayaporn Sangamnarj	The Effect of Hydrophilic Polymers on Release Profiles of Metronidazole Films

PT 1

Andrographolide-Loaded Nanoemulsion and Its Activity against Non-Melanoma Skin Cancer Cells

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Andrographolide (AG) is a diterpenoid lactone found in *Andrographis paniculata* leaves and stems. It has excellent activity against various cancer cells, for example, skin cancer cells. The skin cancer is the most common malignancy in the Caucasian population. However, application of AG for skin cancer treatment in clinical trials is limited due to its poor water solubility. To overcome this problem, the oil in water AG-loaded nanoemulsion (NE) (AG-NE) would be prepared. The objectives of this study were to investigate physicochemical properties of AG-NE and to determine its activity against non-melanoma skin cancer cells. NE containing AG (0.1%w/w), which was dissolved in a mixture of various oils, i.e. coconut oil, sesame oil, jojoba oil, □-tocopherol including a mixture of Tween 80 and Span 80 (5:1) (10% w/w) as an emulsifier and NE base (NE without AG) were formulated and prepared using high-pressure homogenization technique. Both NE base and AG-NE were investigated their physical stability after preparation by centrifugation and observed the appearance of phase separation. Their droplet size, zeta potential and FTIR spectra were determined. Cytotoxicity of AG and AG-NE to non-melanoma skin cancer cells (A-431 cells) and normal skin fibroblast cells (HFF-1 cells) were investigated. The apoptosis induction of A-431 cells by AG and AG-NE was estimated using flow cytometry technique. The results showed that NE base and AG-NE had droplet size in a nanometer range. They had low viscosity with the flow behavior consistent with the Newtonian liquids. Although their zeta potential values were slightly low, they showed good physical stability against centrifugal force. AG and AG-NE were not toxic to HFF-1 cells, but they could induce apoptosis of A-431 cells with IC_{50} of 25.83 μg/ml and 58.32 mg/ml, respectively. Therefore, AG-NE has become possible to use for further investigation of its efficacy and safety in animal models and clinical trials.

Keywords: Andrographolide, Nanoemulsion, Non-melanoma skin cancer, Apoptosis

PT 2

Development of ganciclovir-loaded liposomes incorporated ion-sensitive in situ gels for ophthalmic applications

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Ganciclovir (GCV) is one of antiviral drugs used for treatment of cytomegalovirus (CMV) retinitis. GCV is currently available in the drug market as an injectable drug and an ophthalmic gel. Unfortunately, GCV injection sometimes causes serious systemic side effects and trauma at the injected organs, whereas the ophthalmic gel is difficult to administer. It must be applied on the lower conjuctival sac. Furthermore, it is suitable for relieving CMV infection in the anterior segment of the eye only. Consequently, the GCV ophthalmic preparation, which can be instilled into the eye for treatment of CMV infection in anterior and posterior eye segment in particular, should be developed. The aims of this study were to develop ophthalmic GCV-loaded liposomes (GCV-LPs) incorporated ion-sensitive in situ gels (GCV-LPs in situ gels) and to investigate their physicochemical properties. GCV-LPs targeting posterior eye segment were prepared by reverse-phase evaporation technique. Their particle size and zeta potential were measured by a Zetasizer. They were characterized by differential scanning calorimeter (DSC) and Fourier transform infrared spectroscopy (FT-IR) technique. After they were concentrated, GCV-LPs were incorporated in ionic-sensitive in situ gels containing various concentrations of sodium alginate and polyvinylpyrrolidone K30. The release of GCV to simulated tear fluid (STF) was performed by using modified Franz diffusion cells. Cytotoxicity of GCV-LPs and GCV-LPs in situ gels to human retinal (ARPE-19) cells and rabbit corneal (SIRC) cells was determined by MTT assay. It was found that GCV-LPs prepared in this study had particle size of 98 nm with a zeta potential of -27 mV. DSC Thermograms and FT-IR Spectra indicated that GCV was entrapped in GCV-LPs in an amorphous form with chemical interactions with the compositions consisting of the LPs. GCV-LPs were not toxic to ARPE-19 cells. The ionic-sensitive in situ gels showed phase transition after exposure to STF at 37 °C. However, their gelling capacity was dependent on the concentration of the gelling agents and ratios of sodium alginate to polyvinylpyrrolidone K30. After incorporation of GCV-LPs in the optimized in situ gel containing sodium alginate and polyvinylpyrrolidone K30 at a ratio of 1.5 to 0.5 (%w/w), the obtained product showed liquid characteristics with a viscosity of 20 cps at 25 °C. It became gel for 25 seconds at 37 °C before completely dissolving. It was not toxic to SIRC cells. The release profile of GCV from the GCV-LPs in situ gel obeyed the Higuchi's kinetic release model with a rate of 3.28 mg/min$^{1/2}$. Therefore, GCV-LPs in situ gel became possible for using in further study to investigate its efficacy and safety in the animal models.

