Thai Journal of Pharmacology

www.thaipharmacol.org

Official Publication of
Pharmacological and Therapeutic Society of Thailand

Proceeding of 33rd Pharmacological and Therapeutic Society of Thailand Meeting

17-19 March 2011

Vol.33, Suppl. 1, 2011 ISSN 0125-3832

Thai Journal of Pharmacology

is owed and published every four months by the Pharmacological and Therapeutic Society of Thailand.

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Printed at Ruen Kaew Press, 947 Arun-Amarin Road, Bangkok 10700.Tel: 024126552

Thai Journal of Pharmacology

Vol. 33, Supplement 1, 2011

สารจากนายกสมาคมเภสัชวิทยาแห่งประเทศไทย

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เรียน สมาชิกสมาคมเภสัชวิทยาฯ และผู้เข้าร่วมประชุมทุกท่าน

การประชุมวิชาการประจำปีสมาคมเภสัชวิทยาแห่งประเทศไทย ได้จัดขึ้นเป็นครั้งที่ 33 ในปีนี้ ระยะเวลากว่า 3 ทศวรรษของการดำเนินงานของสมาคมเภสัชวิทยาแห่งประเทศไทย สะท้อนให้เห็นถึงความร่วมแรง ร่วมใจ และความมุ่งมั่นของสมาชิกชาวเภสัชวิทยาทั้งหลาย ในการที่จะเผยแพร่ความรู้ความก้าวหน้าด้านเภสัชวิทยาให้แก่สมาชิกและสังคม ในทุกครั้งของการประชุมฯ คณะกรรมการจัดการประชุมและสมาคมฯมีความตั้งใจอย่างยิ่งที่จะนำเสนอหัวข้อทางวิชาการที่สำคัญและทันสมัย กิจกรรมของสมาคมฯมิได้มีเฉพาะการประชุมวิชาการประจำปีเท่านั้น แต่ยังมีการนำเสนอหัวข้อทางวิชาการที่เป็นที่สนใจในขณะนั้นแก่ผู้สนใจด้วยเป็นครั้งคราว

ดิฉันรู้สึกยินดีเป็นอย่างยิ่งที่ได้เห็นสมาชิกชาวเภสัชวิทยารวมทั้งผู้ที่สนใจในศาสตร์แขนงนี้ ได้มารวมตัวกันเป็นจำนวนมากในสถานที่เดียวกันอีกครั้งในปีนี้ ซึ่งจะเกิดขึ้นไม่ได้หากไม่ได้รับการประสานงานจากคณะกรรมการผู้จัดงาน ภาควิชาเภสัชวิทยา คณะวิทยาศาสตร์ มหาวิทยาลัยสงขลานครินทร์ รวมทั้งวิทยากรทุกท่านที่สละเวลาอันมีค่ามาให้การบรรยาย ผู้ให้การสนับสนุนจากทุกหน่วยงาน และผู้เข้าร่วมประชุมทุกท่าน ดิฉันจึงขอขอบคุณ มา ณ ที่นี้

ในนามของสมาคมเภสัชวิทยาดิฉันขอต้อนรับทุกท่านสู่การประชุมวิชาการประจำปีสมาคมเภสัชวิทยาแห่งประเทศไทย ครั้งที่ 33 ด้วยความเชื่อมั่นว่าทุกท่านจะได้รับทั้งสาระวิชาการและความสุขใจที่ได้มีโอกาสได้พบกับเพื่อนสมาชิกชาวเภสัชวิทยาที่ท่านอาจจะไม่ได้พบกันมานานอีกครั้ง

รองศาสตราจารย์ ดร.มยุรี ตันติสิระ
นายกสมาคมเภสัชวิทยาแห่งประเทศไทย

สารจากประธานจัดงานประชุมวิชาการประจำปีครั้งที่ 33

.....

