

## Scientific Posters Session 1 Abstracts (#101-133)

Thursday, May 29  
11:45 a.m. - 1 p.m.

### 101. Analysis of multiclass antimicrobial residues in feed water by liquid chromatography and ion trap mass spectrometry\*

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**Background:** This project was the collaboration between Mahidol University and Veterinary Drugs Assay Division (VDA), Department of Livestock Development, Thailand to ensure food safety measurement. According to EU Commission Regulation residues of antimicrobials are not allowed in any food products due to their toxicity. Thus, there is an urgent need for a confirmatory method with higher sensitivity for simultaneous analysis these residues.

**Objective:** This work aimed to develop a liquid chromatography-mass spectrometric method (LC-MS) for the quantitation of nitrofurans (e.g. nitrofurazone (NFZ), nitrofurantoin (NFT), furazolidone (FZD) and furaltadone (FTD)), nitroimidazoles (e.g. metronidazole (MNZ), ronidazole (RNZ) and dimetridazole (DMZ)) and chloramphenicol (CAP) in animal feed water.

**Methods:** Optimization of solid phase extraction (SPE) procedures (e.g. sorbent and eluting solvent), HPLC conditions (e.g. mobile phase composition and gradient elution) and MS parameters were performed. The method was validated and applied to analyze the drug residues in forty feed water samples collected from animal farms in Thailand.

**Results and Discussion:** HPLC analysis was performed on a Prodigy ODS-3 column, 2.0 × 150 mm, 5 μm at a flow rate of 0.2 mL/min, column temperature of 40°C, and an injection volume of 10 μL. After an off-line SPE by the OASIS HLB cartridges (with an enrichment factor of 400), the eight antimicrobials were separated in 18 min using a gradient elution of acetonitrile in acidified water (pH 5.0). MS detection was by an ion trap MS coupled with electrospray ionization (ESI) in tandem MS mode (MS/MS) using the nebulizer gas at 35 psi, drying gas at 9 L/min and drying temperature of 325°C. Method linearity was good ( $r^2 = 0.979 - 0.999$ ) with acceptable precision (%RSDs = 3.4 to 26.6%) and accuracy (%recovery = 88.4 to 110.1%). Very low limits of detection (LOD) and quantitation (LOQ) were achieved in ranges of 0.002 to 0.06 μg/L and 0.005 to 0.25 μg/L, respectively. The established method was successfully employed to analyze 40 feed samples collected by the VDA.

**Conclusion:** A HPLC-MS method has been established for residue analysis of eight multiclass antimicrobial drugs at sub-ppb levels in feed water. In addition to its high efficiency, the method is simple, fast and cost-effective, which can be applied to routine analysis in regulatory departments, where sample throughput and sensitivity are priority.

\*This work has been previously published in the *Journal of Chromatography B* 2014 (945-946): 31-38.

## 102. Click Chemistry, 1,2,3-Triazoles as Selective and Potent $\alpha 7$ Nicotinic Acetylcholine Receptor Agonists\*

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**Background:** The  $\alpha 7$  nicotinic acetylcholine receptor (nAChR) is a member of pentameric ligand-gated ion channel (LGIC) receptors and a novel candidate target for treatment of Alzheimer's disease, schizophrenia, other CNS disorders, along with peripheral pain and inflammation. Previous *in vitro* screening of 1,2,3-triazole derivatives has identified lead compounds (TTIn-1) possessing  $\alpha 7$ -nAChR agonistic properties.

**Objective:** To enhance the selectivity and potency profiles of lead compound by structure based drug design.

**Methods:** Approximately 50 molecules were designed based on the binding poses of  $\alpha 7$ -nAChR agonists obtained from x-ray crystal structures and previous *in vitro* screening results. Homologous proteins of nAChR extracellular domain from *Aplysia californica* (Ac) and *Lymnaea stagnalis* (Ls) acetylcholine binding proteins (AChBPs) are expressed and purified as templates for drug design, binding affinity assays, and x-ray crystallography. Lead optimization of 1,2,3-triazole products started with an azide building block modification to obtain a suitable cationic center followed by a variation of alkyne building blocks to fit a hydrophobic region in the binding pocket of  $\alpha 7$ -nAChRs. All modified compounds were synthesized by copper-catalyzed azide-alkyne cycloaddition (CuAAC) or click chemistry. The pharmacological properties were evaluated by binding affinity and functional assays using the AChBPs and fluorescent cell-based detection in LGIC expressed cell lines.

**Results and Discussion:** Both selectivity and potency profiles of the modified compounds were superior to the lead molecule. IND1, a six-membered monocyclic ring with a 2 methylene linker, is the most potent and selective  $\alpha 7$ -nAChR agonist in this series. Its potency is the same as PNU-282987 and 3-fold greater than the lead compound with high selectivity for  $\alpha 7$ -nAChR over the  $\alpha 4\beta 2$ -nAChR and 5HT<sub>3A</sub> receptors. Three compounds (IND8, QND2, and QND8) from a quinuclidine azide building block are the most potent compounds. Their potencies are equal to PHA-543613 increased 20-fold compared with lead compound, where the selectivity is maintained.

\*This work was presented at the 8<sup>th</sup> Annual Drug Discovery for Neurodegeneration Conference: An Intensive Course on Translating Research into Drugs, Miami, February 2-4, 2014.

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## 103. An Economic Burden of Central Nervous System Inflammatory Demyelinating Disorder Patients In Thailand: A Preliminary Report on Patients' Perspective

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**Background:** Central Nervous System Inflammatory Demyelinating Disorder (CNSIDD) is a burden disease affecting patients' quality of life and their families, though it considers as rare disease in Thailand. However, the burden from opportunity cost and out of pocket expenses due to CNSIDD has never been explored in Thailand yet.

**Objective:** This study aimed to evaluate the economic burden of CNSIDD on patients' perspective for each disease state and type and to determine the correlation of economic burden with disease severity and quality of life.

**Methods:** One hundred thirteen patients were recruited at MS clinic in Siriraj hospital, Bangkok during September 2011 through April 2013. Interviews were conducted with patients and/or families on cost related to hospitalization (e.g., food, traveling, etc.), facility modification, homecare cost and other alternative treatment cost. Descriptive statistical method was used to analyze the data.

**Results:** The average age of patients was 40 years and disease duration was 3.3 years. The annual number of outpatient visits was 5.9 times and patients spent 11.4 hours per visit. Annual total direct non-medical cost per patient was \$US1,979, informal care cost was \$US711 (95% CI: 420 to 1012), facility modification was \$US423 (95% CI: 137 to 710), cost related to hospitalization was \$US276 (95% CI: 199 to 352), while annual total indirect cost was \$US2,839 (95% CI: 983 to 4,695). The overall cost was significantly correlated with quality of life score ( $p=0.01$ ). The overall cost of CNSIDD patients was significantly increased with disease severity, while quality of life negatively correlated with disease severity significantly.

**Discussion:** The major part for overall cost was an indirect cost due to earning lost followed by an informal cost and cost related to hospitalization. The economic burden of CNSIDD on patients' perspective was high as relative to the gross domestic product (GDP) due to earning lost and out of pocket expenses which was correlated with patient disability and disease severity.

**Keywords:** Cost of illness, Cost, Quality of life, Multiple sclerosis, Thailand

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#### 104. Chemical stability determination of *Cassia fistula* pod pulp extract by TLC- densitometric method

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**Background:** *Cassia fistula* Linn. (Fabaceae) is a medium-sized tree, native to Southern Asia. The ripe pod pulp has long been used as a traditional laxative drug due to anthraquinone glycosides constituent. The major anthraquinone derivative in the pulp is rhein.

**Objective:** The aims of our study was to develop and validated a TLC densitometric method for quantitative analysis of rhein content in the *C. fistula* pod pulp extract stored at different conditions (in

glass vial and in aluminum foil, at room temperature and at 40°C) for 3 and 6 months. Physical characteristics e.g. color, odor and solubility of the extracts were also determined.

**Methods:** The pulp from the ripe pods of *C. fistula* was extracted by decoction. The filtered extract was evaporated to dryness to yield a crude extract. Three batches of the crude extract were stored in glass vials and in aluminum foil bags under accelerated condition and at room temperature as described in ASEAN guideline on stability study of drug product. For TLC densitometric method, the separation was carried out on an aluminum sheet of silica gel60F<sub>254</sub> using ethylacetate/methanol/water (100:17:10, v/v/v) as a mobile phase. The wavelength of the detector was set at 435 nm. The method was validated by evaluation of linearity, precision, accuracy, limit of detection (LOD) and limit of quantitation (LOQ).

**Results:** The proposed TLC densitometric method showed acceptable validation parameters. The correlation coefficient value was  $\geq 0.999$ , confirming the linearity of the method. The R.S.D value was lower than 2% and the average recovery of rhein was 101.21%, indicating the precision and accuracy of the method. The content of rhein in the crude extract remained more than 95% (95.22%-100.20%) of the initial content for all storage conditions. From the results, there was no significant change of the extracts and the acceptance criteria were met. Regarding physical attributes, all pod pulp extracts had brownish-black with characteristic odor and mild sweet taste. After 6 months of storage under previously mentioned conditions, no significant changes were found.

**Discussion:** TLC densitometric method is a simple, rapid, sensitive and economical alternative method for a routine analysis of rhein content in *C. fistula* pod pulp extract. The pulp extracts were chemically stable after 6 months of storage at room temperature and at 40°C. This indicated a good stability of the pod pulp extract which could potentially be developed as a herbal laxative drug.

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### 105. HPLC analysis of rhein content in *Cassia fistula* pod pulp

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**Background:** *Cassia fistula* Linn. belongs to Fabaceae family. In Thai traditional medicines, the ripe pod pulp has long been used as a laxative drug. The major anthraquinone derivative in the ripe pods is rhein. For the quality assessment of herbal preparation, HPLC is the most widely used method for both quantitative and qualitative analysis of plant materials .

**Objective:** The aims of this study are to develop and validate HPLC method for quantitative analysis of the rhein content in the pod pulp of *C. fistula* and to perform analysis of its HPLC fingerprints.

**Methods:** The pulp from the ripe pods was extracted with distilled water by decoction. The filtered extract was evaporated to dryness on a water bath to yield a crude decoction extract. Instrument and Chromatographic condition: HPLC method was performed on a Shimadzu SCL-10A HPLC system, equipped with a model LC-10AD pump, UV-vis detector SPD-10A. A Hypersil® BDS C-18 column (4.6 x 150 mm, 5 µm size) with a C-18 guard column was used. The isocratic mobile phase was 0.5% aqueous acetic acid solution and methanol (40:60). The total running time was 30 min and a flow rate was 1.0 mL/min. The UV detector monitored at 435 nm while the injection volume was 20 µL. The method was validated by evaluation of linearity, precision, accuracy, limit of detection (LOD) and limit of quantitation (LOQ) according to the International Conference on Harmonization guideline, ICH, 1996.

**Results:** The proposed HPLC method showed acceptable validation parameters. The correlation coefficient value was  $\geq 0.999$ , confirming the linearity of the method. The R.S.D value was lower than 2% and the average recovery of rhein was 99.12%, indicating the precision and accuracy of the method. Average yield of the crude extract was 64.21% wet weight while extract ratio was 1.6:1. The content of rhein in the crude decoction extract was  $0.0926 \pm 0.0073$  %w/w while in the fresh pod pulp was  $0.0594 \pm 0.0047$  %w/w. HPLC chromatograms of the extract showed similar pattern with a major peak of rhein at retention time of 13.6 minute.

**Discussion:** The HPLC method for quantitative analysis of rhein content in *C. fistula* pod pulp is reliable and accurate with validated repeatability, reproducibility and recovery testing. The proposed HPLC quantitative analysis would be useful for quality assessment and standardization of *C. fistula* pop pulp raw materials and products containing its extracts.

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### 106. Evaluation of rhein chemical stability in *Cassia fistula* pod pulp extract by HPLC

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**Background:** *Cassia fistula* Linn. (Fabaceae) is an ornamental plant widely grown in tropical and subtropical area. The ripe pod pulp has long been used as a traditional laxative drug due to anthraquinone glycosides content. Rhein is the major anthraquinone in the pod pulp.

**Objective:** This study was aimed to evaluate chemical stability of *C. fistula* pod pulp extracts which kept under the storage condition as described in ASEAN guideline on stability of drug product.

**Methods:** The ripe pod pulp of *C. fistula* was extracted by decoction method. HPLC method was developed and validated for quantitative analysis of rhein content in these extract. Three batches of crude extract were stored for 6 months under accelerated (at 40°C) and real time storage conditions.

**Results:** The proposed HPLC method showed acceptable validation parameters and the content of rhein in the decoction extract was remained more than 95% (96.88% - 99.62%) of the initial amount for all storage conditions. From the results, there was no significant change of the extracts and the acceptance criteria were met.

**Discussion:** The extract from *C. fistula* pod pulp had good stability and suitable to be further developed as an alternative laxative product.

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### 107. Stability study on antioxidant activity of standardized *Cassia fistula* pod pulp extract

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**Background:** *Cassia fistula* Linn. (Fabaceae) is a medium-sized, deciduous tree widely grown in tropical and subtropical areas as an ornamental plant. It is native to southern Asia and can be found in every part of Thailand. In Ayurvedic medicinal system, *C. fistula* has been used against various disorders such

as haematemesis, pruritus, diabetes and other ailments. Various biological activities of *C. fistula* pods such as antibacterial, antifungal, antioxidant, antileishmanial, and hypolipidemic properties were reported.

**Objective:** The aim of this study is to determine antioxidant activity of standardized *C. fistula* pod pulp extract at various storage conditions of stability study.

**Methods :** The pulp from the ripe pods of *C. fistula* was extracted by decoction method. The crude extract was stored in glass vials and in aluminum foil bag under the condition described in ASEAN guideline on stability study of drug product. For antioxidant activity assay, the extract was determined using DPPH scavenging assay and ferric reducing antioxidant power (FRAP) method. Total phenolic content of the stored extracts was also investigated.

**Results:** The extract exhibited antioxidant activity with  $EC_{50}$  of  $6.86 \pm 0.56$  to  $9.38 \pm 0.19$  mg/mL by DPPH scavenging assay and  $19.59 \pm 0.16$  to  $21.24 \pm 2.04$  g gallic acid equivalent/100 g extract using FRAP method. Total phenolic content ranged from  $2.50 \pm 0.40$  to  $2.89 \pm 0.50$  g gallic acid equivalent/100 g extract.

**Discussion:** These results would be useful for the development of standardized *C. fistula* extract as pharmaceutical products.

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### 108. Comparison of HPLC and TLC densitometric methods for the quantification of rhein in *Cassia fistula* pod pulp extract

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**Background:** *Cassia fistula* Linn. (Fabaceae) is commonly known as “Khun” and “Ratchapruerk” in Thai. *C. fistula* pod pulp is used in traditional medicine as a purgative/laxative drug. The major anthraquinone derivative in the pod pulp is rhein. Although HPLC is the most widely used method for quality assessment of herbal preparations, it requires high operational cost and skilled operator.

**Objective:** The purpose of this study is to compare the quantitative results obtained by validated HPLC and TLC densitometric methods in the analysis of rhein content in the extracts of *C. fistula* pod pulp.

**Methods:** HPLC Method: A validated HPLC analysis was performed on a Shimadzu Technologies modular model Class VP system. The analysis was carried out using a BDS Hypersil C18 column (150×4.6 mm, i.d. 5 µm) with a BDS Hypersil C18 guard column. The isocratic mobile phase was 0.5% aqueous acetic acid solution and methanol (40:60). The total running time was 30 min and the flow rate was 1.0 mL/min. The UV detector monitored at 435 nm while the injection volume was 20 µL.

TLC Densitometric Method: TLC was performed on an aluminum sheet of silica gel60 F<sub>254</sub> (20 cm x 10 cm). Sample and standard solutions were applied on the plate as 7 mm band with a Linomat V automatic sample spotter (Camag, Switzerland). The mobile phase consisted of ethyl acetate-methanol-water (100:17:10, v/v/v). The plate was developed to a distance of 8 cm in a Camag twin trough chamber. The densitometric scanning was performed by using a TLC Scanner 3 with winCATS software. The wavelength of the detector was set at 435 nm. The sample was applied at 10 µL/spot.

**Results:** The contents of rhein in the six samples of *C. fistula* pod pulp extracts analyzed by both methods were compared. The paired *t*-test showed no statistically significant difference ( $P > 0.05$ ) between the mean contents of rhein performed by HPLC method and TLC densitometric method.

**Discussion:** The proposed TLC densitometric method could be used as an alternative method for the quantitative analysis of rhein content in *C. fistula* pod pulp extract. This method showed several advantages such as simplicity, fast data acquisition, and high efficacy.