Keywords: Ganciclovir; Liposome; Ophthalmic drug delivery; In situ gel; Posterior segment of the eye

PT 3

Optimization of production process of nanoemulsions containing alpha mangostin from mangosteen rinds by high pressure homogenization

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This study was aimed to investigate the effect of production parameters on physicochemical properties of nanoemulsion (NE) containing alpha-mangostin (AMG) (AMG-NE) and to determine anti-inflammatory activities and skin toxicity of the obtained AMG-NE in cell lines. Blank NEs (NEs without AMG) were prepared by high-pressure homogenization technique with varying in 3 production parameters, i.e. pressures, numbers of homogenization cycle and temperatures following the face-centered central composite design. They were observed the effect of these parameters on their droplet size and polydispersity index (PDI). The optimized production parameters were used for investigation of production scale-up on droplet size and PDI of AMG-NEs. A representative AMG-NE was determined its anti-inflammatory activity and skin toxicity in murine macrophage (RAW 264.7) cells and human skin fibroblast (HFF) cells, respectively. The results showed that the pressure, the number of homogenization cycle and the temperature significantly affected droplet size and PDI of Blank NEs. After addition of AMG to the optimized Blank NE, the obtained AMG-NE had comparable droplet size and PDI to those of Blank NE. However, an increase in batch size of AMG-NE production by using optimized production parameters caused changes in particle size and PDI but they were still within acceptable criteria. AMG-NE showed anti-inflammatory activity with IC50 of 7.908 μg/ml. In addition, HFF cells could tolerate AMG-NE at various concentrations with %cell viability more than 70%. These suggested that AMG-NE could be prepared for large scale by using the optimized production parameters. Furthermore, AMG-NE had anti-inflammatory activity without toxicity to human skin cells. AMG-NE thus had a potential for using in further investigation of the efficacy and safety in animal models and clinical studies.

Keywords: Production, Nanoemulsions, Alpha-mangostin, High-pressure homogenizer, scale-up

PT 4

The Effect of Hydrophilic Polymers on Release Profiles of Metronidazole Films

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Thin film is one of the promising drug delivery systems that has drawn immense interest in recent years and has become an alternative delivery system for local treatment of periodontitis. The objective of this study was to determine the effects of type and concentration of hydrophilic polymers, i.e. hydroxypropyl methylcellulose (HPMC), sodium carboxymethyl cellulose (SCMC), hydroxyethyl cellulose (HEC) and polyethylene glycol MW6000 (PEG) on the release profiles of metronidazole films. The films were prepared by hot melt extrusion in total of 20 formulations. Each formulation contained 10 %w/w metronidazole as an active drug. In addition, 5 %w/w glyceryl monostearate and polycaprolactone 70 – 82 %w/w were used as a plasticizer and a polymer matrix, respectively. The hydrophilic polymers were varied from 3, 6, 9, 12 and 15 %w/w. The physiochemical properties of the films i.e. weight variation, thickness variation, content uniformity and drug release were investigated. As a result, the obtained films were thin round white glossy sheets with 6 mm in diameter. An average weight was 6.06 ± 1.01 mg, an average thickness was 317.87 ± 3.15 □m and an average drug content was 97.42 ± 6.39 %. The drug release study showed that the films could release metronidazole over 48 hours continuously. The films containing SCMC had rapid drug release rate while the films containing HEC had the slowest drug release rate. Moreover, an increasing of polymer concentration affected in slower drug release rate. The release coefficient of the film was closed to 0.5, indicating that the release mechanism of this films followed Fickian diffusion. This result shows that diffusion is the primary mechanism of drug release.