เรียนท่านนายกสมาคมเภสัชวิทยาแห่งประเทศไทย สมาชิกสมาคมฯ และผู้เข้าร่วมประชุมทุกท่าน

การประชุมวิชาการสมาคมเภสัชวิทยาแห่งประเทศไทยได้จัดให้มีขึ้นเป็นประจำทุกปี เพื่อเป็นการเผยแพร่ความก้าวหน้าทางวิทยาการด้านเภสัชวิทยาแก่สมาชิกสมาคมฯ และผู้สนใจ การจัดประชุมฯ นี้ไม่เพียงจะมุ่งเน้นสาระในด้านวิชาการเท่านั้น แต่ยังเป็นการแสดงความระลึกถึงเกียรติคุณของ รองศาสตราจารย์ ดร.จิรวัฒก์ สดาวงศ์วิวัฒน์ นายกสมาคมเภสัชวิทยาแห่งประเทศไทยคนแรก และครูบาอาจารย์ผู้มีพระคุณที่ได้อบรมสั่งสอนนักเภสัชวิทยารุ่นต่าง ๆ นอกจากนี้ยังเป็นการสร้างโอกาสอันดีแก่ชาวเภสัชวิทยาซึ่งส่วนใหญ่เป็นคณาจารย์ในสถาบันต่าง ๆ ทั้งในฐานะเพื่อน พี่ น้อง อาจารย์ และลูกศิษย์รุ่นต่าง ๆ ได้มาพบปะสังสรรค์กัน

สำหรับปีนี้การประชุมจัดขึ้นในหัวข้อ Pharmacological Researches for the Benefit of Mankind เพื่อเป็นการสื่อให้เห็นว่าผลที่ได้รับจากงานวิจัยด้านเภสัชวิทยานั้นบังเกิดแก่เพื่อนมนุษย์ทั้งหลายนั้นเอง โดยการประชุมมีเนื้อหาครอบคลุมหลากหลายประเด็นสำคัญทางเภสัชวิทยาที่เกี่ยวข้องกับ ความเจ็บปวด โรคมะเร็ง โรคเมตาโบลิค โรคติดเชื้อ นอกจากนี้ยังมีเนื้อหาเกี่ยวกับ บทบาทของเภสัชวิทยาจีโนมต่อผลอันไม่พึงประสงค์จากการใช้ยา รวมทั้งการวิจัยและพัฒนาด้านสมุนไพร เป็นต้น การประชุมในครั้งนี้ได้รับเกียรติบรรยายโดยวิทยากรทั้งชาวไทยและต่างประเทศซึ่งเป็นผู้ที่มีชื่อเสียงเป็นที่ยอมรับอย่างกว้างขวางในแวดวงวิชาการ

การประชุมในครั้งนี้ ภาควิชาเภสัชวิทยา คณะวิทยาศาสตร์ มหาวิทยาลัยสงขลานครินทร์ได้รับมอบหมายจากสมาคมเภสัชวิทยาแห่งประเทศไทยให้เป็นผู้จัดการประชุมฯ ซึ่งถือว่าเป็นเกียรติอย่างยิ่ง ดิฉันในนามของประธานคณะกรรมการจัดการประชุม ขอขอบคุณคณะกรรมการทุกท่าน นายกสมาคมฯ และคณะกรรมการบริหารสมาคมฯ วิทยากรผู้ทรงเกียรติ ผู้ให้การสนับสนุนจากทุกภาคส่วน รวมทั้งผู้เข้าร่วมประชุมทุกท่าน ซึ่งล้วนแต่มีความสำคัญที่ทำให้มีการประชุมในครั้งนี้ขึ้นได้ ดิฉันหวังเป็นอย่างยิ่งว่าผู้เข้าร่วมประชุมทุกท่านจะได้รับประโยชน์จากการประชุมฯ ในครั้งนี้ไม่มากก็น้อย หากมีข้อผิดพลาด หรือมีความไม่สะดวกประการใดก็ตาม ดิฉันขออภัยไว้ ณ ที่นี้ และขอน้อมรับคำติติงและคำแนะนำด้วยความยินดียิ่ง

รศ.ดร.เบญจมาศ จันทร์ฉวี

ประธานคณะกรรมการจัดการประชุมฯ

คำปราศรัยของ รองศาสตราจารย์ ดร.จุฑามาส ศตสุข
คณบดีคณะวิทยาศาสตร์ มหาวิทยาลัยสงขลานครินทร์
เนื่องในพิธีเปิดการประชุมวิชาการประจำปี ครั้งที่ ๓๓
สมาคมเภสัชวิทยาแห่งประเทศไทย
วันพฤหัสบดีที่ ๑๗ มีนาคม พ.ศ. ๒๕๕๔
ณ โรงแรมไดมอนด์พลาซ่า อ.หาดใหญ่ จ.สงขลา

.....