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### 109. A Bayesian Multiple Treatment Comparison of Duloxetine, Pregabalin, Gabapentin, Amitriptyline, and Their Combinations for Painful Diabetic Peripheral Neuropathy Based on Pain Reduction Reported in Clinical Trials

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**Background:** Painful Diabetic Peripheral Neuropathy (PDPN) is a developed long-term complication of diabetes mellitus, which is estimated to occur be 7.8 % of the United States population and 12-14% in people over 40 years. According to American Academy of Neurology, numerous medications, including anti-depressants, antiepileptic, and opioids have been suggested as treatment for PDPN.

**Objectives:** The goal of this study was to compare the performance of treatment of painful diabetic peripheral neuropathy (PDPN) — duloxetine, pregabalin, gabapentin, amitriptyline, and their combinations based upon pain reduction reported in clinical trials, and inform a revised treatment algorithm.

**Methods:** Published studies of PDPN treatment through May 2012 were identified from MEDLINE(PubMed) database and extended manual search was conducted based on citations from identified studies. Inclusion criteria was restricted to randomized controlled trials lasting at least 5 weeks and at most 12 weeks and studies examining 30% pain reduction or equivalent. Direct and indirect pairwise odds ratios (OR) were obtained. The study used Bayesian Analysis Using Gibbs Sampling in Windows (WinBUGS) version 1.4.3. and Monte Carlo Simulations to conduct a multiple treatment comparison.

Results are reported in OR with 95% credible intervals (CI) and the median of ranking.

**Results:** There were a total of 10 studies with 23 treatment arms, representing 2,885 subjects enrolled, that were included in the analysis. The results from fix effects model indicated that duloxetine, pregabalin, gabapentin, and co-administration of duloxetine and gabapentin were significantly better than amitriptyline (OR= 3.22[95%CI, 1.54-7.17], OR = 2.53[95%CI, 1.11-5.94], OR = 4.00[95%CI, 1.33-11.69], OR = 2.86[95%CI, 1.09-7.48], respectively). The results from random effects model suggested that only duloxetine and pregabalin were significantly better than placebo (OR = 2.61[95%CI, 1.37-4.95] and OR = 0.97[95%CI, 1.01-3.62], respectively). There was no significant difference between amitriptyline and placebo in either fixed or random effects models. With regard to the median ranking, gabapentin was ranked first, followed by duloxetine, co-administration of duloxetine and gabapentin, pregabalin, placebo, and amitriptyline from the fix effects model.

**Conclusion:** Treatment of PDPN with amitriptyline does not appear to be significantly different from placebo. Duloxetine and pregabalin appear to be better than both amitriptyline and placebo

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### 110. Modulation of drug release kinetics from shellac-based matrix tablets

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The aim of this research was to evaluate the factors and their consequences on mechanism of drug release through fitting with various kinetic models. The matrix tablets containing different amount of shellac (SHL) were prepared by direct compression method and theophylline was selected as a model drug. The tablets were annealed at various temperatures. Kinetics of drug release was investigated in 0.1 N HCl (pH 1.2) and phosphate buffer pH 6.8 by fitting curve with zero order kinetic model, first order kinetic model, Higuchi model and power law equation model, respectively. The result demonstrated that the kinetics of drug release in 0.1N HCl (pH 1.2) and phosphate buffer pH 6.8 were both fitted with Higuchi model and power law equation model. The drug released in pH 6.8 more rapid than in 0.1N HCl (pH 1.2). The value of release exponent (n) in power law equation model had a tendency to decrease when using the high content of SHL and annealed temperature. The main mechanism of drug release in 0.1N HCl (pH 1.2) was well fitted with diffusion process while the mechanism of drug release at pH 6.8 should be the combination of diffusion and erosion.

**Keywords:** shellac, annealing temperature, kinetics of drug release

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### 111. Medicare Outreach Program: Engaging Pharmacy Students Through Service Learning

*Salisa C. Westrick, PhD*

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**Background:** In the United States, prescription drug coverage (Medicare Part D) for Medicare beneficiaries is provided by private plans. These Part D plans vary greatly in terms of their premiums, patient cost sharing, and medication coverage. The plan selection process places a great reliance on computer literacy and can be challenging to many Medicare beneficiaries. The Medicare outreach project is a collaborative project between Harrison School of Pharmacy and Alabama State Health Insurance and Assistance Program and was launched in October – November 2013. A total of 17 enrollment events in 10 counties in Alabama were offered to provide assistance for Medicare beneficiaries in Part D plan selection.

**Objectives:** This program was evaluated in terms of participants' and students' outcomes. The specific objectives were to 1) identify participants' characteristics, preferences and enrollment decisions, and

potential out-of-pocket cost savings and 2) describe pharmacy students' experiences after volunteering at enrollment events.

**Methods:** For enrollment event participants, data were collected using interviewer-administered questionnaire. Potential annual cost-saving was the cost difference between switching to the least expensive plan and continuing with the 2013 plan. For students' reflections, students who interacted with Medicare beneficiaries wrote a paragraph to reflect on their experience. Reflections were coded independently by two coders using ATLAS.TI and merged for comparison. A final coding scheme was determined through discussion and consensus.

**Results:** Of 146 participants, the majority of participants were female (64.3%). The average age was 66.9 (SD = 8.5) and had 5.6 prescription drugs for chronic conditions (SD = 3.8). The majority (59.1%) preferred plans with the lowest overall out-of-pocket cost while some preferred no deductible plans (23.5%) and plans with lowest monthly premiums (17.4%). The potential annual savings per person was \$488.50 (SD = \$879.23). Of those who selected a plan, the vast majority (78.1%) selected the overall least expensive plan while 21.9% would pay \$207.6 (SD = \$204.7) more on average annually. As for students' outcomes, 80 participating students provided written reflections. The majority of students felt the outreach project was a great learning experience that allowed them to apply information learned in class in the real world. They described their experience helping patients and the realization of need for programs like this in the community. The most common theme among the students was aspirations for future participation in enrollment events.

**Discussion:** The program has positive participants' and students' outcomes and should be sustained over time.

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## 112. Sunitinib-treated dendritic cells promoted Th1 phenotype in CD3<sup>+</sup>CD56<sup>+</sup> subset of CIK cells

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Background: CIK cells have been clinically used for the treatment of leukemia and solid tumors. Their anti-tumor cytotoxicity has been intensified after the co-culture with dendritic cells.

**Objectives:** Since the enhancing function of dendritic cells to the anti-tumor cytotoxicity of cytotoxic T cells had been observed and could be further augmented with sunitinib pretreatment, we asked whether the *in vitro* pre-treatment of dendritic cells with sunitinib could drive the anti-tumor activity of CIK cells.

**Results:** We observed a strikingly enhanced cytotoxicity of CIK cells toward HubCCA1, a cholangiocarcinoma cell line. This enhancing action could be attributed to the heightening activity from CD3<sup>+</sup>CD56<sup>+</sup> subset of CIK cells. This activity coincided with the polarization toward Th1 differentiation within CD3<sup>+</sup>CD56<sup>+</sup> subset as evidenced by the heightening expression of interferon- $\gamma$  and T-bet. The Th2

differentiation were lessened as evidenced by decreasing IL-4 and GATA3 expressions; and so were the Th17 differentiation as evidenced by decreasing ROR $\gamma$ t and STAT3 expressions.

**Discussion:** It is concluded that sunitinib-treated dendritic cells drove CD3<sup>+</sup>CD56<sup>+</sup> subset toward Th1 phenotype and enhanced its anti-tumor cytotoxicity.

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### **113. The role of pharmacist in multidisciplinary diabetes care team, Naresuan University Hospital, Thailand**

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**Background:** Inter-professional collaborative work has proved benefit to patients with chronic diseases. Diabetes clinic, Naresuan University Hospital was established in 2011 to deliver a holistic care by the multidisciplinary care team, which included an endocrinologist, three pharmacists, four nurses and one dietitian. Three pharmacists were rotated to work in diabetes clinic.

**Objective:** The aim of this study was to assess the role of pharmacists in a multidisciplinary care team in diabetes clinic.

**Method:** This retrospective study collected data from pharmacist's note. Patients' data were also reviewed from diabetes clinic records, outpatient profiles and computerized medication records between October 2011 and September 2012.

**Results:** Pharmacist activities included medication history interview, drug related problems assessment, and consultation with physician where necessary. Patient counseling was performed following physician appointment if needed. One hundred and forty-seven patients were enrolled to the clinic with the mean age of 52.5±10.3 years. The median hemoglobin A1C (HbA<sub>1C</sub>) was significantly decreased from 8.4 (Interquartile range (IQR); 7.2, 10.2) mg/dL to 7.9 (IQR; 7.1, 9.0) mg/dL ( $p < 0.0001$ ) after registered to the clinic. Non-adherence (62.6%) and adverse drug reaction (42.7%) were the main drug related problems identified. Seventy two percent of patients who used insulin were reviewed for their insulin injection technique by the pharmacists. Incorrect insulin injection technique was found in 40.0% of those using insulin pen and 37.5% of insulin syringe users, which required further follow up.

**Discussion:** Pharmacist plays an important role in the multidisciplinary diabetes care team to detect and resolve drug related problems. These will help the team to provide the quality use of medicines and assist patients to achieve their blood glucose target.

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#### **114. Development of an international PharmD program**

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*University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences*

**Background:** There is an increasing awareness and desire for advancing pharmacy education worldwide to better prepare graduates to provide patient-centered pharmacy care (PCPC). Recognizing this need, we developed the internationally-trained PharmD (ITPD) degree program which is an innovative hybrid PharmD degree curriculum for international pharmacists. The ITPD program, which received ACPE accreditation as an entry-level degree pathway, is modeled after our on-campus entry-level PharmD (ELPD) program and our online post-BS North American Trained PharmD (NTPD) program.

**Objective:** The ITPD program aims to educate and train internationally-based non-PharmD practicing pharmacists to be advocates for PCPC in their communities.

**Methods:** Applicants must demonstrate plans to provide local PCPC. Successful candidates will pass English proficiency tests, and pre-admission secure online, proctored foundational sciences competency exams to establish baseline knowledge from global pharmacy education variances. Admitted students complete an initial one-month on-campus session including orientation, courses in pharmacy skills and US-based patient-centered pharmacy practice, and introductory pharmacy practice experiences. Successful students then enter the online curriculum, allowing for maintaining their home country-based practices while learning integrated clinical sciences and US-practice, through online lectures, Discussions, cases and simulations. Case-based teleconferences develop PCPC skills. The University's online ethics course will provide interprofessional education. Upon successful completion of online coursework, students return to the US for additional professional skills courses, and introductory and advanced pharmacy practice experiences. The program is designed to be completed in three years but allows for flexibility up to six years. The inaugural ITPD class begins Summer 2014.

**Results:** Success of the program will be assessed through demographic (inquiry, applicant, admission, retention and graduation), student learning compared to our other pathways and graduate data. Total inquiries to date = 74 (2009=5, 2010=1, 2011=7, 2012=11, 2013=32, 2014 (Jan-March)=18); applications to date=10. Student learning: Assessed at the school level (performance in identical or like-courses and overall school educational outcomes, across ELPD, NTPD and ITPD programs; admissions criteria compared to performance in didactic and experiential courses) and national level (Pharmacy Curriculum Outcomes Assessment exam).

**Discussion:** Our ACPE-accredited innovative hybrid ITPD curriculum addresses the increasing demand and the global awareness for and complexity of educating pharmacists for PCPC.

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#### **115. Addressing local pharmacy educational needs through use of the FIP Global Competency Framework (GbCF) in an ACPE-accredited internationally-trained PharmD (ITPD) degree program.**

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**Background:** Pharmacy education and professional needs of each country vary. To address individual country pharmacy education needs, while providing global consistency of practice expectations, FIP has put forth the GbCF. Concurrently, we developed an ACPE-accredited ITPD degree program for international pharmacists to be educated in providing patient-centered pharmacy care (PCPC). Admission to the ITPD program requires demonstration of plans to advance pharmacy practice toward PCPC in the applicants' home countries. The learning plans are to be based on local pharmacy practice needs.

**Objective:** To address students' individual and local educational and practice needs through implementation of the GbCF in our ITPD curriculum.

**Methods:** The ITPD curriculum includes a longitudinal Professional Development Portfolio course. In this course, students will identify their individual and local educational needs at the start of the curriculum from one or more behavior(s) for each competency of the GbCF. These GbCF competencies will be included in their online (E-Value™) professional portfolio, in addition to the ITPD program-specific required competencies. Students will document their achievement of each chosen GbCF competency through identification of didactic and experiential activities, with accompanying written reflection on how each activity allowed them to achieve the competency and how this will improve their ability to locally provide PCPC. Students will be assessed on their achievement of each GbCF competency through rubric-guided and individualized review of each submitted activity and reflection. Portfolios will be reviewed after completion of approximately half of the didactic courses have been completed, just prior to advanced pharmacy practice experiences, and prior to graduation, when all must have been achieved. A post-graduation survey sent to each graduate will assess the impact of their education and GbCF competency achievement on their local practice.

**Results:** Results are pending the implementation of the ITPD program in summer 2014.

**Discussion:** Implementing the GbCF into coursework of our ACPE-accredited ITPD program will allow the addressing of local educational needs of our international pharmacist students, while also meeting our accreditation and program goals.

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## 116. Novel preparation technique for floating drug delivery based on sublimation technique

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The present study aims to develop floating drug delivery system which can prolong gastric residence time and increase bioavailability of the active drug. The core tablets containing a model drug, hydrochlorothiazide, were prepared by wet granulation method. Various levels (i.e., 0-50% w/w) of ammonium carbonate (AMC) were incorporated in the core tablets. The tablets were then coated with different amounts of the polyacrylate polymers (i.e., Eudragit® RL100, Eudragit® RS100, and the mixture

of Eudragit® RL100 and Eudragit® RS100 at 1:1 ratio). The coated tablets were kept at room temperature or cured at 70°C for 12 hours. The floating and drug release behaviors of the tablets were performed in simulated gastric fluid USP without pepsin (SGF) at 37°C. The results showed that high amount of AMC induced the floating of the tablets. The coated tablets containing 40 and 50% AMC floated longer than 8 hours with a time-to-float of about 3 minutes. The sublimation of AMC from the core tablets decreased the density of system, causing floating of the tablets. The tablets coated with Eudragit® RL100 floated at a faster rate than those of Eudragit® RS100. Even the coating level of polymer did not influence the time to float and floating time of coated tablets containing the same amount of AMC, the drug release from the tablets coated with higher level of coating the polymer showed the slower drug release. The results suggested that the gas formation and sublimation technique using AMC is promising for the development of floating drug delivery system.

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### **117. Modification of tricomponent and dicomponent poly( $\epsilon$ -caprolactone)-co-poly(ethylene glycol) with methotrexate and folic acid**

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Regarding polymer-drug conjugation, the reaction and drug characteristics are of important since they reflect the possibility of conjugation. In addition, the different composition and the relative length of copolymer block may affect molecular and thermal characteristics of copolymer. Therefore, this study aimed to investigate an appropriate condition including solvent systems and catalysts used for conjugating methotrexate (MTX) and folic acid (FOL) molecules onto poly( $\epsilon$ -caprolactone)-co-poly(ethylene glycol) and to evaluate the molecular and thermal characteristics of MTX- and FOL-conjugated copolymers. Initially, tri- and dicomponent azido-functionalized copolymers were synthesized. Tricomponent copolymers consisted of caproyl, azido-substituted caproyl and ethylene glycol repeating units whereas dicomponent ones contained solely the last two repeating units. In parallel, the terminal alkyne derivatives of MTX and FOL were synthesized by coupling reaction using DCC and DMAP with an addition of NHS for FOL coupling. By click reaction, MTX and FOL were successfully conjugated with tri- and dicomponent copolymers, respectively, without polymer chain degradation. The grafting efficiencies of MTX and FOL were higher than 77% and 68% by using CuI/DBU and CuSO<sub>4</sub>·5H<sub>2</sub>O/sodium ascorbate, respectively. According to the differential scanning calorimetry thermograms, MTX did not change the semi-crystalline property of copolymers except for high % molar grafting whereas the presence of FOL affected thermal properties of copolymer except at 5 molar grafting. The resultant copolymers could be further employed as polymer-drug conjugate delivery system for cancer therapy.