Keywords: metronidazole, films, hydrophilic polymer, drug release mechanism

Pharmacognosy & Chemistry (PC)

Poster No.	Presenters	Title
PC 1	Rinnara Krongsil and Waritsara Chaichanasap	Effect of structural modification of isoquinoline derivatives on cytotoxic activity
PC 2	Suwapat Chatwachirawong and Panadda Sangyang	The α-glucosidase inhibitory activity and chemical constituents of Neem (*Azadirachta indica*) leaves extracts
PC 3	Napasorn Ransibrahmanakul and Nontapat Sarovath	Determination of insecticidal activity and development of prototype product against American cockroach from *Stemona collinsiae* root extract
PC 4	Nawakarn Chitchai and Apissara Mingmuang	Analytical method development and validation of new ion-pair reagent for quantitation of Aspirin and Salicylic acid by HPLC method
PC 5	Ratchaneewan Aunpad	Structural and Biological Features of A Novel Plant Defensin from *Brugmansia* x *candida*
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PC 7	Thanyaphat Sirilertpitak and Thitiyaporn Choosuwan	The β- secretase inhibition activity of various colors water lily petal extracts

PC 1

Effect of structural modification of isoquinoline derivatives on cytotoxic activity

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Cancer is the leading cause of death worldwide and increasing incident and resistant rate. Presently, several researchers attempt to find out new effective drugs or new targets. Lophocladine B was one example derived from marine organisms which inhibit depolymerization process of microtubule. In the previous study, structure of lophocladine B was modified to isoquinoline scaffold and obtain most potent cytotoxicity agent, compound **2** and **7**. The binding mode of the synthesized compound in tubulin receptor was also examined. The aims of this research were study the structural modification of isoquinoline to evaluate cytotoxicity activity. The chemical reactions were applied such as Sonogashira coupling reaction; and click reaction. All eight synthesized compounds were characterized and elucidated by many approaches; melting point, IR spectroscopy, and ^{1}H-NMR. All compounds were evaluated for cytotoxic activity in HeLa and MRC-5 cell and calculated for IC_{50} values. Furthermore, binding interaction between microtubule and synthesized compound were investigated by molecular docking approach. The results had shown **RW9** were the most potent cytotoxic activity with IC_{50} 67.07 μM compared with compound **2** and **7** which had IC_{50} 14.34 and 65.15 μM, respectively. **RW9**, compound **2**, and **7** showed less cytotoxicity in MRC-5 cell than HeLa cell. The binding mode from molecular docking results showed the isoquinoline and triazole linker were critically required for microtubule inhibition activity and we assume that side chain modification to hydrogen bond acceptors can improve binding affinity. Therefore, this study provided information of cytotoxic activity on cancer cells and the results of computational docking assisted for design and development of further new anticancer agents.

Keywords: isoquinoline, synthesis ,anticancer, structural modification, molecular docking

PC 2

The α-glucosidase inhibitory activity and chemical constituents of Neem (*Azadirachta indica*) leaves extracts

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Neem *or Azadirachta indica* A.Juss (Family Meliaceae) is widely distributed in Thailand and is commonly used as food for a long time. According to traditional medicine, it has been utilized as antipyretic, antiemetic, antidiarrheal, hemorrhoid treatment, antihelminthic and tonic herb. The aim of this study was to determine the α-glucosidase inhibitory activity and the constituents from Neem (*Azadirachta indica*) leaves extracts. Eight crude extracts were obtained from maceration then subsequent solvent partitions and soxhlet extraction with various solvents. The phytochemical test and thin layer chromatography fingerprints of each extracts were determined. All extracts were screened the α-glucosidase inhibitory action. In the results, the crude extract of dichloromethane partition (CEDP) and the crude extract of soxhlet extraction using methanol (CESM) showed a high α-glucosidase inhibition. Further study, the CEDP were isolated by using column chromatography to give 4 fractions (F1 to F4). In the results, F4 exhibited the highest inhibitory action with 82.73% (0.167 mg/mL). Meanwhile, the F1 showed a higher inhibitory action than F2 and F3 with 64.43 % (0.167 mg/mL), 62.46% (0.033 mg/mL) and 52.10% (0.167 mg/mL), respectively. Therefore, Neem has a potential herb for α-glucosidase inhibitory activity. For further research, the CESM and some potent fractions should be studied and the active compounds was clarified for quality control marker.