ท่านประธานคณะกรรมการจัดประชุมวิชาการ ท่านนายกสมาคมเภสัชวิทยาแห่งประเทศไทย
ท่านวิทยากร และท่านผู้เข้าร่วมประชุมผู้มีเกียรติทุกท่าน

ดิฉันรู้สึกเป็นเกียรติและยินดีอย่างยิ่ง ที่ได้มีโอกาสมาเป็นประธานในพิธีเปิดการประชุมวิชาการประจำปี ครั้งที่ ๓๓ ของสมาคมเภสัชวิทยาแห่งประเทศไทยในวันนี้ ขอแสดงความยินดีที่สมาคมเภสัชวิทยาได้ดำเนินงานจนประสบความสำเร็จมาตลอดระยะเวลากว่า ๓๐ ปี

ศาสตร์ด้านเภสัชวิทยามีความสำคัญต่อการนำยาไปใช้ในทางการแพทย์เพื่อการรักษา ป้องกัน หรือวินิจฉัยโรค นักเภสัชวิทยามีความตั้งใจ ทุ่มเท และอุทิศเวลาในการศึกษา ค้นคว้า วิจัย ในทุก ๆ แง่มุม เพื่อให้ได้มาซึ่งยาที่มีประสิทธิภาพและปลอดภัยทั้งนี้ก็เพื่อประโยชน์ของเพื่อนมนุษย์ ดังจะเห็นได้จากหัวข้อของการจัดประชุมในครั้งนี้ “Pharmacological Researches for the Benefit of Mankind” นั้นตรงกับทิศทางของมหาวิทยาลัยที่ว่า “Our Soul is for the Benefit of Mankind” ซึ่งมาจากการน้อมนำพระราโชวาทของเจ้าฟ้ามหิดลอดุลยเดช กรมหลวงสงขลานครินทร์ที่ว่า “ขอให้ถือผลประโยชน์ส่วนตัวเปนที่สอง ประโยชน์ของเพื่อนมนุษย์เปนกิจที่หนึ่ง ลาภ ทรัพย์ และเกียรติยศ จะตกมาแก่ท่านเองถ้าท่านทรงธรรมะแห่งอาชีพย์ไว้ให้บริสุทธิ์”

เนื่องจากองค์ความรู้ด้านเภสัชวิทยามีความก้าวหน้าไปอย่างรวดเร็วประกอบกับความก้าวหน้าทางด้านวิทยาศาสตร์และเทคโนโลยี การประชุมวิชาการจะทำให้นักวิชาการและบัณฑิตได้ติดตามวิทยาการได้ทันเพื่อประโยชน์ในการพัฒนาตนเอง หน่วยงานและประเทศชาติต่อไป

มหาวิทยาลัยสงขลานครินทร์มีความยินดี และขอต้อนรับผู้เข้าร่วมประชุมทุกท่าน และขอให้ผู้เข้าร่วมประชุมทุกท่านได้นำความรู้ที่ได้ กลับไปพัฒนาทั้งด้านการเรียนการสอนและงานวิจัยตามที่ได้

ตั้งใจไว้ บัดนี้ได้เวลาอันสมควรแล้ว ดิฉันขอเปิดการประชุมวิชาการ ครั้งที่ ๓๓ ของสมาคมเภสัช-วิทยาแห่งประเทศไทย และขออวยพรให้การประชุมครั้งนี้บรรลุตามวัตถุประสงค์ และสำเร็จสมดังเจตนารมณ์ที่ตั้งไว้ทุกประการ