**Keywords:** PEGylated poly( $\epsilon$ -caprolactone), polymer-drug conjugation, click reaction, methotrexate; folic acid

### **118. Herbal formulation adjuvant with antidiabetic drugs for treatment of type II diabetic patients at Bantakhun Hospital, Thailand**

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Diabetes is a chronic disease that must be treated consistently. Initial treatment includes control of diets, exercise, and medication. Many patients who cannot control their blood sugar levels turn to alternative medicine, such as herbal therapy. This study is a descriptive research and the data were collected from patient medical records. This study aimed to assess the efficacy of herbal remedies to control the level of fasting blood sugar (FBS) in patients with type 2 diabetes at Bantakhun hospital, Thailand. Inclusion criteria of the study were age over 18 years old, the FBS levels in the range of 126-300 mg/dl, and receiving 600 mg of herbal remedy (capsule consisting of 26 ingredients). The study was divided into two periods, before and after receiving the herbal remedy. Nineteen patients were included in this study. Most patients were 40-60 years old, and had FBS levels in the range of 126-199 mg/dl. Patients use a combination of metformin and glibenclamide(47.36%). After the herbal remedy was used in combination with diabetes drugs, the FBS levels were decreased significantly (25.57, 95%CI 3.70-47.45, p=0.024). When various factors were analyzed, women, 40-60 years of age and above 60 years demonstrated a significantly decreased in the FBS levels. The herbal remedy in combination with insulin, insulin and metformin, and metformin produce a significant decrease in the FBS levels (p=0.006, 0.028, and 0.034, respectively). In conclusion, the herbal remedy is beneficial in reducing the FBS level especially in females and patients at the age above 40. It can also be used with other diabetes drugs. However, future long term studies on efficacy and safety are required.

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### **119. The Multifunctional Tryptoline and Tryptamine Triazole Derivatives that Enhanced the Neurite Outgrowth of Cultured P19-Derived Neurons**

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Alzheimer's disease (AD) is a common neurodegenerative disorder for which one of the hallmarks is the deposition of aggregated  $\beta$ -amyloid peptides (A $\beta$ 40,42) as plaques in brain. Oligomers of these peptides can react with biological metal in brain to generate free radicals resulting in neuronal cell death. We have previously reported tryptoline and tryptamine triazole derivatives (6h, 12c and 12h) as lead compounds acting on multiple targets, namely  $\beta$ -secretase (BACE1),  $\beta$ -amyloid peptides (A $\beta$ ), metal chelation and antioxidant. The multifunctional lead compounds inhibited BACE1, the key enzyme to generate  $\beta$ -amyloid peptides, and also interacted with A $\beta$  and prevented the amyloid self-aggregation to form amyloid oligomers and plaques. In addition, metal chelation and antioxidant properties helped in reducing radical formation and scavenged the generated radicals. The multifunctional activities of compound 6h included anti-amyloid aggregation and antioxidant effects while those of compound 12c

were  $\beta$ -secretase inhibitory action, anti-amyloid aggregation and metal chelating. Compound 12h acted as  $A\beta$  aggregation blocker, chelator and antioxidant. As neurite dystrophy has been found in AD brain, and this significant loss of connectivity of neuron relates to cognitive decline, the multifunctional lead compounds (6h, 12c and 12h) were evaluated for neurotogenic activity using P19-derived neurons. The morphology of P19-derived neurons was observed and the length and number of neurites was measured comparing to geldanamycin, a positive control. At the noncytotoxic concentration of 1 nM, lead compounds 6h, 12c and 12h showed significant increase in neurite length and neurite number. The results suggested that the multifunctional lead compounds not only acted as neuroprotectants against neurotoxicity from  $A\beta$  on neuronal cells but also enhanced the survival and neurite outgrowth of P19-derived neurons.

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## 120. In Vitro Cytotoxicity of Novel Cc-CATH3 Analogues against Human Cancer Cell Lines

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**Background:** Cc-CATH3 is an antimicrobial peptide with 29 amino acid residues in length and demonstrated broad-spectrum antimicrobial activity against a variety of microorganisms including bacteria, fungi as well as some drug-resistant bacterial strains with MIC values in the range 0.3–2.5  $\mu$ M, higher potency than ampicillin, kanamycin, and LL-37. However, the cytotoxic activity of Cc-CATH3 against human cancer cell line has never been reported.

**Objectives:** The objectives of this study are to explore the cytotoxic activity of Cc-CATH3 and its analogues against human cancer cell lines human hepatoma cells (HepG2) and human non-small cells lung cancer (NCI-H460) and to investigate the effect of amino-terminal truncation on cytotoxic effect of Cc-CATH3 peptide.

**Method:** A series of Cc-CATH3 analogues with progressive truncations of four amino acid residues from the N-terminal region was generated namely Cc-CATH3(5-29), Cc-CATH3(9-29) and Cc-CATH3(13-29) in order to investigate the effect of N-terminal truncation on its biological activity. The *in vitro* cytotoxicity of these analogues have been investigated by using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) cell proliferation assay in human hepatoma cells (HepG2) and human non-small cells lung cancer (NCI-H460).

**Results:** The results demonstrated that Cc-CATH3(1-29) and Cc-CATH3(5-29) exhibited cytotoxic activity against HepG2 and NCI-H460 cell lines. In contrast, Cc-CATH3(9-29) and Cc-CATH3(13-29) demonstrated no toxicity even at the maximum tested concentration of 50  $\mu$ M. Cc-CATH3(1-29) displayed the cytotoxicity for HepG2 and NCI-H460 with the values of  $IC_{50}$  18.38 and 17.74  $\mu$ M, while Cc-CATH3(5-29) exhibited the cytotoxicity for HepG2 and NCI-H460 with the values of  $IC_{50}$  6.58 and 4.4  $\mu$ M, respectively.

**Discussion:** All Cc-CATH3 analogues were demonstrated prerequisite factors that fit to the classical characteristics of AMPs. However, only the native and the four amino acid truncation analogue, Cc-CATH3(5-29), are demonstrated the cytotoxicity. Therefore, the eight amino acid residues at the N-terminal region are important to its function. Interestingly, the four amino acid truncation analogue

illustrated higher cytotoxic against human cancer cell lines than that of the parent peptide Cc-CATH3(1-29).

**Keywords:** Cc-CATH3 analogues; cytotoxicity; antimicrobial peptide

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### **121. Role of $\alpha$ -mangostin in VEGF induced neovascularization and hypoxia induced oxidative stress**

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Retinal neovascularization is a major cause of the vision loss and is characterized by the development of abnormal leaky blood vessels. Vascular Endothelial Growth Factor (VEGF) is known to play an important role in this process. Oxidative stress has been strongly implicated in up regulation of VEGF associated with neovascularization in various tissues. Hence, compounds with the anti-oxidant actions can prevent neovascularization.  $\alpha$ -mangostin, a component of mangosteen (*Garcinia mangostana* Linn) has been shown to have an anti-oxidant property in pathological conditions involving angiogenesis such as cancer. However, the specific effect of  $\alpha$ -mangostin on angiogenesis has not been studied. Using bovine retinal endothelial cells (BRECs) and *ex-vivo* models, the present study investigated the anti-oxidant and anti-angiogenic activity of  $\alpha$ -mangostin. Dihydroethidium (DHE) assay was used to study the effects of  $\alpha$ -mangostin on superoxide formation in BRECs treated with hypoxia. 3D matrigel tube formation and aortic ring assay were performed to study whether  $\alpha$ -mangostin can reduce neovascularization and western blot was performed to determine the signaling mechanisms involved. We observed that  $\alpha$ -mangostin significantly and dose-dependently reduced superoxide formation in hypoxia-treated BRECs.  $\alpha$ -mangostin also significantly inhibited VEGF-induced phosphorylation of VEGFR2 and suppressed neovascularization in the 3D matrigel tube formation and aortic ring assays of angiogenesis. According to our results,  $\alpha$ -mangostin reduces oxidative stress and inhibits angiogenesis through blockade of VEGFR2 activation.

**Keywords:** Angiogenesis,  $\alpha$ -mangostin, oxidative stress

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### **122. Influence of chemical penetration enhancers on skin permeability of ellagic acid-loaded niosomes**

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This study aimed to develop niosomes of ellagic acid (EA), a potent antioxidant phytochemical substance, for dermal delivery and investigate the influence of chemical penetration enhancers on the physicochemical properties of EA-loaded niosomes. The EA niosomes were prepared by reverse phase evaporation method using Span 60, Tween 60 and cholesterol as vesicle forming agents and Solulan C24 as a steric stabilizer. Polyethylene glycol 400 (PEG) was used as a solubilizer while dimethylsulfoxide (DMSO) or *N*-methyl-2-pyrrolidone (NMP) was used as a skin penetration

enhancer. It was found that the mean particle sizes of EA-loaded niosomes were in the range of 312-402 nm with PI values of lower than 0.4. The niosomes were determined to be spherical multilamellar vesicles as observed by transmission electron microscope and optical microscopy. All niosomes were stable after 4 months storage at 4 °C. In vitro skin permeation through human epidermis revealed that the skin enhancers affected the penetration of EA from the niosomes at 24 h. The DMSO niosomes showed the highest EA amount in epidermis; whereas the NMP niosomes had the highest EA amount in the acceptor medium. Concomitantly, the skin distribution by confocal laser scanning microscopy showed the high fluorescence intensity of the DMSO niosomes and NMP niosomes at a penetration depth of between 30-90  $\mu\text{m}$  (the epidermis layer) and 90-120  $\mu\text{m}$  (the dermis layer) under the skin, respectively. From the results, it can be concluded that the DMSO niosomes are suitable for epidermis delivery of EA while the NMP niosomes can be used for dermis delivery of EA.

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### **123. Protective effect of Teaw (*Cratoxylum formosum*) against amyloid-beta toxicity in *Caenorhabditis elegans* model of Alzheimer's disease**

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Alzheimer's disease (AD), an age-related neurodegenerative disorder, is widely recognized as a serious public health problem. As lifespan increases, greater proportions of our population are affected by AD. The accumulation of amyloid  $\beta$  (A $\beta$ ) is one of the histopathological hallmarks of AD. A $\beta$  is aggregated to form oligomers which are toxic to neurons and are critical to the onset and progression of AD. Currently, there is still no approved drug with a proven disease-modifying effect. This leads to the need for the development of effective compounds that can provide disease-modifying property. Oxidative stress is known to play an important role in AD, and there is strong evidence linking oxidative stress to A $\beta$ . Thai dietary herbal plant Teaw (*Cratoxylum formosum*) is an indigenous Thai vegetable that is mostly grown in the Northeast of Thailand. Many evidences suggested that the extract from *C. formosum* possess antioxidant property. Previous studies demonstrated that the extract from *C. formosum* have protective effect against various conditions including acid/alcohol-induced gastric mucosal damage, and phenylhydrazine-induced oxidative stress and vascular injury. The purpose of this study is to investigate the protective effect of the leaf extract from *C. formosum* against A $\beta$  toxicity using transgenic *Caenorhabditis elegans* (*C. elegans*) model. In *C. elegans* model, human A $\beta$  is expressed intracellular in the body wall muscle. The expression and subsequent aggregation of A $\beta$  in the muscle lead to progressive paralysis. We found that the extract significantly delayed A $\beta$ -induced paralysis. The results also showed that chlorogenic acid, the main component of the extract significantly delayed A $\beta$ -induced paralysis. Both extract and chlorogenic acid ameliorated oxidative stress by reducing the level of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). Using genetic approach, we found that DAF-16/FOXO transcription and HSF-1 were required for the protective effect of the extract. These findings suggest that leaf extract from *C. formosum* may have benefit effect for the treatment of AD.

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#### 124. Economic Evaluation of Colorectal Cancer Screening: A Systematic Review

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**Background:** Colorectal cancer (CRC) is a major public health problem worldwide. CRC screening in average-risk population aims to prevent new cases of CRC by detecting and removing pre-malignant lesions or to discover CRC at its early stage. Implementation of CRC screening program requires enormous of resources; therefore, it is important to carefully assess value for money of the program.

**Objective:** This study aimed to systematically review the economic evaluation studies of different CRC screening methods in order to identify the optimal screening modality.

**Method:** A search was carried out using PubMed and ScienceDirect databases. Full economic evaluations assessing CRC screening in average-risk population from January 2003 to July 2013 were retrieved.

**Results:** Sixteen publications identifying optimal screening modalities were included in the review. Of 16 included studies, the studies were performed in ten different countries used four modeling approaches. Fifty percent of included studies used cost-effectiveness analysis, whereas the others used cost-utility analysis. The method of gFOBT was the most assessed option, while FIT-biennial screening was the most reported optimal strategy. It was found that CRC screening was considered as a cost-effective or even cost-saving when compared with no screening. Although, the studies did not find the consensus conclusion on which screening method was the most effective or the modality of choice.

**Discussion:** Of implementing screening program in the country, the evaluation should be conducted to assess the benefits against the society acceptable costs because the transferability of results from one setting to another is limited.

**Keywords:** Colorectal cancer, screening, economic evaluation

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#### 125. Effect of $\gamma$ -oryzanol on antioxidant genes of human prostate cancer cells

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**Objective:** To assess the effect of  $\gamma$ -oryzanol on antioxidant genes of human prostate cancer cells.

**Materials and Methods:** Cytotoxic activity of gamma-oryzanol on human prostate cancer cells, DU145 and PC3, was performed by proliferation assay using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) reagent. mRNA levels of genes involved in the intracellular antioxidant system, superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) and

glutathione reductase (GSR) were determined by reverse transcription-polymerase chain reaction (RT-PCR).

**Results:** All concentrations of  $\gamma$ -oryzanol, 0.1 - 2.0 mg/ml, significantly inhibited cell growth in a dose- and time-dependent fashion in both prostate cancer cell lines, DU145 and PC3. The gene expression of catalase in DU145 and PC3 exposed to  $\gamma$ -oryzanol at 0.5 mg/ml for 14 days were down regulated, mRNA of GPX was also down regulated in PC3.

**Conclusion:** This study highlighted the effect of  $\gamma$ -oryzanol via the down-regulation of antioxidant genes, catalase and GPX, not the cytotoxic role. This might be interesting for adjuvant chemotherapy to make prostate cancer cells more sensitive to free radicals. It might be useful for the reduction of cytotoxic agent and cancer chemoprevention.

**Keywords:**  $\gamma$ -oryzanol, cytotoxicity, superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase

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## 126. Identification of *Stemona* by Microscopic Characterization

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**Background:** *Stemona* plants are widely used for insecticides and antitussive remedy. *Stemona* in Thailand comprises 11 species which can be separated into 2 main groups according to their morphological characteristics and bioactive components, i.e. *tuberosa* group (*S. tuberosa* and *S. phyllantha*) and non-*tuberosa* group (*S. aphylla*, *S. burkillii*, *S. collinsiae*, *S. cochinchinensis*, *S. curtisii*, *S. kerrii*, *S. pierrei*, and *S. ruprestis*). There is confusion when the powder of *Stemona* is used.

**Objective:** This study was investigated the characters of each group of *Stemona* for separation of its species.

**Methods:** Cross-sectional histology of fresh root samples of 6 species of *Stemona*, i.e. *S. burkillii*, *S. cochinchinensis*, *S. curtisii*, *S. kerrii*, *S. phyllantha* and *S. tuberosa* were examined. Powdered drug characteristics were studied under a microscope using mounting reagents.

**Results:** Cross-sectional histology showed that *tuberosa* group had a non-lignified pith, while the non-*tuberosa* group had the smaller lignified one. Powder drug of both groups appeared as creamish-yellow color containing vessels, fibers, starch grains and parenchyma cells. *Tuberosa* group can be discriminated from the others by numerous of parenchyma cells.

**Discussion:** Cross-sectional histology and powder drug characteristics of various *Stemona* species growing in Thailand showed that *tuberosa* group had a non-lignified pith and contained numerous parenchyma cells, while non-*tuberosa* group had smaller lignified pith and less abundant of parenchyma cells. These microscopic characters can be used as a tool to identify *Stemona* groups.

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### 127. Optimization of Extraction Method for High Content of Didehydrostemofoline from *Stemona collinsiae* Roots

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**Background:** *Stemona* plants have been traditionally used as natural pesticides and medicinal plants in South-East Asian countries. Among *Stemona* plants in Thailand, *S. collinsiae* Craib is one of the most interesting species. It contains didehydrostemofoline as a major alkaloid resulting in insecticidal activity and making it suitable for bio-pesticide. It also possesses anticholinesterase inhibitory activity that may be useful for pharmaceutical uses. Optimizing the extraction process will economize its production in practical application.

**Objective:** This study was aimed to optimize the extraction methods as well as various extracting solvents with different polarity on *S. collinsiae* roots.

**Methods:** Various extraction methods such as sonication, reflux, Soxhlet extraction, maceration and percolation, as well as various extracting solvents with different polarity, i.e. absolute methanol, absolute ethanol, acetonitrile, acetone, 30, 50, and 70% of methanol-water mixtures and 30, 50, 70, and 80% of ethanol-water mixtures, were performed on *S. collinsiae* roots and monitored with validated-HPLC analysis using didehydrostemofoline as a marker compound.