Keywords: Neem tree, *Azadirachta indica* A.Juss and α-glucosidase

PC 3

Determination of insecticidal activity and development of prototype product against American cockroach from *Stemona collinsiae* root extract

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Stemona collinsiae root have been used in pesticide and vector control for long time. However, the insecticide activity against American cockroach (*Periplaneta americana*) have not been studied. In this study, the insecticidal activity using bait method and repellent activity were tested. Hexane, dichloromethane, ethanol and water crude extract were prepared using reflux extraction method and extractants as hexane, dichloromethane, ethanol and purified water were used. Temperature of the extraction was controlled not more than 70 ^{0}C. The four crude extracts at concentration of 10 mg/cockroach were used for bait method. Ethanol crude extract showed the highest mortality rate as 96.56% corrected mortality while hexane, dichloromethane and purified water crude extracts presented at 3.45%, 68.97% and 44.83% corrected mortality, respectively. Ethanol crude extract at range of concentration $6.25x10^{-3}$- 0.1 g extract/g fructose showed percent of corrected mortality in range 20.69-96.56% and LC_{50} was 0.0233 ± 0.0000 g extract/g fructose. For the repellent test, concentration of dichloromethane crude extract in range 1-10% w/w in cream base could repel American cockroach calculating as 100% repellent activity and this activity had maintained for more than 2 hours.

Conclusion, ethanol and dichloromethane crude extracts showed insecticidal activity via oral administration and repellent activity, respectively. Thus, dichloromethane crude extract at concentration 4% w/w was prepared as active ingredient in repellent cream. Repellent cream could repel American cockroach having duration of repellent activity more than 2 hours with 90% repellent activity

Keywords: Americana cockroaches, insecticidal activity, *Stemona collinsiae, Periplaneta americana*

PC 4

Analytical method development and validation of new ion-pair reagent for quantitation of Aspirin and Salicylic acid by HPLC method

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The Ion-pair chromatography is used for quantitation of aspirin and salicylic acid in The United States Pharmacopeia 37. Sodium 1-heptanesulfonate used as ion-pair reagent was recommended in the USP37. However, the price of sodium 1-heptanesulfonate is high. Sodium citrate has similar properties, is easy to purchase and also cheaper, therefore, it is considered to be a good choice to study. The purpose of this project is to search for a new ion-pair reagent to use instead of sodium heptanesulfonate. To prove this analytical method is appropriate for quantitation of aspirin and salicylic acid. The HPLC analytical method validation was performed by using C18 (4.6 x 250 mm, 10 μm) and mobile phase consisted of 2 g of sodium citrate in a mixture of water: acetonitrile (85:15 %v/v) adjusted to pH 3.4 by glacial acetic acid. The analysis performed at a flow rate of 2 mL/min with UV detector at 280 nm. The retention times were 6.48 and 4.25 min for aspirin and salicylic acid, respectively. Calibration curve were linear (r2=1.00) over the concentration range 0.1-0.9 and 0.005-0.025 mg/mL for aspirin and salicylic acid, respectively. The repeatability and Intermediate precision were within acceptable criteria (%RSD≤2.0). The recovery for aspirin and salicylic acid were found in the range of 98.28- 102.2% and 99.52-100.59%, respectively which demonstrated the accuracy of this method. The LOQ of salicylic acid are 0.013 mg/ml. The proposed method was successfully searched for a new ion-pair reagent to use instead of sodium 1-heptanesulfonate and appropriate used for quantitation of aspirin and salicylic acid.

Keywords: analytical method development, validation, ion-pair reagent, aspirin, salicylic acid

PC 5

Structural and Biological Features of A Novel Plant Defensin from *Brugmansia* x *candida*

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Data from both the laboratory and clinic in the last decade indicate that antimicrobial peptides (AMPs) are widely regarded as potential sources of future antibiotics owing to their broad-spectrum activities, rapid killing, potentially low-resistance rate and multidirectional mechanisms of action compared to conventional antibiotics. Defensins, a prominent family of AMPs, have been found in a wide range of organisms including plants. Thailand is a rich source of plants including medicinal plants used therapeutically, however there is no report of defensin from among these plants. In this study, a novel plant defensin gene, *BcDef*, was successfully cloned from *Brugmansia* x *candida* (Bc). *BcDef* cDNA was 237 bp in length, encoding 78 amino acids with a putative 31-amino acid residue signal peptide at the N-terminal followed by the mature sequence. BcDef shared high sequence identity (78-85%) with Solanaceae defensins and belonged to the class I plant defensins. From homology modeling, BcDef shared a conserved triple stranded β-sheet (β1-β3) and one α-helix (α1) connected by a loop (L1-L3). BcDef1 peptide, designed from the γ-core motifs of BcDef located in loop 3, showed antibacterial activity against both Gram-positive and Gram-negative pathogens with the lowest MIC (15.70 μM) against *Staphylococcus epidermidis*. This peptide affected cell membrane potential and permeability, and caused cell membrane disruption. Moreover, BcDef1 also exhibited antioxidant activity and showed low cytotoxicity against mouse fibroblast L929 cells. These findings may provide an opportunity for developing a promising antibacterial agent for medical application in the future.