รองศาสตราจารย์ ดร.จุฑามาส ศตสุข
คณบดีคณะวิทยาศาสตร์
มหาวิทยาลัยสงขลานครินทร์

บรรณาธิการแถลง

เรียนท่านสมาชิกและผู้เข้าร่วมสัมมนา

วารสารสมาคมเภสัชวิทยาแห่งประเทศไทย (Thai Journal of Pharmacology) ฉบับนี้ จัดเป็นฉบับ Supplement ของปี 2554 และเป็น Proceeding สำหรับการประชุมวิชาการประจำปีครั้งที่ 33 ของสมาคมเภสัชวิทยาแห่งประเทศไทย ซึ่งภาควิชาเภสัชวิทยา คณะวิทยาศาสตร์ มหาวิทยาลัยสงขลานครินทร์ ได้รับเป็นเจ้าภาพจัดการประชุม ภายใต้หัวข้อ "Pharmacological Researches for the Benefit of Mankind" การประชุมวิชาการในปีนี้มีผู้เข้าร่วมเสนอผลงานวิชาการเป็นจำนวนมาก จึงหวังเป็นอย่างยิ่งว่าจะนำไปสู่การทำความรู้จัก แลกเปลี่ยนประสบการณ์ด้านความรู้งานวิจัยทางด้านเภสัชวิทยา อันส่งผลให้เกิดความร่วมมือในการพัฒนาวิชาชีพ และการสร้างสรรค์งานวิจัยต่อไปในอนาคต

ขอขอบคุณ คณะกรรมการจัดการประชุมวิชาการทุกท่าน ที่ได้รวบรวมข้อมูล เนื้อหา และรายละเอียดต่าง ๆ จนสามารถจัดเป็นวารสารฉบับนี้ได้

รองศาสตราจารย์ ดร.ลัดดาวัลย์ ผิวทองงาม

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รองศาสตราจารย์ พญ.ศศิกานต์ นิมมานรัชต์	คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์
นพ.พิสุทธ์ ศิริไพฑูรย์	คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์
ภญ. วิมล สุวรรณเกษาวงษ์	ศูนย์เฝ้าระวังความปลอดภัยด้านผลิตภัณฑ์สุขภาพ สำนักงานคณะกรรมการอาหารและยา
รองศาสตราจารย์ ดร.วิจิตรา ทัศนียกุล	คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น
นพ. พงศธร เนตราคม	โรงพยาบาลวิชัยยุทธ และเลขาธิการสมาคมจิตแพทย์แห่งประเทศไทย
ดร.กฤษณา ไกรสินธุ์	คณะการแพทย์แผนตะวันออก มหาวิทยาลัยรังสิต
รศ.ภก.ดร.ภาคภูมิ พาณิชยูปการนันท์	คณะเภสัชศาสตร์ มหาวิทยาลัยสงขลานครินทร์
ผศ.ภก.ดร.จินดาพร ภูริพัฒนาวงษ์	คณะเภสัชศาสตร์ มหาวิทยาลัยสงขลานครินทร์

รองศาสตราจารย์ ภญ.ดร.มยุรี ตันติสิระ **คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย**

รองศาตราจารย์ นพ.สุภมัย สุนทรพันธ์ **คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์**

รองศาตราจารย์ พญ.รัตนา ลีลาวัฒนา **คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์**

กำหนดการจัดประชุมวิชาการประจำปี ครั้งที่ 33
สมาคมเภสัชวิทยาแห่งประเทศไทย ร่วมกับ
ภาควิชาเภสัชวิทยา คณะวิทยาศาสตร์ มหาวิทยาลัยสงขลานครินทร์
ระหว่างวันที่ 17-19 มีนาคม 2554
ณ ห้องประกายเพชร โรงแรมไดมอนด์พลาซ่า อ.หาดใหญ่ จ.สงขลา

"Pharmacological Researches for the Benefit of Mankind"

วันพฤหัสที่ 17 มีนาคม 2554

7.45-8.15 ลงทะเบียน

8.15-8.45 ประธานการประชุมกล่าวรายงาน
พิธีเปิดการประชุม โดย อธิการบดีมหาวิทยาลัยสงขลานครินทร์
นายกสมาคมฯกล่าวต้อนรับผู้เข้าร่วมการประชุม

8.45-10.15 **The 18th Dr.Chiravat Sadavongvivad Memorial Lecture:**
Antioxidants and free radicals in health, life, disease and death
Professor Barry Halliwell
Deputy President (Research and Technology), National University of Singapore