**Results:** Using a single solvent, the recovery of didehydrostemofoline was clearly increased with the increased polarity solvent (acetone < acetonitrile < ethanol < methanol). Methanol and seventy percent of ethanol were shown to be good solvents for extracting didehydrostemofoline with nearly the same yield. Comparative analysis of didehydrostemofoline in the root extracts of *S. collinsiae* by different extraction **Methods** (sonication, reflux, Soxhlet, maceration, percolation) using 70% ethanol showed that refluxing and sonication gave the highest amount of didehydrostemofoline.

**Discussion:** Methanol and seventy percent ethanol were shown to be good solvents for extracting didehydrostemofoline. Seventy percent ethanol which has a safety profiles over methanol was chosen as the appropriate solvent for *Stemona* extraction. Using 70% ethanol, refluxing and sonication gave the highest amount of didehydrostemofoline. Reflux promoted high yield of crude extract, required short extracting time and less amount of solvent. It is also simple, inexpensive, and convenient for upscaling industrial process. Thus, refluxing with 70% ethanol was the recommended method and solvent for extracting *S. collinsiae* roots.

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### 128. Variation of Insecticidal Didehydrostemofoline and Stemofoline Contents in *Stemona collinsiae* Roots in Thailand

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**Background:** *Stemona* plants have been traditionally used as natural pesticides and medicinal plants for a long time. *S. collinsiae* Craib has been interested for its insecticidal activity supported by many scientific research studies. The roots contain didehydrostemofoline and stemofoline as active components. Variation of active compounds affects their promised biological activities. The study of variability of didehydrostemofoline and stemofoline contents could provide a basis for standardization of *S. collinsiae* extract for a better source and for further development as pharmaceutical and insecticidal products.

**Objective:** The aim of this study was to quantitatively analyze and compare didehydrostemofoline and stemofoline contents in *S. collinsiae* roots collected from various locations in Thailand.

**Methods:** Eight samples of *S. collinsiae* roots were collected from various wild forests in the eastern, southeastern, and central floristic regions of Thailand. Each sample was dried, ground and separately extracted with 70% ethanol by refluxing, which was found to be the appropriate extraction method. The extract was concentrated under reduce pressure at 45°C using a rotary vacuum evaporator. The concentrated extract was then evaporated on a boiling water bath until a constant weight was obtained. The crude extract was dissolved in 70% ethanol and analyzed by the validated HPLC method.

**Results:** The contents of didehydrostemofoline and stemofoline in the dried powder of *S. collinsiae* ranged from 0.37 to 0.78 and 0.012 to 0.119 %w/w while in the 70% ethanolic extracts contained 0.53 to 1.08 and 0.016 to 0.167 %w/w, respectively. Characteristic fingerprints of the components in the extracts provided a powerful tool for identification of this *Stemona* species.

**Discussion:** The contents of didehydrostemofoline and stemofoline in various sources of *S. collinsiae* roots collected from different floristic regions of Thailand and their characteristic fingerprints could be used as guidance for standardization of *S. collinsiae* extracts. The data also indicated better sources of *S. collinsiae* roots in Thailand as active raw materials for pharmaceutical and insecticidal products development.

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### 129. Inhibitory Effect of *Stemona* Alkaloids on Acetylcholinesterase Activity

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**Background:** Acetylcholinesterase (AChE) is one of the most important enzymes in many living organisms. It plays an important role in nerve signal transmission, and therefore cholinesterase inhibition is the treatment of choice for Alzheimer's disease. In searching for potential lead compounds for further development, we investigate the acetylcholinesterase inhibition effect of *Stemona* alkaloids.

**Objective:** This study was aimed to investigate the acetylcholinesterase inhibitory activity of *Stemona* alkaloids.

**Methods:** Eleven *Stemona* alkaloids belonging to three skeletal types, i.e., protostemonine-type (didehydrostemofoline, stemofoline, stemocurtisine, stemocurtisinol, stemokerrine, oxystemokerrine), croomine-type (croomine), and stichoneurine-type (tuberostemonine, tuberostemonine-A,

tuberostemonine N, neotuberostemonine), were isolated from the roots of various *Stemona* plants. The AChE activity was determined using the Ellman's colorimetric assay in 96-well plate. Activity of the enzyme was calculated as percentage of velocities compared to that of the assay using buffer without any inhibitor.

**Results:** At the concentration of 0.1 mg/ml, protostemonine alkaloid-derivatives could inhibit AChE more than 50% whereas stichoneurine-derivatives and croomine could inhibit AChE in a wide range close to 50%, and 25.68%, respectively. Therefore, serial dilutions were conducted to determine IC<sub>50</sub> of protostemonine-derivatives. Didehydrostemofoline, stemofoline, stemocurtisine, stemocurtisinol, stemokerrine, and oystemokerrine inhibited AChE with IC<sub>50</sub> of 50.55, 39.53, 96.13, 104.75, 78.96, and 88.12 µg/ml, respectively. Galanthamine, which was used as a positive control, inhibited AChE with IC<sub>50</sub> of 0.48 µg/ml.

**Discussion:** Protostemonine-type alkaloids of *Stemona* plants could possess acetylcholinesterase inhibitory activity. The highest effect was observed in stemofoline and didehydrostemofoline with IC<sub>50</sub> of 39.53 and 50.55 µg/ml, respectively. However, the inhibition activity of these compounds was lower than that of galanthamine standard (IC<sub>50</sub> 0.48 µg/ml). Our results provide useful information on further structural modification and utilization of these natural products

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### 130. TLC-Densitometric Analysis of Didehydrostemofoline in *Stemona collinsiae* Roots

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**Background:** *Stemona collinsiae* has been traditionally used as a natural pesticide for a long time. Didehydrostemofoline is a major active component, which possesses potent insect toxicity. In order to standardize good quality raw material form *S. collinsiae* root, a thin layer chromatography (TLC)-densitometric method was developed and validated for quantitative analysis of major active component didehydrostemofoline.

**Objective:** This study was aimed to develop and validate a TLC-densitometric method for quantitative analysis of didehydrostemofoline in *S. collinsiae* roots.

**Methods:** A TLC-densitometric method has been developed for determination of didehydrostemofoline in *S. collinsiae* root extract at UV maximum absorption 300 nm. The analysis was performed on TLC aluminum sheets precoated with silica gel 60 F<sub>254</sub> using dichloromethane: ethyl acetate: methanol: ammonium hydroxide (70:25:5:1) as a mobile phase. The method was validated for linearity, precision, accuracy, limit of detection (LOD), and limit of quantitation (LOQ).

**Results:** Didehydrostemofoline showed linearity within the concentration range of 40-320 ng/spot with correlation coefficient (r) 0.995. Intraday and interday precision studies showed the relative standard deviation (RSD) < 4%. Accuracy of the method was determined by a recovery study of didehydrostemofoline at 3 different levels and found to be 95.9, 104.3, and 103.5%, with an average of 101.2%. The LOD and LOQ were 6.88 and 22.94 ng, respectively. The contents of didehydrostemofoline in the methanol extract and dried root powder of *S. collinsiae* were 1.27 ± 0.089 and 0.735 ± 0.048 %w/w, respectively.

**Discussion:** The developed method is simple, precise, specific and accurate and can be used for quantification of didehydrostemofoline in plant materials, extracts and products containing this compound. It is suitable for routine analysis of many samples of *S. collinsiae* extract and its products at the same time.

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### 131. Species-specific Accumulation Trends of Alkaloids in *Stemona* species

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<sup>c</sup>Department of Agronomy, Faculty of Agriculture, Kasetsart University, Thailand

<sup>d</sup>Chemodiversity Research Group, Faculty Center of Biodiversity, University of Vienna, Austria

**Background:** *Stemona* spp. have traditionally been used as medicinal plants and insecticides. The Thai vernacular name “Non Tai Yak” generally refers to various *Stemona* spp, but they were shown to possess a great chemical diversity. *Stemona* raw material purchased from the local markets are often not properly identified or may be mixtures of various species. Therefore, a broad-based phytochemical comparison was carried out to detect species-specific accumulation trends of *Stemona* alkaloids which should contribute as chemical markers for natural grouping

**Objective:** This study was aimed to establish a phytochemical comparison of *Stemona* plants in Thailand.

**Methods:** 42 samples of *Stemona* roots representing eight species were collected from different locations in Thailand. Major alkaloids were isolated and their structures elucidated by NMR- and MS-analyzes. The methanolic extracts of all samples were compared by HPLC coupled with diode array or evaporative light scattering detectors.

**Results:** Thai *Stemona* were mostly characterized by alkaloids derived either from a protostemonine- or stichoneurine-type skeleton. The latter characterized *S. tuberosa* and *S. phyllantha* accumulating species-specific isomers of tuberostemonine. *S. collinsiae* clearly deviated by protostemonine-type derivatives dominated by didehydrostemofoline and small amounts of stemofoline. *S. kerrii* were distinguished by stemokerrine and small quantities of oxystemokerrine, whereas *S. curtisii* showed an infraspecific variation accumulating either the pyrroloazepine stemofoline or the pyridoazepine stemocurtisine. By contrast, *S. cochinchinensis*, *S. aphylla*, and *S. rupestris*, mainly distributed in the dry habitats, showed a general reduction of alkaloids, mostly consisting of traces of protostemonine only.

**Discussion:** The present survey showed a clear chemical segregation between protostemonine- and stichoneurine-type alkaloids in Thai *Stemona* species, simultaneously informing about the distribution of the biologically highly active stemofoline derivatives of the former and tuberostemonine derivatives of the latter structural type.

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### 132. Variation of Alkaloids Content in *Stemona curtisii* Roots in Thailand

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**Background:** *Stemona* plants (Stemonaceae) have been traditionally used as natural pesticides and medicinal plants. *S. curtisii*, the dominant species distributed in the South and Southwest of Thailand, has been of interest for its insecticidal properties. Variation of active components affects their promised biological activities. Therefore, the study of variability of the contents of bioactive components was done.

**Objective:** This study was aimed to determine and comparison the alkaloid contents in *Stemona curtisii* roots in Thailand.

**Methods:** Ten samples representing *S. curtisii* were obtained from various locations in Thailand. Each powdered sample of *S. curtisii* roots was accurately weighed and exhaustively extracted with methanol in an ultrasonic bath. The concentrated extract was adjusted the volume with methanol and analyzed with the validated HPLC method.

**Results:** The contents of the major alkaloids oxystemokerrine, stemocurtisine, stemocurtisinol, and stemofoline in dried powder of *S. curtisii* roots ranged from 0.0458 to 0.3299, 0.0354 to 0.2368, 0.0149 to 0.1040, and 0.0849 to 0.2139% (w/w), respectively.

**Discussion:** A remarkable infraspecific variation of alkaloid composition was observed in *S. curtisii* collected from different geographical provenances in the South and Southwest of Thailand with a humid climatic condition almost all year round. This study would provide a basis for standardization of *S. curtisii* raw materials for a better source for further insecticidal development.

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### 133. Insecticidal Activity and Alkaloids Composition of *Stemona curtisii* Roots Growing in Thailand

Sumet Kongkiatpaiboon<sup>a,b</sup>; Stefan Mikulicic<sup>c</sup>; Vichien Keeratinijaka<sup>d</sup>; Harald Greger<sup>c</sup>; Wandee Gritsanapan<sup>a</sup>

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<sup>c</sup>*Chemodiversity Research Group, Faculty Center of Biodiversity, University of Vienna, Austria*

<sup>d</sup>*Agronomy Department, Faculty of Agriculture, Kasetsart University, Thailand*

**Background:** *Stemona curtisii* Hook. f., a traditional insecticide plant distributed in South and Southwest of Thailand, attracted attention for its insecticidal properties caused by specific alkaloids. *S. curtisii* root extracts and their formulations have been commercially used as bio-pesticide in agriculture by farmers in Thailand. However, a variation in phytochemical constituents was observed in *S. curtisii* and the effectiveness of the local-made preparations is always a concern.

**Objective:** This study was aimed to determine the insecticidal activity of *Stemona curtisii* roots in Thailand and their alkaloids composition.

**Methods:** Ten samples of *S. curtisii* roots, collected from various localities in Thailand, were analyzed for their major components oxystemokerrine, stemocurtisine, stemocurtisinol, and stemofoline with the validated HPLC method. Chronic feeding bioassays against neonate larvae of the polyphagous pest

insect *Spodoptera littoralis* Boisduval (Lepidoptera, Noctuidae) was done to evaluate their insecticidal properties.

**Results:** Insecticidal activities of ten *S. curtisii* extracts were evaluated. The highest insect toxicity with 100% lethality and 0% growth rate at 2.5 mg/g was found in a collection from Surat Thani accumulating only stemofoline as major component, whereas less activity was found in samples without detectable amounts of this compound, inferring its stronger insecticidal effect than other alkaloids.

**Discussion:** Stemofoline possesses stronger insecticidal effect than other alkaloids, suggesting its suitability to be used as a bioactive chemical marker for the quality assessment and standardization of *S. curtisii* raw materials, extracts, and finished products from this plant. The present study serves a basis for further development of *S. curtisii* roots as a high potential natural insecticidal product.

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## Scientific Posters Session 2 Abstracts (#134-170)

Friday, May 30

11:45 a.m. - 1:15 p.m.

### 134. Quantification of Bioactive Chemical Markers in *Stemona collinsiae* Roots by HPLC Method

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<sup>b</sup>Drug Discovery and Development Center, Thammasat University, Thailand

**Background:** *Stemona* plants have been traditionally used as an insecticide, scabicide, for the treatment of skin and respiratory diseases. *S. collinsiae* Craib is one of the most interesting species in *Stemona* genus that is widely used in Central, East, Northeast, and Southeast of Thailand. The accumulation of didehydrostemofoline and stemofoline in the roots leads to high insecticidal activity of this plant. In order to standardize good quality raw material from *S. collinsiae* root extracts, a HPLC method was developed and validated for quantitative analysis of major active components didehydrostemofoline and stemofoline.

**Objective:** This study was aimed to develop and validate a HPLC method for quantitative analysis of didehydrostemofoline and stemofoline in *S. collinsiae* roots.

**Methods:** Eight samples of *S. collinsiae* roots were collected from various locations in Thailand. Each sample was dried, ground and separately extracted with 70% ethanol by refluxing. HPLC was carried out using a Hypersil BDS C<sub>18</sub>-column eluted with methanol: 1 mM ammonium acetate (55:45) with a flow rate of 1 ml/min and detection at 295 nm. Method validation was performed to assure its linearity, precision, accuracy, and limits of detection and quantitation.

**Results:** A HPLC method was developed for analyzing the contents of didehydrostemofoline and stemofoline in *S. collinsiae* root extracts. From the various mobile phases trialed, the system containing 55% methanol in 1 mM ammonium acetate solution gave symmetric peaks and provided the most efficient separation and speed. Didehydrostemofoline and stemofoline showed a linear relationship within the range of 0.5-432.3 and 0.5-188.4 µg/ml, respectively. The method was shown to be precise

with RSD <2%. The average recovery of didehydrostemofoline and stemofoline were 98.80 and 99.97%, respectively.

**Discussion:** The developed and validated HPLC method was found to be appropriate for the analysis of didehydrostemofoline and stemofoline in *S. collinsiae* root extracts. This work would be useful as a guide for the standardization of *S. collinsiae* root extract raw materials and their finish pesticidal products.

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### 135. Insecticidal Activities of Traditional Insecticide Plants “Non Tai Yak” (*Stemona* spp.) in Thailand

Sumet Kongkiatpaiboon<sup>a,b</sup>; Stefan Mikulicic<sup>c</sup>; Vichien Keeratinijakal<sup>d</sup>; Harald Greger<sup>c</sup>; Wandee Gritsanapan<sup>a</sup>

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<sup>d</sup>Agronomy Department, Faculty of Agriculture, Kasetsart University, Thailand

**Background:** *Stemona* plants have been traditionally used as natural pesticides and medicinal plants. Despite their diversity, the same vernacular name of “Non Tai Yak” has been used for various species in Thailand because of their similar root shapes. However, a variation in phytochemical constituents in different species was observed and leads to the different biological activities.

**Objective:** This study was aimed to evaluate the insecticidal activities of various *Stemona* species growing in Thailand.

**Methods:** Thirty-three samples representing 7 species and one unidentified species was tested using chronic feeding bioassays with neonate larvae of the polyphagous pest insect *Spodoptera littoralis* Boisduval (Lepidoptera, Noctuidae).