Keywords: Defensin, Brugmansia x candida, structure, γ-core motif

PC 6

Synthesis of Bivalent SFTI-1 Microprotein Based on the Diaminopimelic Acid Scaffold and Biological Activities

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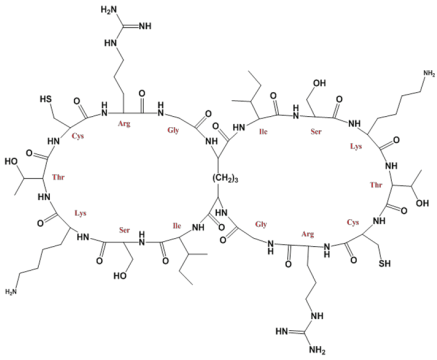
The sunflower trypsin inhibitor (SFTI-1) is a protease inhibitor isolated from sunflower seeds. Its structure is consisted of 14 amino acids and a cyclic backbone. SFTI-1 also demonstrated an ability to inhibit human-β-tryptase, which causes allergic and inflammatory disorders in human. To this work, A bivalent peptide inhibitor derived from SFTI-1 was designed and synthesized through a few branched precursors via a one pot 'double' macrolactamization. The newly synthesized bivalent scaffold was generated using the combination of 2,6-diaminopimelic acid scaffold grafted by two SFTI-I inhibitory epitopes. Finally, this bivalent SFTI-1 will be tested against human- beta tryptase and other serine protease enzymes.



Keywords: Bismacrocyclic peptide, Solid Phase Peptide Synthesis (SPPS) , Sunflower trypsin inhibitor-1 (SFTI-1)

PC 7

The β- secretase inhibition activity of various colors water lily petal extracts

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This research is a study on β- secretase inhibitory effect of various colors *Nymphaea* spp. or known as water lily petal (red, pink, yellow, white, and violet) extracts. The aim of this study is to evaluate the β- secretase inhibition activity of extracts by using FRET assay at excitation wavelength 380 nm and emission wavelength 510 nm. The violet water lily exhibited the highest activity with IC_{50} value of 0.05 ng/ml. The red water lily showed the highest total alkaloids content (4.855 %w/w) on gravimetric methods. According to the results, the β- secretase inhibition effect does not relate to amount of total alkaloid content from various colors of water lily petal which may indicate that the β- secretase inhibition activity may be caused by other important substances or the active alkaloids that is not the most abundant. Therefore, we recommended further investigation is to be conducted to clarify which alkaloid is responsible for β- secretase inhibition activity.

Keywords: *Nymphaea* spp. petal extracts, *Nymphaea* spp. stamen extracts, β- secretase inhibitory effect, alkaloid

Pharmacy Practice (PP)

Poster No.	Presenters	Title
PP 1	Chanokneth Yospanya and Chetthida Sutthiprapa	The effects of printed material compared with educational video on knowledge of cancer patients receiving chemotherapy
PP 2	Fitriya Yusof and Siriprapha Sanguanhong	Pattern and cost of the use of proton pump inhibitors in out-patients at a university hospital
PP 3	Chavalit Varongkriengkrai and Navapol Kanjanaboworn	A study of health literacy in pharmacy service utilization among consumers around Thammasat University

PP 1

The effects of printed material compared with educational video on knowledge of cancer patients receiving chemotherapy

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Over the past decade, the number of cancer patients at Thammasat University Hospital has been dramatically increasing. Hence, there are challenges for healthcare professionals in a hospital to equip cancer patients in terms of knowledge for their self-care and side effects of cancer chemotherapy regimens.