**Results:** Potent insect toxicity was observed in all *S. collinsiae* samples, unidentified *S. sp.* sample and some samples of *S. curtisii*. *S. kerrii* possessed moderated insecticidal activity while *S. aphylla* and *S. rupestris* showed low to moderate insecticidal activity. *S. tuberosa* and *S. phyllantha* showed insignificant insecticidal activity. Stemofoline and its derivatives didehydrostemofoline were found to be the key active compounds which can be found as major components in the active samples, while less activity was found in samples without detectable amount of this compound, inferring their stronger insecticidal effect than other alkaloids.

**Discussion:** *Stemona* samples containing stemofoline and didehydrostemofoline showed potent insecticidal activities. Hence, these compounds can be used as bioactive chemical markers for the quality assessment of *Stemona* raw materials, extracts, and their finished products for further pharmaceutical and agricultural development.

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### 136. “Vote & Vax” Student Pharmacist Initiative for Free Immunization Clinic on Election Day

Lisa Lebovitz, JD, Assistant Dean for Academic Affairs; Cherokee Layson-Wolf, PharmD, CGP, BCACP, FAPhA, Associate Dean for Student Affairs and Associate Professor, Department of Pharmacy Practice and Science

*University of Maryland School of Pharmacy*

The objectives of this student-led initiative were to provide a free influenza vaccination clinic on Election Day, increase immunization rates among an underserved population, and demonstrate pharmacists' roles in health promotion and disease prevention. The national Vote & Vax initiative works with local public health providers to launch vaccination clinics at or near polling places. In 2010, Maryland student pharmacist organizers analyzed vaccination and polling site statistics and then contacted local health departments to identify clinic locations, obtain sponsorship for vaccinations, and finalize immunization protocols. The event was promoted through media outlets. In 2010, the Vote & Vax clinic provided 153 vaccinations; 42 individuals received an influenza vaccination for the first time. It was the only Vote & Vax initiative held in Maryland during the 2010 election season. During the 2012 elections, a total of 221 free flu shots were given at two locations. More than 30 students and faculty were involved each time. The University of Maryland School of Pharmacy's Vote & Vax initiative was honored in 2011 with an Immunization Excellence Award by the Maryland Partnership for Prevention, and recognized by the Maryland Legislature's House of Delegates with a resolution. Lessons learned were published for schools of pharmacy who wish to conduct similar programs. The Vote & Vax initiative reinforces the benefits of expanding pharmacists' roles and provides student pharmacists with experience implementing a public health event and interacting with other health care practitioners and the public. Plans are underway for Maryland Vote & Vax 2014.

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### **137. An Effective Programmatic Assessment Process for Continuous Quality Improvement**

*Lisa Lebovitz, JD, Assistant Dean for Academic Affairs; Richard Dalby, PhD, Professor and Associate Dean for Academic Affairs*  
*University of Maryland School of Pharmacy*

The University of Maryland School of Pharmacy leads pharmacy education, scientific discovery, patient care, and community engagement in the state of Maryland and beyond. This mission is reflected in the programmatic outcomes of the institutional assessment plan that was developed and endorsed as part of 2010 strategic planning process. Through programmatic assessment, the school seeks to understand and improve curricular effectiveness and peripheral factors that impact the learning environment. Tools used to understand program-level quality include course evaluations, instructor evaluations, and academic performance campus comparisons. Simple graphs enable faculty to quickly analyze their results. Established metrics include academic performance between campuses, course evaluation completion rate and documentation of course evaluation review by course managers, faculty and the department chair, vice chair, and mentors as needed. Benchmarks for each metric include equivalent academic performance between campuses, 80% course evaluation response rate, and 100% documentation of faculty review to assure completion of the feedback loop. High benchmarks were intentionally set for each metric because continuous quality improvement of a PharmD program is best measured through the success of its students and faculty. In the last six semesters, the overall course evaluation response rate has been between 67% and 78% each semester. The return rate for documentation of review by faculty and vice chairs is 100%. Students benchmark their performance against their peers by reviewing their class rank, which is provided to each individual via email by the Office of Academic Affairs every semester. The school benchmarks graduating class performance on the North American Pharmacist Licensure Examination (NAPLEX) against peer institutions and longitudinally, as well as between campus cohorts. Faculty can benchmark themselves against other faculty who taught during the given semester by reflecting on their average instructor rating in conjunction with the other

ratings on the graph. This process is easily transferable to other colleges and schools of pharmacy, regardless of the type of academic records and registration system and online survey tool for course evaluations. It is evident that students at the main campus and the distance campus continue to perform equivalently and with excellence throughout all four years of the program, faculty and vice chairs are actively engaged with the review of their courses and teaching effectiveness, and although the course evaluation response rate tends to fluctuate, students are aware that their perspectives are heard and valued.

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### **138. Metabolic syndrome screening in drugstore, Pathum thani Province, Thailand**

*Kusawadee Maluangnon<sup>1</sup>, Ph.D.; Natthida Kanama<sup>3</sup>; Wanichaya Meesiroj<sup>3</sup>; Wathanyuta Keawwichian<sup>3</sup>*

<sup>1</sup> *Lecturer, Faculty of Pharmacy, Thammasat University, Thailand*

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**Background:** Metabolic syndrome is a serious health condition which can lead to coronary heart disease, heart attack, and stroke. National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (NCEP ATP III) defines the criteria for metabolic syndrome if any of 3 risk factors present 1) waist circumference > 102 cm in men, >88 cm in women 2) blood pressure  $\geq$ 130/85 mmHg 3) fasting blood glucose  $\geq$  110 mg%. 4) HDL cholesterol <40 mg% in men, <50 mg% in women 5) Triglycerides >150 mg%.

**Objective:** The study aimed to screen the patient for metabolic syndrome at the drugstore.

**Method:** Survey study, using the guideline developed by Community Pharmacy Association (Thailand) and National Health Security Office (Thailand) according to the NCEP ATP III, the criteria for the screening in Thai population including 1) waist circumference > 90 cm. in men, >80 cm. in women 2) blood pressure  $\geq$ 130/85 mmHg/ patient with hypertension taking hypertensive agents and 3) fasting blood glucose  $\geq$  110 mg%. These three criteria for screening metabolic syndrome at the drugstore are easy and not consume time. The patient, age over 34, who met 3 of the risk factors, was considered to have a condition of metabolic syndrome. Three drugstores in Pathum thani province were selected as study sites by simple random sampling technique. The screening project started from August to September, 2013. The subjects of the study were well-informed about the objective of the screening and signed the inform consent.

**Results:** From 132 subjects (87 men and 45 women) with the average age of  $52.3 \pm 11.8$ , three of them have metabolic syndrome condition (achieved 3 of the risk factors). In addition, 23 (17.42%) and 66 (50%) subjects have 2 and 1 risk factors, respectively. These high-risk groups were suggested to have their blood cholesterol and triglyceride tested at the hospital since they had the possibility of the metabolic syndrome. Forty subjects (30.30%) have none of the risk factors and were informed about the risk of metabolic syndrome and how to promote their health. The satisfaction evaluation found that all subjects were satisfied with the screening project (average score  $4.28 \pm$  out of 5).

**Conclusion:** The result showed that community pharmacist's roles of chronic disease screening are important since there is benefit in early detection of metabolic syndrome and appropriate treatment can prevent the patient from cardiovascular disease.

**Keywords:** Metabolic syndrome, screening, drugstore

### 139. Risk Factors for recurrent atrial fibrillation after cardiac surgery

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**Background:** Postoperative atrial fibrillation (POAF) is the most common complication after cardiac surgery. Its prevalence is approximately 30% after coronary artery bypass grafting (CABG) surgery, 40% after valve replacements or repair, and 50% after combined procedures. POAF is generally transient and self-limited but it can result in increased risk of stroke, renal failure, heart failure and increased mortality. When it causes complications or requires additional treatment it prolongs hospital stay and increases costs. Beta-blockers are considered the first-line treatment in the postoperative period hyperadrenergic state. Amiodarone, a class III antiarrhythmic agent, with additional adrenergic blocking activity is an alternative agent for the management of POAF. Amiodarone can cause conversion to sinus rhythm, control heart rate and improve hemodynamic status. POAF can recur despite treatment with amiodarone.

**Objective:** The objective of this study was to (1) determine the incidence of recurrent POAF, (2) identify the risk factors of recurrent POAF, and (3) define the dose and duration of amiodarone therapy for treatment for POAF. **Method:** This is a retrospective cohort study. The medical records of patients who had atrial fibrillation after heart surgery at the University of Arizona Medical Center from January 1, 2011 through December 31, 2013 will be reviewed for recurrent POAF event until patient discharged from hospital. Multiple logistic regression analysis will be performed to develop a prognostic model and to evaluate the impact of variation of amiodarone therapy on the outcome.

**Results and Conclusions** of this study will be presented.

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### 140. Use of Videoconferencing to Advance US-Thai Collaboration: The Chulalongkorn Experience

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**Background:** Videoconferencing can promote collaboration by linking of geographically separated faculty and students. The Department of Social and Administrative Pharmacy (SAP), Faculty of Pharmaceutical Sciences, Chulalongkorn University has used videoconferencing for nearly 10 years to facilitate teaching/learning and research efforts.

**Objectives:** 1) Describe and categorize SAP videoconferencing activities, 2) discuss outcomes of these activities, and 3) recommend strategies for enhancing international collaboration using videoconferencing.

**Methods:** In-depth interviews of ten key informants (SAP faculty, graduate students, staff) were content analyzed. Experience with videoconferencing uses (teaching, learning, research), process evaluation (feasibility, cost, satisfaction), and outcomes were analyzed.

**Results:** Videoconferencing has been used as a communication channel for teaching/learning in the SAP graduate program since 2005. Various commercial (i.e., Telepresence, Microsoft Lync) and non-commercial (e.g., Skype, Google Hangout) software programs have been used. Since 2012, Microsoft Lync has been used because of its robust presentation features (e.g., PowerPoint, Word, Excel), pointing and annotation tools, advanced meeting scheduling, recording, content sharing (e.g., desktop, whiteboard, polls), and instant messaging. The SAP program used videoconferencing in 4 ways: 1) having local instructors teach evening or weekend classes that accommodate work schedules of adult learners, 2) inviting instructors in foreign countries give lectures or presentations, 3) having remote experts serve on thesis committees or as thesis advisor/co-advisor, and 4) facilitating research activities among national and/or international collaborators. Teaching/learning activities were the most common use. During 2013-14, videoconferencing was used in most graduate courses and in all graduate seminars. MS Lync's synchronous communication facilitated high-level **Discussion** that is central to graduate courses. The most complex use involved team-teaching of a Medication Use Behavior course by US and Thai instructors. The US instructor recorded lectures and hosted them on an LMS for self-study before class then gave remote lectures and **Discussion** with students for 8 weeks. The Thai instructor taught remaining sessions and course wrap-up with face-to-face sessions. Continuing research topic consultation involving a US professor and a Thai student was found in one case. Involvements remain limited in number and scope due to instructors' lack of experience and training, and need for time to get accustomed to new technology.

**Discussion:** Videoconferencing enhances and advances teaching/learning and research activities in pharmacy, opening collaboration opportunities that are flexible in place and time, and relatively low cost. Reducing barriers and training users will increase educational opportunities and expand learning. Leader support (e.g., resources, budget) is needed for enlarging national and international collaborations.

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#### **141. The cost efficiency analysis of biosimilar compared with originators erythropoiesis-stimulating agents (ESAs) to manage chemotherapy-induced anemia in Thailand**

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**Background:** Cancer-induced anemia is a common complication of cancer treatment that Results in decreased quality of life. Erythropoiesis-stimulating agents (ESAs) was found significantly associated with increase in hemoglobin levels and quality of life.

**Objectives:** To estimate the cost efficiency of the originator and biosimilar ESAs in a range of different fixed and weight-based dosing schemes; to determine the relative cost savings of treatments with biosimilar epoetin  $\alpha$  over the originator ESAs; and to estimate the incremental number of patients access to primary antineoplastic therapy in a hypothetical panel of 10,000 ESA-treated cancer patients.

**Methods:** The direct costs of ESAs regimen of 6 cycles at 3-week intervals with ESAs initiated at week 4 and continued for 15 weeks were calculated and subsequently applied to five scenarios with both fixed and weighted-based dosing schemes. The 5 scenarios included: 15-week continuous standard dose (CSD); sustained dose escalation (SDE) to 1.5 times or double of the standard dose at week 7, continued for 12 weeks; and discontinued dose escalation (DDE) to 1.5 times or double of the standard dose at week 7 for a 3-week period, followed by a standard dose for 9 weeks.

**Results:** Compared with originators, biosimilar epoetin  $\alpha$  yielded the lowest average total costs of 136,500 Baht and 96,915 Baht for fixed and weight-based dosing, respectively. In fixed-dosing scheme, the average saving cost with use of biosimilar epoetin  $\alpha$  ranged from 51,264.14 Baht (27.30%) to 114,749.24 Baht (45.67%). While, it ranged from 36,397.53 Baht (27.30%) to 117,149.37 Baht (54.73%) in weight-based dosing. Biosimilar epoetin  $\alpha$  conversion saving from darbepoetin  $\alpha$  once weekly and once every 3 weeks in both schemes led to the greatest incremental number of patients access to rituximab (119.76 to 156.54 patients), bevacizumab (224.86 to 293.91 patients) and trastuzumab (282.63 to 369.43 patients).

**Discussion:** The biosimilar epoetin  $\alpha$  is the most cost-efficient to manage chemotherapy-induced anemia in cancer patient over the originator ESAs. The cost savings of treatment with biosimilar epoetin  $\alpha$  potentially leads to increase in accessibility to primary antineoplastic therapy.

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#### 142. *In Vivo* and *In Vitro* Hemostatic Activity of *Chromolaena odorata* Leaf Extracts

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**Background:** *Chromolaena odorata* (L.) R.M.King & H.Rob. (Asteraceae) or Siam weed has long been used to stop bleeding in Thailand and many countries. Only the aqueous leaf extract was investigated in *in vivo* and there have been conflicting results of *in vitro* hemostatic mechanisms of this plant.

**Objective:** The most appropriate *C. odorata* leaf extract that promoted the highest hemostatic activity and the hemostatic mechanisms of these plant extracts will be investigated.

**Methods:** The lyophilized aqueous leaf extract and alcoholic (50, 70, and 95% ethanol) extracts from the fresh and dried leaves were investigated both *in vivo* and *in vitro*. The bleeding time in male Wistar rats was measured to investigate the hemostatic effect. The hemostatic mechanisms were tested using *in vitro* platelet aggregation and blood coagulation tests in sheep plasma.

**Results:** All extracts displayed significantly reducing bleeding time (<2.5 min) in rats but did not induce platelet aggregation or blood clotting in the *in vitro* study. The *in vitro* blood clotting times of all extracts were > 0.6 min. Seventy percent of ethanolic extract from the dried leaves proved to be the extract producing the highest hemostatic activity *in vivo* with the bleeding time of 1.85 min.

**Discussion:** The *in vivo* study with rats confirmed the significant ability of this plant extract to stop bleeding. However, the sufficient amount of calcium and active compounds which are aggregating and clotting agents to enhance blood coagulation and platelet aggregation in *in vitro* tests should be further studied.

**Keywords:** *Chromolaena odorata*, Siam weed, hemostatic activity, bleeding time, Wistar rats

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### 143. *In Vivo* Anti-inflammatory Activity of Extracts from *Chromolaena odorata* Leaves of Different Thai Provenances

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**Background:** *Chromolaena odorata* (L.) R.M.King & H.Rob. (Asteraceae) or Siam weed has long been used for treatment of wounds in Thailand and many countries. Anti-inflammatory activity is one of the mechanisms enhancing wound healing.

**Objective:** This study focused on the *in vivo* anti-inflammatory activity of 70% ethanolic extracts from *C. odorata* leaves collected from different provenances in Thailand.

**Methods:** Seventy percent ethanolic extracts, which extracted from the mature leaves collected from different provenances in 4 parts of Thailand, i.e. Samut Sakhon (Central), Nakhon Ratchasima and Yasothon (North-East), Chanthaburi (East) and Surat Thani (South). The anti-inflammatory effect of 10% w/v extracts was conducted using ethylphenylpropiolate (EPP)-induced ear edema model in male Sprague-Dawley rats. The percentage of swelling and inhibition were calculated and compared with the standard and control groups.

**Results:** All 70% ethanolic extracts showed significance difference on anti-inflammatory activity. While percentage of inflammatory inhibition of indomethacin was set at 100%, the 70% ethanolic extract from Yasothon (North-East) presented the highest activity at 42.73% inflammatory inhibition. Whereas, other extracts from Samut Sakhon, Chantaburi, Nakhorn Ratchasima and Surat Thani showed similar percentage of inflammatory inhibition at 38.92, 38.01, 37.04 and 32.58, respectively ( $p < 0.001$ ).

**Discussion:** *C. odorata* leaf extracts showed moderate anti-inflammatory activity in *in vivo*. The different effectiveness on this activity of *C. odorata* leaf extracts might be from different amounts of active compounds in the extracts. Therefore, the contents of active components in *C. odorata* leaf extracts should be further investigated.

**Keywords:** Anti-inflammatory activity, Asteraceae, *Chromolaena odorata*, Siam weed

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#### 144. Determination of Calcium Content and Hemostatic Activity of Siam Weed Leaf Extracts

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**Background:** Siam weed (*Chromolaena odorata*) has been used as a hemostatic agent to stop bleeding in rural areas of Thailand for centuries. The blood coagulation activity is due to 4',5,6,7-tetramethoxyflavone, which has been isolated and identified. Working synergistically with this compound, calcium is a significant contributor to enhance blood coagulation. However, there has been no report comparing the calcium content in Siam weed leaves collected from different provenances as of now.

**Objective:** The aims of this study were to determine the calcium content in Siam weed leaf extracts collected from 10 different locations in Thailand and to compare the hemostatic activity of the extracts containing the highest and lowest calcium quantities.

**Methods:** The 70% ethanolic leaf extracts of Siam weed which leaves were collected from 10 provinces in Thailand were determined. The calcium content in each extract was analyzed by atomic absorption spectrophotometer (AAS). The highest and lowest calcium containing extracts were chosen for investigation of the hemostatic activity in Sprague-Dawley rats while 70% ethanol was used as a control. The incision was made at a foot pad of each rat using a No.11 blade. Length and depth of each wound were 1x0.1 cm. The 20 µl of each extract or control was applied to the wound. Bleeding time was recorded immediately after making the wound until the blood stop.

**Results:** Calcium contents in 10 Siam weed leaf extracts were in the range 1 to 7 ppm. The leaf extract containing the highest (6.58 ppm) and the lowest (1.46 ppm) calcium levels were from Yasothon and Nakhon Ratchasima provinces, respectively. The time it took to completely stop bleeding of the extracts with the highest and the lowest calcium contents and the control were found to be 1.52, 1.37 and 3.34 min, respectively. The results showed that the extract containing lower amount of calcium could stop bleeding faster than the higher calcium extract. This implied that some other chemical constituents were responsible for hemostasis.

**Discussion:** We concluded that calcium content in Siam weed leaves was not the only one factor that promoted the hemostatic activity. Therefore, active compounds in the leaf extract should be further separated and identified. Standardization based on amount of the active components should be determined.

**Keywords:** Siam weed, calcium content, stop bleeding

#### **145. HPLC Quantitative Analysis of Scutellarein Tetramethyl Ether: the Active Component of *Chromolaena odorata* Leaf Extract**

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**Background:** *Chromolaena odorata* (L.) King and Robinson (Siam weed) is a medicinal herb used for stop-bleeding, anti-inflammation and wound healing in tropical countries for centuries. It contains various bioactive components. Among them, scutellarein tetramethyl ether has been reported as a bioactive component for blood coagulation.

**Objective:** In our previous study, it was shown as a bioactive component for anti-inflammation. In this study, we developed the HPLC analytical method for quantitative determination of this compound in *C. odorata* leaf extract.

**Methods:** The method was validated for its linearity, precision, accuracy, limit of detection (LOD) and limit of quantitation (LOQ). HPLC was carried out using a BDS Hypersil C18-column eluted with methanol:1% acetic acid (60:40) with a flow rate of 1 mL/min and detection at 268 nm.

**Results:** Scutellarein tetramethyl ether showed a linear relationship within the range of 12.5–500 µg/ml. The method was shown to be precise with RSD < 2%. The average recovery was > 98%. The average content of scutellarein tetramethyl ether in the extract was 102.9 µg/ml.

**Discussion:** The proposed HPLC method was appropriate for the analysis of scutellarein tetramethyl ether in *C. odorata* extract and would be useful for standardization of this plant extract.

**Keywords:** *Chromolaena odorata*, Siam weed, HPLC, Scutellarein tetramethyl ether, standardization

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#### **146. Hemostatic and Anti-inflammatory Components from *Chromolaena odorata* Leaf Extract in Rat Models**

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**Background:** *Chromolaena odorata* (L.) King and Robinson (Siam weed) has been used as hemostatic agent to stop bleeding and anti-inflammatory agent when the scutellarein tetramethyl ether has been reported as an active component. However, it has no report on hemostatic and anti-inflammatory activities of this component in animal models.

**Objective:** In this study, we studied both hemostatic and anti-inflammatory activities in rats of scutellarein tetramethyl ether and two more major compounds; stigmasterol and one unknown compound which were isolated from *C. odorata* leaf extract.

**Methods:** The hemostatic and anti-inflammatory activities were assessed using a bleeding time and ethyl phenylpropionate (EPP)-induced ear edema models in Sprague-Dawley rats, respectively.

**Results:** The scutellarein tetramethyl ether at 0.2 mg/10  $\mu$ l/paw could immediately stop the bleeding. In contrary, stigmasterol and unknown at the same concentration did not have ability to stop bleeding. The 70% ethanolic extract at 2 mg/20  $\mu$ l/ear exhibited low relative percent inhibition of indomethacin (37.61%) on ear edema within 2 h after application. However, all components at 0.4 mg/20  $\mu$ l/ear exhibited high relative percent inhibitions (> 70%).

**Discussion:** Our data presented that scutellarein tetramethyl ether is hemostatic component of *C. odorata*. This compound, stigmasterol and unknown are also active anti-inflammatory components of this plant. This is the first report on an active hemostatic component of *C. odorata* in animal model.

**Keywords:** *Chromolaena odorata*, hemostasis, anti-inflammatory activity, bioactive component, animal model

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#### **147. Relationship Between Scutellarein Tetramethyl Ether and Calcium Amounts in *Chromolaena odorata* Leaf Extracts on Hemostatic Activity in Rat Model**

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**Background:** *Chromolaena odorata* (L.) King and Robinson (Siam weed) is a medicinal herb used as hemostatic agent to stop bleeding in tropical countries for centuries. Scutellarein tetramethyl ether and calcium have been reported as active components for stop-bleeding. From our investigation using a bleeding time model in rat, The 70% ethanolic dried leaf extract displayed the highest hemostatic activity which could stop bleeding within  $1.85 \pm 0.05$  min. Furthermore, the scutellarein tetramethyl ether could immediately stop bleeding after 0.2 mg/10  $\mu$ L application to the wound.

**Objective:** In this study, we investigated the relationship of scutellarein tetramethyl ether and calcium amounts to the hemostatic activity of extracts from those various solvent extractions.

**Methods:** The scutellarein tetramethyl ether and calcium contents were determined using validated HPLC analytical method and atomic absorption spectroscopy, respectively.

**Results:** The results displayed the positive correlation between the active components and the hemostatic activity. However, the scutellarein tetramethyl ether seemed to have more influence on this activity. The 70% ethanolic dried leaf extract which exhibited the highest hemostatic activity yielded the highest amount of scutellarein tetramethyl ether (308 ppm) and moderated amount of calcium (4.57 ppm). In contrary, the lyophilized aqueous extract from fresh leaves which exhibited the lowest hemostatic activity ( $2.47 \pm 0.02$  min) yielded the lowest amount of scutellarein tetramethyl ether (1 ppm) although it yielded the highest amount of calcium (11.97 ppm). We have also determined the amounts of both active components in the extracts, whose leaves were collected from various parts of

Thailand. The results presented that various amounts of active components did not depend on the geographical feature. Scutellarein tetramethyl ether varied in the range of 116-420 ppm while the calcium content varied in the range of 1.46-6.58 ppm.

**Discussion:** These data suggested that standardization of plant extracts on both contents of scutellarein tetramethyl ether and calcium are necessary for further development.

**Keywords:** *Chromolaena odorata*, Hemostatic activity, Scutellarein tetramethyl ether, calcium, standardization

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#### **148. Effect of Siam weed extract and its bioactive component scutellarein tetramethyl ether on anti-inflammatory activity through NF- $\kappa$ B pathway**

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**Background:** Siam weed (*Chromolaena odorata* (L.) King and Robinson) is a medicinal herb used for wound healing and inflammation-related diseases.

**Objective:** In this study, we evaluated the molecular mechanism by which Siam weed extract (SWE) and its bioactive components, scutellarein tetramethyl ether (scu), stigmaterol, and isosakuranetin affect anti-inflammatory activity.

**Methods:** The expression of several inflammatory proteins in RAW 264.7 (murine) macrophages was assessed by Western blot and reverse transcription-polymerase chain reaction (RT-PCR). Biochemical assays including prostaglandin E2 (PGE2) and nitric-oxide (NO) quantification were performed. Luciferase promoter activity and immunocytochemistry of Nuclear factor- $\kappa$ B (NF- $\kappa$ B) were investigated.

**Results:** Cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) are critical proinflammatory proteins. The level of protein and mRNA expression of these enzymes induced by lipopolysaccharide (LPS) was dramatically suppressed by treatment with SWE, scu, or stigmaterol compounds in a dose-dependent manner. They also reduced PGE2 and NO release. We further analyzed the NF- $\kappa$ B pathway and found that the scu compound suppressed I $\kappa$ B kinase complex alpha/beta (IKK $\alpha$ / $\beta$ ) and Inhibitory- $\kappa$ -B-alpha (I $\kappa$ B $\alpha$ ), thereby suppressing COX-2 and iNOS expression.

**Discussion:** This is the first report of the anti-inflammatory molecular mechanism in SWE and/or its bioactive component scu, indicating alteration NF- $\kappa$ B pathway and further providing potential uses in the treatment of inflammation-related diseases.

**Keywords:** Siam Weed, *Chromolaena odorata*, Scutellarein tetramethyl ether, Stigmaterol, Isosakuranetin, NF- $\kappa$ B pathway

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### 149. Hemostatic and Wound Healing Properties of *Chromolaena odorata* Leaf Extract

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**Background:** *Chromolaena odorata* (L.) King and Robinson (Siam weed) extract has been used to stop bleeding and in wound healing in many tropical countries. However, its detailed mechanisms have not been elucidated.

**Objective:** In this study, we examined the molecular mechanisms by which Siam weed extract (SWE) affected hemostatic and wound healing activities.

**Methods:** The effect of SWE on cell migration and proliferation were investigated using scratch assay in Balb/c 3T3 fibroblast cells. The expression of several hemostatic and wound healing proteins in undifferentiated promonocytic cell lines (U937) and Balb/c 3T3 fibroblast cells, respectively were assessed using Western blot and reverse transcription-polymerase chain reaction (RT-PCR)/ or Quantitative Real-Time-PCR. Luciferase promoter activity of heme oxygenase-1 (HO-1) was investigated.

**Results:** SWE promoted Balb/c 3T3 fibroblast cell migration and proliferation. Subsequently, we found that heme oxygenase-1 (HO-1), the accelerating wound healing enzyme, was increased at the transcriptional and translational levels by SWE treatments. The HO-1 promoter analyzed with luciferase assay was also increased by treatment of SWE in a dose-dependent manner. This induction may be mediated by several kinase pathways including MEK, p38MAPK, AKT, and JNK. Quantitative real-time PCR using U937 cells revealed that thromboxane synthase (TXS), a potent vasoconstrictor and platelet aggregator, was increased and MMP-9, an anti-platelet aggregator, was decreased in the presence of SWE.

**Discussion:** Our studies presented that SWE accelerated hemostatic and wound healing activities by altering the expression of genes, including HO-1, TXS, and MMP-9.

**Keywords:** *Chromolaena odorata*, Siam weed, Balb/c 3T3 cells, U937 cells, HO-1, Wound healing

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### 150. Development of supporting clinical skills by e-learning in drug therapy monitoring

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**Background:** E-learning platforms are cost-effective, consistent, faster, supportive to cognitive retention, easy updating by instructors and manageable with self-pace by students as learning-center. Authors incorporated an e-learning to enhance clinical skill in pharmacotherapy for Parkinson's disease.

**Objective:** To develop e-Learning for pharmacy students enrolled in pharmacotherapy, a platform for Parkinson's disease with subsequent assessment of: (1) Success of learning before/after participation based on test-score results. (2) Participant satisfaction based on satisfactory score.

**Methods:** The fourth year pharmacy students enrolled in pharmacotherapy course during the year 2013 were prospectively for e-Learning. The course contents were adapted from physician manual for diagnosis and treatment in general practice from Parkinson's disease and Movement disorders Research and Training Center of Thailand published in 2010. The assessment tools consist of the equivalent 20-item pre-test and post-test examination papers and the 20-item, five domains satisfactory survey questionnaire. Descriptive statistics to compare test scores for pre-learning, post-on-ground learning and post-online learning with 95% CI significant at  $p < 0.05$  were analyzed. The dependency of tested score employed Spearman's rank correlation coefficient. The reliability test of total satisfaction score employed intra-class correlation with Chronbach's alpha coefficient.

**Results:** The contents of e-Learning developed is equivalent to 2 hours of on-ground learning which comprises of introduction, epidemiology, etio-pathophysiology, clinical presentation, differential diagnosis, treatment algorithms, common motor complications, clinical monitoring and assessment. The pre-test on-ground learning score and post-test on-ground learning score, post-test on-ground learning score and post-test e-learning score of the same student set reflected Spearman's rank correlation coefficient of 0.289 ( $p=0.231$ ) and 0.252 ( $p=0.298$ ) respectively, indicating independency of score. The mean (SD) of test score at different tests for the same student set were 3.526(1.896), 6.894(1.629) subsequent to on-ground learning and 9.473(0.841) subsequent to e-Learning respectively. The score reflected mean score difference (SD), [95% CI] at -3.368(2.290)[-4.472, -2.264],  $p < 0.001$  and -5.947(1.899)[-6.862, -5.031],  $p < 0.001$  respectively. The reliability of 20-item, 5 domains of score reflected with Chronbach's alpha coefficient of 0.867 indicating consistent total score with item score.

**Discussion:** The e-learning project should foster further development with other subjects. There were some shortcomings in terms of small sample size and the test results should be validated against actual score of final examination.

**Conclusion:** The e-Learning support clinical skill developments are beneficial to the pharmacy student education. The 4<sup>th</sup> year pharmacy student performed better after subsequent e-Learning.

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### 151. Experimental and Theoretical Studies of the Interaction between Lipid Membrane and Ceragenin CSA-13

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**Background:** Ceragenin CSA-13, a cholic acid derivative, has been proposed as a novel template for development of more potent and specific antibiotics. It exerts a rapid bactericidal activity against a broad range of bacterial species, while its hemolytic activity is relatively low. Unfortunately, the precise

mechanism of action is not entirely clear. It has been speculated that CSA-13 interacts with lipid components of the bacterial cell membrane, causing membrane disruption.

**Objective:** The purpose of the study was to investigate the mechanism of membrane perturbation by ceragenin CSA-13 using MD simulation and the leakage experiments.

**Methods:** By means of MD simulations, single component POPG or POPE lipid bilayers were used to mimic cell membranes. The initial conformations of the ceragenin CSA-13 was modeled using the Discovery 2.5 studio. All simulations were performed using the CHARMM program. Simulations were carried out using explicit solvent, counter ions, periodic boundary conditions, with the NPT ensemble at a temperature of 303 K and a pressure of 1 atm. The leakage experiments were performed with calcein-loaded single-component liposomes comprised of anionic POPG, anionic DOPG, and zwitterionic DOPC lipids; and with two-component liposomes including, DOPG:DOPE, DOPC:DOPG, DOPE:DOPC, and POPG:POPE lipids. Leakage of calcein from liposomes was monitored after 5-min incubation with ceragenin CSA-13 by measuring fluorescence intensity at 520 nm (excitation at 490 nm). For determination of 100% dye-release, 1% of Triton X-100 solution (1% in HEPES buffer) was added to dissolve the vesicles.

**Result and Discussion:** Studies on single-component liposomes demonstrated that ceragenin CSA-13 effectively induced calcein leakages by interacting with negatively charged POPG and DOPG vesicles, while also exhibiting weak dye-leakage activity in DOPC vesicles. Using two-component vesicles, leakage varied showing a higher leakage for POPG:POPE than DOPG:DOPE vesicles. This can be explained by a difference in the packing characteristic of the lipid acyl chains in which DO species contain two unsaturated chains giving loose packing density. The experimental results were in good agreement with the MD calculations indicating that the positively charged parts of ceragenin CSA-13 preferentially bind to the negatively charged PG headgroup, leading to increases of ceragenin CSA-13 at the membrane-water interface, and subsequently causing membrane destabilization by the increased membrane fluidity. Moreover, the MD simulations revealed that the hydrophobic portions of the ceragenin CSA-13 enhanced its penetration into membrane lipid core. Using a combination of experiments and simulations can help to better understand the mechanism of membrane perturbation by ceragenin CSA-13.