This study is aimed at comparing the effects of printed materials and videos on knowledge of cancer patients receiving five regimens of chemotherapy. The regimens consisted of AC (doxorubicin and cyclophosphamide), CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisolone), RCHOP (CHOP with rituximab) Carboplatin/paclitaxel, and Cisplatin weekly. Cancer patients within the first three cycles of chemotherapy were recruited. In addition, this study also aimed to assess the effectiveness, attitudes and satisfaction of the role of pharmacist advice on cancer chemotherapy knowledge. This study was conducted at oncology short stay department in collaboration with registered nurses and approved by University's ethic committee.

A pre-test was conducted and then rectify correctness after the first test. At the next cycle of chemotherapy, patients were tested for a post-test followed by the effectiveness, attitude and satisfaction questionnaires. The number of cancer patients in this study was 25 patients completing the study during the period of February 2019 to March 2019. Printed materials, videos and structured questionnaires for assessing knowledge of subjects on chemotherapy and patient's satisfaction sheet were developed and approved by expert panel.

The participants were divided into two groups. There were 10 patients in video group and 15 patients in printed material group. The independent t-test comparing the mean pre-test score between 2 group gave indifferent results as same as comparing mean difference scores between 2 group. Comparison pre- and post- test scores within the group demonstrated that both printed material and video had a statistically greater improvement in knowledge scores ($P<0.05$).

Although receiving printed materials or videos had indifferent result in improving knowledge score in patient, each group understood their chemotherapy regimens they received and self-care management. There is still a need for another approach of each material to improve patient's long-term knowledge. Indeed, these efforts may have a positive impact in terms of cancer chemotherapy in cancer patients at Thammasat University Hospital.

Keywords: printed material, videos, pharmacist, chemotherapy, knowledge

PP 2

Pattern and cost of the use of proton pump inhibitors in out-patients at a university hospital

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This study aimed 1) to determine the quantity and cost of prescriptions for proton pump inhibitors (PPIs) in out-patient population at a university hospital. Three clinics were studied, i.e., the orthopedic, the cardiovascular and the gastrointestinal clinics; 2) to identify prescribing of PPIs in orthopedic patients receiving an NSAID or other ulcerogenic agents, who had risk factors for gastrointestinal ulcers. The study was conducted at Thammasat University Hospital. The quantity and cost of the prescriptions of the fiscal year 2016 to 2018 were collected. Three-hundred and ninety-six electronic medical records of the orthopedic outpatients were randomly selected to explore the risk factors in patients receiving co-prescriptions of a PPI and an NSAID or other ulcerogenic agents. Proportion of the patients in whom a PPI may be prescribed against gastro-prophylaxis criteria was determined. Quantity and cost of the prescriptions were estimated.

The results showed the highest volume of PPIs prescription were from the orthopedic clinic (45.96%), followed by the cardiovascular (32.86%) and the gastrointestinal (21.17%) clinics. The most frequently prescribed PPIs was omeprazole (77.34%) followed by lansoprazole (10.76%). The cardiovascular clinic had the highest cost of PPIs prescribing (19,156,380 baht; 45.75%) to which lansoprazole was contributed. The corresponding figures for the gastrointestinal and the orthopedic clinics were 16,154,042.50 baht (38.58%) and 6,559,920 baht (15.67%), respectively. Among the orthopedic patients studied, 28.54% (113/396) may be receiving a PPI without the gastro-prophylaxis criteria. This accounted for 20.21% of the amount of PPIs prescribing and 11.38% of the cost.

In conclusion, the orthopedic clinic had the highest volume of PPIs prescribing. The cardiovascular clinic generated the highest cost. Co-prescriptions of a PPI and an NSAID or an ulcerogenic agent were not in accordance with the gastro-prophylaxis criteria in over 1 in 4 of the orthopedic patients.

Keywords: Proton Pump Inhibitors (PPIs), Prescribing, Cost, Quantity, Gastro-prophylaxis

PP 3

A study of health literacy in pharmacy service utilization among consumers around Thammasat University