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## 152. Model of integrating community learning into Thai PharmD curriculum

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**Background:** Consumer protection and providing home health care are important roles for Thai pharmacists. These roles normally involve working in community in order to detect and tackle community health problems. PharmD students need to understand community culture and lifestyle to be able to work better in this setting. Training students is thus necessary to enhance this competency.

**Objective:** To describe details of community learning program used in Thai PharmD curriculum and to demonstrate primary outputs of the program.

**Methods:** Community learning program was developed by Social and Administrative Pharmacy (SAP) teaching group, Faculty of Pharmacy, Mahasarakham University. One community, 200-household size and within a 10-kilometer radius of the pharmacy school, was selected to be a learning place. The program was integrated into 2-credits modules run in two consecutive semesters for year-2 students. Social Pharmacy, describing principles of health, health behaviors and medical anthropology, was a keystone module in semester I. At the first visit, students invited one family to be their host for a regular meeting. For the next two, they learned this community in all aspects using the 7-community learning tools, a well-known tool used in anthropology and social health in Thailand. Public Health Pharmacy was set in semester 2, explaining principle of public health, health system and policy. Students visited the community twice in this semester to investigate health status and use of medicines and health products. They were assigned to interview one or two members ( $\geq 18$  years) of the host family using a survey form developed by SAP team.

**Results:** Students produced community information following the 7-instruments including (1) geo-social map, (2) family trees of host families, (3) structure of community board, (4) community health system, (5) community calendar, (6) community history, and (7) autobiography of key persons. Students interviewed 162 community members. Of those, 112 forms were usable. Participated members age ranged from 18 to 83 years. Majority were female (73.0%), married (79.3%), primary school educated (69.4%), and farming/agriculture (61.3%). Almost one-fifth were drinkers (18.9%), while 1 in 10 were smokers (12.6%). About a third had high risk of diabetes (33.9%). Inappropriate use of medicines and advertising health products improperly were found.

**Discussion:** Community learning program integrated in PharmD curriculum provides students an opportunity to gain experience of working in community. Activities included in the program can help identify community health problems, which will be useful for planning interventions/campaigns to promote healthy community in the next academic year.

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### 153. Quality evaluation of turmeric capsules prepared in Thai hospitals

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Turmeric rhizome capsules are popularly used for treatment of flatulent and dyspepsia. Standardized turmeric is recommended by Thai Herbal Pharmacopoeia (THP). This study evaluated physical and chemical properties, i.e. weight variation, disintegration time, contents of moisture, volatile oil, total curcuminoid and microbial contamination, of turmeric capsules prepared by 10 different hospitals in Thailand. The results revealed that weight variation, disintegration time and moisture content of all samples were conformed with the THP standard while 90% of the samples contained volatile oil and total curcuminoids within the recommended amounts. For microbial contamination, 70% of samples contained exceeded amounts of total aerobic bacteria, yeasts and molds. However, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Clostridium* spp. were not found in all samples. The results showed that most of turmeric capsules prepared in hospitals in Thailand have high standards in terms of

physical and chemical qualities. However, a sanitary in manufacturing process of turmeric capsules has to be more concern.

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#### 154. Polysaccharide extraction from *Parkia timoriana* seeds

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**Background:** *Parkia timoriana* seeds give mucilaginous polysaccharide when soaking in water and the seeds are interesting to be the sources of purified polysaccharide.

**Objectives:** To compare between extraction with hot and cold water for selection in an appropriate method which made the most yield of polysaccharide extract from *Parkia timoriana* seeds and to analyze the monosaccharide compositions of polysaccharide by Thin Layer Chromatography.

**Methods:** including step 1: *Parkia timoriana* seeds was divided into 2 groups for hot and cold extraction with distilled water. Then, add 70% Ethanol to collect the precipitate. The precipitate was evaporated and freezes dry to calculate the yield of polysaccharide. Step 2: Purification of polysaccharide was done by dialysis method to get the polysaccharide. Step 3 : Determination of polysaccharide was done with Dubois' reaction and determination with UV spectrophotometer at 480 nm. The protein in the polysaccharide was determined with UV spectrophotometer at 260 nm. Step 4: The polysaccharide was hydrolyzed and examined monosaccharide composition by Reverse Phase Thin Layer Chromatography to compare with 8 standard monosaccharides.

**Results:** The result showed that hot extraction of *Parkia timoriana* seeds had pure polysaccharide more than cold extraction 2.43 times. The proportion of polysaccharide to protein by hot and cold extraction was 0.188 and 0.155 respectively. The galactose was the major monosaccharide composition in the polysaccharide. The conclusion and discussion of this study were the hot extraction was the most appropriate method and galactose was monosaccharide composition in the polysaccharide extract from *Parkia timoriana* seeds. This study data can be used for extraction of polysaccharide in other plants. In addition, the biological test and health products development was interested.

**Keywords:** *Parkia timoriana*, Polysaccharide, extraction

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#### 155. The influence of hydroxycarboxylic acids on the solubilization of haloperidol

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**Background:** Haloperidol, an antipsychotic drug, is a basic compound with low water solubility which is a major problem of drug formulation. The interaction with acid species is one strategy to enhance solubility of basic drugs.

**Objective:** The aim of this study was to investigate the influence of hydroxycarboxylic acids (i.e., citric acid, tartaric acid and lactic acid) on the drug solubilization.

**Methods:** The studied acids contain different chain lengths and numbers of hydroxyl and carboxyl groups. Haloperidol solubility was determined in various concentrations (0-270 mM) of different acids in water.

**Results:** It was found that the addition of acid in water incremented the drug solubility which further increased with the increasing acid concentration. The drug solubility was enhanced by 51 to 751 times compared to the solubility in water without acids. Additionally, the solubility of haloperidol was further investigated in 0.1 mM citrate buffer pH 3 and 6 with the addition of acids. The result showed that the haloperidol solubility significantly increased in buffer pH 3 but decreased in buffer pH 6 as compared to that in water. However, the highest drug solubility enhancement was observed in both buffered and non-buffered systems added with citric acid, followed by the systems with lactic acid and tartaric acid, respectively. The solubilization of haloperidol by the addition of acids in water and buffer pH 3 took place predominantly via the presence of unionized species of added acids at low pH. Meanwhile the buffer pH 6 reduced the amount of unionized species available for drug solubilization and decreased the haloperidol solubility.

**Discussion:** From the results, it can be concluded that the solubility of haloperidol depended on concentration and type of added acids, but the main effect on drug solubility is the pH of medium. Ultimately, these obtained data can be further used for the development of haloperidol delivery system.

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## 156. Standard Cost Lists for Health Economic Evaluation in Thailand

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This analysis was undertaken to generate a set of standard costs for medical services and those incurred by patients receiving treatment, for use in health economic evaluations. Medical service unit cost data were derived from a survey of 3,091 hospital medical services in five hospitals, disaggregated by type of hospital (district or provincial/regional) and analyzed using the relative value unit method. Patient-borne ambulatory cost values were derived from data gathered through 905 patient interviews that took place in six health centers, three district hospitals and three provincial/regional hospitals. The survey gathered data on costs arising from the distance travelled to access the medical service, the time spent in the healthcare facility, as well as travel and meal costs. The analysis generated a set of standard cost data for Thailand that will make conducting economic evaluations more accurate, faster and more convenient, as well as allowing better comparability between studies. This is the first standard cost menu that has been developed specifically for Thailand, and as such should be revised and refined in the future. Some areas that would benefit from revision are suggested.

**Keywords:** Medical service, unit cost, standard cost list, health economic evaluation, Thailand

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### 157. Measurement of costs for health economic evaluation

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The provision of guidelines on cost measurement for health economic evaluations enable research to be more standardized and hence more comparable, which offers clear benefits for policy formulation and health management. The guidelines herein focus on three aspects—the cost of health intervention/health care programs, the cost of illness/health risks, and use of costs in health economic evaluation. For each aspect, the main concepts and methods are outlined, and recommendations for the Thai context are presented. There is particular focus on how to calculate various costs according to different evaluation methods and perspectives, how to evaluate source of cost data, how to make value adjustments and how to present cost measurement findings.

**Keywords:** Cost, cost measure, methods, guidelines, economic evaluation, Thailand

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### 158. Safety of Intravitreal Bevacizumab Injection for Neovascular Age-Related Macular Degeneration and Diabetic Macular Edema: A Systematic Review

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**Background:** Bevacizumab (IVB) has been widely used as an off-label treatment for treating neovascular age-related macular degeneration (AMD) and diabetic macular edema (DME) because its substantial lower cost than the approved drug named ranibizumab. However, there are concerns about possible serious adverse events (SAEs) of IVB particularly rare events and evidences supporting its safety profile remain inconclusive.

**Objective:** To examine ocular and systemic SAEs of IVB in the treatments of neovascular AMD and DME.

**Methods:** The articles were searched from Pubmed and Centre for Reviews and Dissemination. Randomized controlled trials (RCTs), cohort studies, systematic reviews, or meta-analyses which reported SAEs of IVB compared with placebo or other anti-VEGF drugs in the treatment of neovascular AMD or DME were included. Studies which IVB were given in conjunction with other ocular procedures or therapies and articles published in non-English languages were excluded.

**Results:** Only 11 articles were included in this review. The number of RCTs, retrospective studies or systematic reviews was 3, 2, and 5, respectively. Most studies concluded that the treatment with IVB was safe and well-tolerated. The incidences of endophthalmitis and arteriothrombotic events (i.e., ocular and systemic SAEs) in neovascular AMD and DME patients were low. Non-SAEs commonly found in both IVB and IVR groups are subconjunctival hemorrhage, increased intraocular pressure and mild ocular inflammation. Most studies concluded that IVB and IVR have similar safety profile and low incidence of SAEs.

**Discussion:** The results should be interpreted cautiously due to the limitations of previous studies, particularly small sample size for evaluating rare SAEs. High quality evidence is still required. The valid safety profile of IVB in comparison to IVR might be useful in treatment selection and decision making to allocate the resources for treatment of neovascular AMD and DME.

**Keywords:** intravitreal injection; bevacizumab; neovascular age-related macular degeneration; diabetic macular edema

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### 159. 3D-QSAR studies on chromone derivatives as topoisomerase I inhibitors

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DNA Topoisomerase I play critical roles in cellular processes, in which it is involved in DNA replication, transcription, and chromosome segregation. Topoisomerase I inhibitors are a new class of anticancer agents which aimed to interrupt DNA replication in cancer cells, resulting cell death. The goal of these studies was to identify structural features necessary to increase topoisomerase I inhibitory activity and further use these features to design novel anticancer agents. Comparative Molecular Field Analysis (CoMFA) and Comparative Molecular Similarity Indices Analysis (CoMSIA) based on three dimensional quantitative structure activity relationship (3D-QSAR) studies were conducted on a series of 16 chromone derivatives as topoisomerase I inhibitor agents. The best CoMFA and CoMSIA model obtained from AM1 geometry optimization and database alignment. The satisfactory CoMFA model predicted a cross-validated  $r^2$  ( $q^2$ ) = 0.646 and noncross-validated  $r^2$  = 0.999 indicating that electrostatic and steric properties play a significant role in potency. The best CoMSIA model, based on steric, electrostatic, and hydrophobic fields, gave  $q^2$  = 0.732 and  $r^2$  = 0.995,  $SEE$ =0.009 and  $F$ =155.558. The resulting contour maps produced by the best CoMFA and CoMSIA models could be used to understand the important structural features responsible for the design and development of new highly active topoisomerase I inhibitors

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### 160. Community pharmacist's monitoring on the quality use of medicines in the accredited community pharmacies in Maha Sarakham and Roiet provinces

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Community pharmacists have an important role in monitoring patients to enhance the efficacy of the treatment and quality use of medicines. The purpose of this study was to compare the effects of the community pharmacy service in providing quality use of medicines (drug related problems, drug use behavior and patient satisfaction) between the control and treatment groups. Patients who enrolled to this study came to the accredited community pharmacies during October – December 2011 and were taking at least one medication for common illness or chronic illness. Randomized allocation with

permuted block was designed. The treatment group received a usual pharmacy service plus informative calendar and telephone follow-up every week while the control group received only a usual pharmacy service. The pharmacy service for quality use of medicine was collaborated for referral with 5 community health centers and community health volunteers. This study was done in 9 accredited community pharmacies.

There were 280 patients enrolled to the study. At the pre-test, the treatment group showed 91 drug related problems and 66 problems in the control group. The post-test, the drug related problems were reduced 54.0% in the treatment group and 29.1% in the control group. The most common drug related problems found at the pre-test were 1) noncompliance (38.1% and 26.2%, in the treatment and control groups respectively) 2) miscellaneous (e.g. duplicate medications; 16.5% and 12.8 %, respectively) and 3) adverse drug reactions (5.8% and 5.0% respectively). Most pharmacist interventions were education (74.1% and 87.1% in the treatment and control groups, respectively) and changing drugs were found (7.4% and 6.5% in the treatment and control groups, respectively). Drug use behaviors were better in the treatment group when compared with the control group including reading a label, no double dose when missing, self-dose adjustment, and action if running of medication before the next appointment ( $p < 0.05$ ). The treatment group were more satisfied to the information received by a pharmacist and the counseling area in the pharmacy made them comfortable when compared to the control group ( $p < 0.05$ ). In conclusion, patients who received the quality use of medicine service get benefits from the management drug related problems with a pharmacist including duplicated therapy and adverse drug reaction. Development of long term collaboration between community pharmacies and primary care unit should be further supported.

**Keywords:** quality care of drug use, pharmacist, accredited pharmacy, drug-related problem, Thailand

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### 161. Immersive Faculty Development Program in Interprofessional Education

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**Background:** Currently in the U.S., interprofessional education (IPE) is a required curricular element for accreditation for most health professions education programs. According to the Interprofessional Education Collaborative (IPEC) Expert Panel Report, it is essential that faculty be adequately prepared to deliver effective IPE.

**Objective:** To pilot a faculty development program in interprofessional education and to determine the utility of this program as a valid mode by which to develop faculty for IPE.

**Methods:** Faculty from the University of Kentucky Colleges of Pharmacy and Health Science Physician Assistant (PA) Studies were recruited to participate in a 3-part faculty development program as follows: 1) Online training modules consisting of assigned readings, videos, and reflective writing; 2) Live, 1-hour just-in-time training session; 3) Facilitating physician assistant and pharmacy students in a simulated Team-Based Medical Error Disclosure activity.

**Results:** Thirteen faculty members were enrolled in the faculty development program. Data collection is ongoing and includes surveys and assessments related to knowledge, competence, degree to which the program met learning objectives, and faculty member satisfaction. Data will be used for quality improvement purposes for the faculty development program.

**Discussion:** Current research indicates that active learning and immersive activities such as these are an important aspect to include in faculty development programs as they provide faculty learners an opportunity to actively apply learned skills in a real IPE activity. If this immersive faculty development program is successful, it will be considered for inclusion as a component of the official faculty development program for the University of Kentucky Interprofessional Core Curriculum and would include approximately 120 faculty members from the participating health-care colleges (Communication Sciences and Disorders, Dentistry, Medicine, Nursing, Pharmacy, Physician Assistant, and Physical Therapy).

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## 162. A Cost-Utility and Budget Impact Analysis of Drug Treatments in Pulmonary Arterial Hypertension Associated with Congenital Heart Diseases

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**Background:** Pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) is a rare condition with narrowing coronary arteries in the lungs. Currently, in Thailand, only sildenafil is a pulmonary selective drug included in the National List of Essential Medicines (NLEM) as the first line treatment, while iloprost and bosentan have not been included in the NLEM as the second-line treatment, yet. Nevertheless, until now there has been no economic evaluation information related to these drugs available in Thailand.

**Objective:** This study aimed to assess the cost-utility of drug treatments in PAH-CHD.

**Methods:** The study population was the patients with PAH-CHD with severity in functional class (FC) II and III according to the World Health Organization classification. Cost-utility analysis using a Markov

model was used to estimate the costs and health outcomes over lifetime period using a societal perspective. The first-line treatment compared beraprost and sildenafil with standard treatment. The second-line treatment compared sildenafil combined with iloprost and sildenafil combined with bosentan with sildenafil switched to standard treatment in case of no response to sildenafil as the first-line treatment. Health outcome was quality adjusted life years (QALYs) gained. Probabilistic sensitivity analyses were performed to investigate the effect of parameter uncertainty.

**Results:** In PAH-CHD patients aged  $\leq 30$  years, for the first-line treatment, compared with standard treatment, the ICERs of beraprost were 192,752 (FC II) and 201,308 (FC III) THB per QALY gained and the ICERs of sildenafil were 249,770 (FC II) and 226,802 (FC III) THB per QALY gained. For the second-line treatment, compared sildenafil switch to standard treatment, the ICERs of sildenafil plus iloprost were 1,440,409 (FC II) and 3,298,720 (FC III) THB per QALY gained and the ICERs of sildenafil plus bosentan were 805,528 (FC II) and 2,147,137 (FC III) THB per QALY gained.