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Introduction: Health literacy is an important factor driving consumers to achieve good health. Most consumers tended to use drugstore when they have minor illness. Drugstore services consisted of history taking, problem identification, appropriate drug selection and patient education. Adequate health literacy had a crucial role as it indicates consumer's basic understandings and positive patient-pharmacist communication ensuring efficacious and safe drug utilization.
Purpose: Objectives of the study were to 1. Assess health literacy in pharmacy service utilization among consumers around Thammasat University 2. Compare mean difference between demographic information and health literacy in pharmacy service utilization score.
Method: This study was a survey research. Data was collected in 396 subjects including students, teachers and personnel in Thammasat University using questionnaire derived from literature review. Questionnaire consisted of demographic information (6 questions), consumer's health information reporting behavior during history taking process (14 questions), attention to essential information consumers should receive from pharmacist (10 questions). Data were analyzed by descriptive statistics. Mean difference between demographic information and health literacy in pharmacy service utilization score were compared.
Results: Majority of subjects (47.98%) had good health literacy (mean health literacy score 3.51 - 4.50). Subjects agreed the most with "reporting drug allergy will elevate safe drug utilization since pharmacist won't prescribed that drug" got 4.74 scores out of 5.00. Health information least reported by consumers are past medications during medication history interview which scores 3.92. Demographic information could lead to health literacy score difference in some questions, but no significant difference between demographic information and mean health literacy score had been found.
Conclusions: Our subjects mostly had good health literacy and no significant difference between demographic information and mean health literacy score had been found. This paper suggests universities' community pharmacy store giving priority to educate consumers about pharmacy services process, information reporting during history taking process and essential information consumers should receive from pharmacist in order to maintain consumer's health by effective and safe drug utilization.

Keywords: health literacy, drugstore, pharmacy service, history taking

Pharmaceutical Administration (PA)

Poster No.	Presenters	Title
PA 1	Pakawat Keetawattanakul and Nuntawan Loessaksrisakul	Factor Influencing Stroke Treatment Expenditure at Phramongkutklao Hospital
PA 2	Chayanis Tongsri and Wanwarat Aree	Drug store licensee's perception and opinions toward conducting business as juristic person
PA 3	Varisara Jareanviriyaphab and Totsaporn Loksantisuk	Online marketing promotions of dietary supplements in accordance with Thai law

PA 1

Factor Influencing Stroke Treatment Expenditure at Phramongkutklao Hospital

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Introduction: Stroke is one of a major global health problem. In Thailand, the mortality rate of stroke patients has been increasing every year. Information on factors affecting cost of medical care is necessary for hospital financial status management but the studies in Thailand are still limited.

Purpose: The aim of this study is to determine the factors influencing stroke hospitalization cost at Phramongkutklao Hospital.

Method: A retrospective analytical study was conducted among stroke inpatients who were admitted during the financial year 2017 at Phramongkutklao hospital, identified by ICD-10. The data was collected form Electronic database & Electronic medical records. Multiple regression analysis was used to determine the association between the hospitalization costs and factors that influenced the costs in term of a correlation coefficient. All statistical test were performed using SPSS version 24.0. The methodology was approved by the ethical committee of Institutional Review Board Royal Thai Army Medical department (IRBRTA).

Results: Among 272 in-patients with stroke, the proportion with ischemic stroke, hemorrhagic stroke, transient ischemic attack were 53.3%, 41.5%, and 5.2%, respectively. While the average cost: 136,643 ± 211,005 THB; the median 52,854 THB, the interquartile range 120,233 THB. 57% of the patients were male and their mean age was 69.2 ± 14.2 years, the mean length of stay (LOS) was 25.6 ± 40.2 days. Multiple regression analysis among 13 independent factors revealed that, female patients, had surgery, had a nosocomial infection, use of ventilator, and prolonged LOS had significant positive correlation with stroke hospital costs. (R-square = 0.788)

Conclusions: Surgery, use of ventilator, nosocomial infection, and LOS are the factors related to the stroke treatment cost which the hospital can control the use of resources efficiently.

Keywords: Stroke, factor, hospital cost, inpatients, diagnosis related groups (DRGs)

PA 2

Drug store licensee's perception and opinions toward conducting business as juristic person

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Drugstore business in Thailand can be divided into 2 types, non-juristic person and juristic person. Since 2016, the government has set supporting tax policies as an attempt to promote changing non-juristic person drugstores to juristic person drugstores in a form of limited company. The objectives of the study were to examine Thai drug store licensees' perception and opinions toward conducting business as juristic person. The study was divided into 2 parts. Part 1 was a survey research, collected data through postal questionnaire. Five hundred and sixty six samples were selected from 2016 Thai drugstore licensees which only included licenses that classified as type 1 drug store according to Drug Act B.E. 2510. Part 2 was a qualitative research by a structure in-depth interview. Four juristic person drugstores in a form of limited company were selected as samples. The collected data was analyzed and summarized using descriptive and analytical statistics by Chi-square test and Fisher's exact test. Part 1 of the study got 70 responses consisted of 61 non-juristic person drugstores, 6 juristic person drugstores from the beginning and 3 juristic person drugstores that used to conduct the business as non-juristic person before. The findings indicated that majority of the respondents perceived 'the financial statement helps you to understand your business's status better' and 'expenditure and taxs calculation of non-juristic person and juristic person are different' **(**95.7% and 92.8% respectively**).** The respondents perceived the least on 'non-juristic person and juristic person are supported by the government differently' (51.5%). The findings from non-juristic person respondents showed that 83.6% rated 'agility in business management and finance' and 80.3% rated 'agility in paying taxes' as importance reasons why they chose to conduct business as non-juristic person. 38.6 % and 34.1% rated very-high and high satisfaction respectively in conducting business as non-juristic person. 88.6% didn't have a thought to change their business type to juristic person. Furthermore, status of the respondents (being pharmacist or not) had a statistically significant association with perceptions of 'non-juristic person and juristic person are supported by the government differently' and with choosing to be non-juristic person because 'reducing obstacles in providing the financial statement and hiring auditors'. The findings from juristic person respondents that used to conduct the business as non-juristic person before showed that 66.7% of them rated 'changing standard deduction of 80% to 60%' and 'allowing 200% expenditure deduction for 5 accounting periods for juristic person registration expenditure, financial statement expenditure and hiring auditor expenditure' as important policies from government that convinced them to change their business type to juristic person. The results from in-depth interview showed that majority of the samples chose to conduct business as juristic person because they thought it was better to register as juristic person, while the government started to implement supporting policies, than facing difficulties in changing business type later. Moreover, it also benefited their business activities. Overall, their opinions on the policies were positive. They thought the policies benefited both drugstores and government by increasing convenience of business type changing and paying taxes. Moreover, they thought the juristic person drugstores' obstacles were providing financial statements and documents. In conclusion, non-juristic drugstores' perception toward conducting business as juristic person were still limited and majority of them didn't have a thought to change business type. Even though there were obstacles from conducting business, juristic person drugstores acknowledged benefits from the government's supporting policies.

Keywords: Drug store licensee, Juristic person, Perception, Opinion, Conducting drugstore business

PA 3

Online marketing promotions of dietary supplements in accordance with Thai law

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Marketing promotion through online channels is popular for selling the dietary supplement products. This study aims to analyze various forms of these promotion methods and their compliance with Food Act, BE 2522. Top 100 products under the dietary supplement category from 3 websites, Lazada Shopee 11Street , were selected as samples. Altogether 300 samples were recorded on 5th November 2018. Descriptive and analytical statistics by Chi square and Fisher's exact test with SPSS version 24 were employed. The results shows that among 300 samples under the category of dietary supplement, 31 samples were drugs or medical foods and only 269 samples (89.7%) were dietary supplement products. Subgroup analysis on their components revealed that the most popular, which accounted for 53.6%, were plants such as grapes, acerola cherries followed by vitamins (40.5%) such as Vitamin C, Vitamin B, other substances (40.1 %) such as collagen, *Ganoderma lucidum*, *Cordyceps sinensis*, minerals such as Zinc, Calcium (27.1%) and not showing significant substances (15.9%). All of these online advertisement were not approved by the Food Act, BE 2522, Section 41 and accounted for 93.3% of the claims. Violation of the Food Act, BE 2522, Section 40 was found that they were changes in the body's 68.4%, disease treatment 63.2% and beauty 61.3%. The relationship between the components and efficacy claims was found statistically significant, as follows: grapes and acerola cherries with claims of disease treatment; Vitamin E, *Ganoderma lucidum* and *Cordyceps sinensis* with claims about sexual maintenance; Vitamin C, Zinc, grapes, acerola cherries and collagen with beauty claims. In terms of promotion, it was found that the price discount was the most common sales promotion accounted for 85.5% followed by 48% of free delivery and 10.1% of free gift. In summary, the efficacy claims of dietary supplements through online marketing promotion were found violation of the Food Act, BE 2522. The FDA should consider of the effective strategies to protect the consumers from misunderstanding.

Keywords: online marketing promotion, dietary supplement, claim

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