**Discussion:** As the first-line treatment, both beraprost and sildenafil were close to being cost-effective. If the price of sildenafil 20 mg was decreased to 19-26 THB, it would be cost-effective in the Thai context. Furthermore, in case of no response to sildenafil as the first-line treatment, all second-line treatments were not cost-effective in the Thai context. Therefore, sildenafil should be used as the first-line treatment in PAH-CHD patients in FC II or III if its price was reduced to be cost-effective.

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### 163. Computational model evidence for a complex containing DAT, VMAT, and D2 receptors and for pH regulation of dopamine leak from storage vesicles

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**Background:** The combination of an antipsychotic drug and an inhibitor of dopamine transporter (DAT) exerts several effects on dopamine nerve terminals (varicosities) that have not yet been explained.

**Objective:** The goal of this project is to explain these effects using computer simulation models of dopaminergic varicosities.

**Method:** The simulation model utilizes rate equations for dopamine synthesis and metabolism and for transport of dopamine and its metabolite, DOPAC, between compartments. Drug effects were simulated by changing values of parameters thought to be impacted by the drugs. When such changes failed to provide a model output that matched published experimental data, additional changes were made using a trial and error process until model output matched experimental data. A set of parameters was found that provided model output closely matching published data for extracellular dopamine, extracellular DOPAC, tissue dopamine, tissue DOPAC, and rate of dopamine synthesis.

**Results:** The results document that

- D2 receptor antagonism increases extracellular dopamine by 63% with a compensatory increase in rate of dopamine synthesis
- D2 receptor antagonism increases extracellular DOPAC by 100% with a compensatory increase in rate of dopamine synthesis

- Some but not all antipsychotic drugs increase the rate of passive diffusion of dopamine out of storage vesicles. Rate of dopamine synthesis increases proportionally to the rate of increase of diffusion
- DAT inhibition decreases rate of dopamine removal from signaling space
- DAT inhibition decreases rate of secretion of dopamine by 70%
- Combination of drugs reverses decreased rate of secretion elicited by inhibitors of DAT alone
- Combination of drugs decreases rate of dopamine storage by vesicular monoamine transporter (VMAT) by 60%
- Combination of drugs decreases rate of destruction of DOPAC by 50%

**Discussion:** We postulate the following biological explanation for these observations. (1) Some (but not all) antipsychotic drugs are lipophilic weak bases. These accumulate in storage vesicles, partially alkalinize the vesicle, and increase amount of diffusible neutral dopamine. Some tyrosine hydroxylase is located on storage vesicles, and activity of this enzyme increases in proportion to increases in rate of passive diffusion of dopamine out of vesicles. (2) DAT, VMAT, and D2 receptors exist in a complex such that pharmacological inhibition of both D2 receptors and DAT results in decreased activity of VMAT.

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#### **164. Integration of Interprofessional Simulation to Enhance Communication among Professional Students Caring for the Critically Ill**

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**Objective:** Evaluate the impact of an interprofessional course utilizing high fidelity simulation on student self-reported ability to identify patient problems, assess patient severity, and communicate within an interprofessional team.

**Methods:** A course involving pharmacy, nursing, social work, and respiratory therapy was implemented in fall 2011 and utilized high fidelity simulation in an attempt to enhance communication skills amongst the professions regarding the care of critically ill patients. An IRB approved survey was administered to students on the first and last day of class. Students ranked their ability to perform tasks regarding problem identification, illness severity assessment, and communication skills for three critically ill patient case scenarios. The rating scale was 1-6; 1 represented the least confidence/ability to perform the specified task and 6 represented the most confidence/ability to perform the task. Results were analyzed through Chi-square statistics.

**Results:** 15 students enrolled for the class (6 pharmacy, 6 nursing, 3 social work). 14 students completed the pre-class survey and 11 students completed the post-class survey. There was a significant improvement in student perceived patient problem identification ( $p=0.03$ ). Student perception of communication ability with each of the professions also improved significantly ( $p=0.004$  for communicating with respiratory therapists;  $p=0.01$  for social workers;  $p=0.002$  for nurses and  $p=0.002$  for pharmacists).

**Discussion:** A pilot interprofessional course using high fidelity simulation to teach critical care patient management principles significantly enhanced problem identification and communication amongst the professions involved. Further utilization of this survey in future offerings of this class is needed to ensure validity and reliability.

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### **165. Navigator-Facilitated Care Coordination Algorithm to Improve Outcomes of Underserved Primarily Latino Patients with Uncontrolled Diabetes**

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<sup>3</sup>University of Maryland Eastern Shore School of Pharmacy

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**Objective:** To determine the impact of an interprofessional navigator-facilitated care coordination algorithm on diabetes control in underserved, primarily Latino patients using a safety-net clinic as their medical home.

**Methods:** An algorithm was created by an interprofessional team to coordinate diabetes-related services (diabetes self-management education, medication therapy management, nutrition, endocrinology) based on specific criteria for patients with poorly controlled diabetes. Over a six month period, patients with A1C $\geq$ 9% were identified through an electronic registry and contacted via phone by a navigator to schedule the recommended services based on the algorithm. A tracking tool was designed and included in the patient's medical record, indicating dates of navigator contact, selected diabetes-related services and the appointment dates for such services. A1C was the primary outcome measure evaluated both before and after receiving referral algorithm services (i.e. patients served as their own control). Paired Student's t-test was used to analyze the data.

**Results:** Pre- and post-service A1C data was available for 45 patients. Average A1C decreased from 10.6 $\pm$ 1.2% to 8.8 $\pm$ 2.1% (p<0.001). Among the 34 patients who demonstrated improvement in A1C from baseline (76%), the average decrease was 2.5 percentage points (10.6 $\pm$ 1.1% to 8.1 $\pm$ 1.7%), p<0.001. Thirty-two (76%) of the 45 patients were Latino. In that subset of patients, average A1C improved from 10.6 $\pm$ 1.2% to 9.1 $\pm$ 2.2% (p=0.0013). Average A1C for non-Latino patients improved from 10.4 $\pm$ 1.0 to 8.0 $\pm$ 1.4% (p=0.0004).

**Discussion:** Interprofessional navigator-facilitated care coordination had a positive and rapid impact on A1C for low income, uninsured, primarily Latino patients with poorly controlled diabetes.

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### **166. Promoting Medication Use with Generic Name in Medical and Pharmacy School, Maharakham University, Thailand**

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**Background:** Rational Use of medicines (RUM) requires quality use of medicines with the appropriateness, effectiveness, safety, rational cost and benefit to patients. One of 12 WHO interventions to promote RUM is the problem-based pharmacotherapy training in undergraduate curricula. Moreover, WHO guide to good prescribing recommends health professionals to support RUM by prescribing medicines with their generic names. To promote RUM in school training, both Faculty of Medicine and Faculty of Pharmacy have a joint educational intervention.

**Objective:** To promote medication prescribing and dispensing with generic name in the institutional trainings

**Methods:** This 9-month action research was done by a educational research team between 2 faculties. Samples were medical students and pharmacy students registered in the first semester of the academic year of 2013 (June-October 2013). An study intervention was pre-clinic training by pharmacy and medical lecturers composed of 2 contents; 1) Principles of RUM and prescribing medicines with generic name for students before having internship rotation (51 medical students year 3 and 75 pharmacy students year 5) and 2) problem-based training in courses of pharmacology and pharmacotherapy for 207 pharmacy students (year 3-4).

Results: Two lectures of RUM principle and the benefit of medication prescribing and dispensing with generic name were done; 1) Family medicine 3 course for medical students and 2) Pharmacoeconomics course for pharmacy students. The students' self assessment after the lecture revealed that all of them understood the concepts RUM and medication use with generic name. Students explained the benefits of using generic name of medicine; 1) reducing the potentially duplicated medication 2) reducing medication errors and drug interactions 3) supporting the cost-effective medicine 4) not supporting the sale promotion of pharmaceutical company and 5) supporting the international understanding on medicine within health professionals and between them and patients. After the case study and problem-based training in pharmacology and pharmacotherapy courses, 99.5% of pharmacy students showed the skill of dispensing medicine with generic name. A trade name of sulfonamides (Bactrim<sup>®</sup>) was mostly found. Cephalosporins and Sulfonamides were medicine groups that students (30.4% and 24.2%, respectively) wrote generic names incorrectly.

**Discussion:** The pre-clinic intervention in the lecture courses and problem-based training courses can enhance medical and pharmacy students to concern on RUM and medication use with generic name and to train their skill of writing the correct generic name of medicine. these will be a initiate point for supporting students to be the health professionals for RUM practice.

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### 167. The Effect of Disruption of Circadian Rhythm on Vascular Function in Lean (C57BL/6) and Obese, Leptin Resistant (*db/db*) Mice

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An artificial light or shift work at night might disturb a circadian gene oscillation and behavior which has been known to associate with cardiovascular and metabolic risks. However, the mechanisms of circadian disruption on vascular function still remain unclear. The aim of this study is to determine whether

disruption of the circadian rhythm impairs the vascular function in lean (C57/BL6) mice (LM) and enhances the vascular dysfunction in obese, leptin resistant (*db/db*) mice (OB). Lean and obese male mice, age 10-11 weeks were subjected to normal *12:12 h light-dark cycle* or constant darkness to disrupt the circadian rhythm for 4 weeks. The metabolic parameters, vascular reactivity of thoracic aorta and small mesenteric artery were evaluated. In addition, daily rhythmic expression of clock genes (*BMAL1*, *CLOCK*, *NPAS2*, *PER1*, *PER2*, *CRY1*), clock output gene (*DBP*), vascular relaxation-related genes (*eNOS*, *GTPCH1*), and superoxide-related genes (*NOXs*, *SODs*) were also investigated. Circadian disruption had no effect on glucose metabolism in LM, while marked increase in fasting serum glucose and HbA1C levels in OB. OB had stronger aortic vasoconstriction to 5-HT than LM. Circadian disruption enhanced the response to 5-HT only in LM. In small mesenteric artery, the vasoconstriction to PE was not altered by obesity or circadian disruption. While the endothelium-dependent dilation to Ach was attenuated in OB and depressed in LM subjected to constant darkness. In the presence of L-NAME, the vasodilator responses were attenuated in both LM and OB. SNP-mediated relaxation was impaired in LM subjected to constant darkness but was not observed in OB. In small mesenteric artery, the rhythmic expression of *PER1* and *DBP* was depressed in OB. Circadian disruption altered the daily oscillation of *CLOCK*, *NPAS2*, and *PER1* and depressed gene profile of *DBP* in LM. The vascular profile of *eNOS* expression was depressed and *GTPCH1* rhythmic expression was lost, both in obesity and by constant darkness. The *SODs* expression was also depressed in obesity and by constant darkness, while the *NOXs* components were generally increased in obese subjected to constant darkness. These results suggested that circadian disruption increased the vasoconstrictor property of macrovessel and impaired both endothelium-dependent and independent dilation of microvessel in lean mice without metabolic disturbances. However, circadian disruption exacerbates glycemic load but did not enhance the vascular impairment in obese mice. The interruption of nitric oxide pathways reveals an underlying mechanism of vascular impairment by circadian disruption. Aberrant clock gene oscillation and vascular dysfunction might imply a parallel interconnection.

**Keywords:** Circadian disruption, clock genes, obesity, vascular function, *eNOS*

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### **168. *Pandanus amaryllifolius* Root Extract Reduces Locomotor Activity and Prolongs Sleeping Time and in Mice**

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**Background:** Some plants in *Pandanus* species were reported to be potential as a CNS depressant

**Objective:** To investigate locomotor activity and hypnotic effect of the decoction of *Pandanus amaryllifolius* root in mice.

**Methods:** Locomotor activities were measured by small-animal activity monitor (Animate, MATYS, Toyo Sangyo, Japan).

**Results and Discussion:** The extract at doses of 1- 2 g/kg significantly decreased the spontaneous locomotor activity in a dose-dependent manner during 30 minutes after feeding. The extract at the dose 4 g/kg significantly suppressed the locomotor activity in methamphetamine-treated mice but the lower dose cannot. In addition, the extract at doses of 0.5-2 g/kg feeding prolonged the pentobarbital-induced sleeping time in both sexes of mice. This effect was not attenuated by flumazenil (a selective benzodiazepine receptor antagonist). These results suggest that the water extract of *Pandanus amaryllifolius* root suppressed the spontaneous and amphetamine-activated locomotor activity. The extract also potentiated the effect of pentobarbital sodium on sleep which is not implicated with benzodiazepine receptor system.

**Keywords:** *Pandanus amaryllifolius*, sleeping time, flumazenil, locomotor activity, methamphetamine

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### **169. Safety and quality aspects of Thai fermented herbal beverages with selected probiotic *Lactobacillus plantarum* strain**

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Lactic acid fermented herbal beverages (FHBs) have been widespread used as functional foods in Thailand. Thai people believe that these products are able to relieve disease symptoms and promote health. However, they are still household products distributed in several areas. Moreover, major contaminants which were methanol and fungus were detected in the finished products. In order to solve the problem, it is necessary to use bacterial starter to eliminate the pathogenic microbial and harmful metabolite contamination in order to control the safety and quality of the FHBs. The objectives of study were to isolate *Lactobacillus* spp. from food origins and to examine probiotic properties. The selected strain which possess the probiotic properties was used as starter culture of FHBs for developing the safe functional food products from Thai indigenous plants. Total 763 non-human origin strains isolated from fermented products containing plant were collected. A number of lactic acid bacteria (LAB) strains were isolated and primarily identified for *Lactobacillus* sp. All isolates were then evaluated for some key probiotic properties. The selected *L. plantarum* strain had growth ability in 0.15 and 0.30% (w/v) bile salt, growth ability in pH values between 3-8, exhibited strong antimicrobial activities against *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* ATCC 11778, *Pseudomonas aeruginosa* ATCC 27853 and *Candida albicans* ATCC 90028, utilizations of protein and starch. Moreover, the strain expressed the ability to obstruct the Caco-2 cell adherence of three bacterial pathogens such as *E. coli*, *Salmonella* spp. and *Shigella* spp. with the percentages of inhibition ranged 52.13 to 74.39. For the preliminary safety tests, the strain was susceptible to 9 antibiotics and did not reveal alpha and beta haemolysis. The probiotic strain was prepared to be a potentially starter culture (about  $10^8$  cfu/ml) for FHBs. The strain provides a starter for controlled fermentation of FHBs gave better safety and quality than obtained without starter culture. At the end of 30 day fermentation, lactic acid increased from 0.05 to 1.98% (w/v). The maximum amount ( $5.76 \times 10^9$  cfu/ml) of *Lactobacillus* sp. increased significantly ( $P < 0.05$ ) at 15 days of fermentation. Methanol, fusel oils, harmful metabolites

and food-borne pathogens were not detected during 7-180 days of fermentation period. The selected probiotic strain, *L. plantarum*, could be developed as an effective starter culture for Thai FHBs products. The probiotic *L. plantarum* strain will be developed in further work as easy form of starter culture for Thai functional FHBs manufacturing.

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### **170. Evaluation of Rifaximin Therapy in the Medical Intensive Care Unit**

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**Purpose:** Approximately 5.5 million patients, their families, and healthcare providers bear the burden of chronic liver disease (CLD) in the United States. Hepatic encephalopathy (HE) is a complication that occurs in people with advanced cirrhosis or severe liver damage. Antibiotics have been used to decrease ammonia by reducing the growth of intestinal bacteria. Rifaximin exhibits a high tolerability profile and low clinical drug interactions compared to other antibiotics for treatment of HE. Based on direct observation, the majority of patients admitted to the medical intensive care unit (MICU) at the University of Maryland Medical Center (UMMC) for HE are started on rifaximin therapy. However, due to a lack of data, rifaximin's place in therapy for the treatment of HE is yet to be determined. In addition, no studies have assessed the pattern of rifaximin use. This study will describe the population administered rifaximin in the MICU.

**Methods:** The study was a retrospective chart review from July 1, 2011 to June 30, 2013. This study included adult patients initiated on rifaximin therapy, during their MICU admission. Data collection included patient demographics, etiology of CLD, disease severity, pertinent laboratory data, HE participating factors, rifaximin regimen, and patient outcomes. Statistical analysis will be performed with Microsoft Excel and SPSS software version 11.5 (SPSS, Chicago, IL).

**Results:** Data collection is in progress. The results will be presented at the meeting.

**Conclusions:** This study will describe the utilization of rifaximin therapy in the MICU population and outcomes of these patients.