10.15-10.45 พัก:- อาหารว่าง และชมการแสดงผลงานทางวิชาการโดยโปสเตอร์

10.45-11.45 **Session 1: Emerging data of Targeted Therapies in Hemato-Oncology Cancer**
(ผู้ดำเนินการอภิปราย: ดร.นพ.พงษ์เทพ วิบูลย์จันทร์ มหาวิทยาลัยสงขลานครินทร์)
CML (Chronic Myeloid Leukemia): Improving clinical outcome by 2nd generation TKI in CML
ดร.นพ.พงษ์เทพ วิบูลย์จันทร์
คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์
NET (Neuroendocrine Tumor): How to overcome unmet medical need for pNET (Pancreatic NET) and carcinoid tumors
ผู้ช่วยศาสตราจารย์ พญ.ภัทรพิมพ์ สรรพวีรวงศ์
คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์
สนับสนุนโดยบริษัท โนวาร์ตีส (ประเทศไทย) จำกัด

11.45-12.45 **Luncheon symposium 1:**
Aescin: What's new for the treatment of chronic venous insufficiency?
Lucio Cavicchioli
Director, International Medical Marketing, Rottapharm Madaus Group
ณ ห้องไข่มุก; สนับสนุนโดยบริษัท ร็อตต้าฟาร์ม (ประเทศไทย) จำกัด

12.45-14.00 **Session 2: Molecular drug targets and management of pain**

(ผู้ดำเนินการอภิปราย: ผู้ช่วยศาสตราจารย์ สมสมร ชิตตระการ มหาวิทยาลัยสงขลานครินทร์)

Pain mechanism: ion channels and receptors

รองศาสตราจารย์ ภญ.ดร.จุฑามณี สุทธิสีสังข์

คณะเภสัชศาสตร์ มหาวิทยาลัยมหิดล

Trend in pain management

รองศาสตราจารย์ พญ.ศศิกานต์ นิมมานรัชต์

คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์

14.00-14.45 **Session 3: Update on antimicrobials**

Antimicrobial agents in clinical use: what's new?

นพ.พิสุทธ์ ศิริไพฑูรย์

คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์

14.45-15.15 พัก:- อาหารว่าง และชมการแสดงผลงานทางวิชาการโดยโปสเตอร์

15.15-16.30 **Session 4: Pharmacogenomics of adverse drug reaction**

(ผู้ดำเนินการอภิปราย: ดร.วันดี อุดมอักษร มหาวิทยาลัยสงขลานครินทร์)

Adverse drug reactions in Thailand

ภญ. วิมล สุวรรณเกษาวงษ์

ศูนย์เฝ้าระวังความปลอดภัยด้านผลิตภัณฑ์สุขภาพ สำนักงานคณะกรรมการอาหารและยา

Pharmacogenomics of adverse drug reactions

รองศาสตราจารย์ ดร.วิจิตรา ทัศนียกุล

คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

16.30-17.15 **Session 5: Circadian rhythm and depression: Pharmacology of melatonergic antidepressant agomelatine, an update**

นพ. พงศธร เนตราคม

โรงพยาบาลวิชัยยุทธ และเลขาธิการสมาคมจิตแพทย์แห่งประเทศไทย

สนับสนุนโดยบริษัท เซอร์เวียร์ (ประเทศไทย) จำกัด

18.30-20.30 งานเลี้ยงต้อนรับ ณ ห้องประกายเพชร

วันศุกร์ที่ 18 มีนาคม 2554

8.30-10.00 **Session 6: Medicinal plant utilization: costs, risk and rewards**

ดร.กฤษณา ไกรสินธุ์

คณะการแพทย์แผนตะวันออก มหาวิทยาลัยรังสิต

10.00-10.30 พัก:- อาหารว่าง และประชุมธุรการสมาคมฯ

10.30-11.45 นำเสนอผลงานทางวิชาการโดยโปสเตอร์ของนักศึกษา

พิจารณาผลงานโดย คณะกรรมการพิจารณาผลงานวิจัย

11.45-12.45 **Luncheon symposium 2: Recent advance and future trend in cancer treatment**

ผู้ช่วยศาสตราจารย์ พญ.ภัทรพิมพ์ สรรพวีรวงศ์

คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์

ณ ห้องไข่มุก; สนับสนุนโดย สมาคมผู้วิจัยและผลิตเภสัชภัณฑ์ (PReMA)

12.45-14.15 **Session 7: Medicinal plants: research & development for the community**

(ผู้ดำเนินการอภิปราย: รองศาสตราจารย์ ภญ.ดร.มยุรี ตันติสิระ จุฬาลงกรณ์มหาวิทยาลัย)

Active constituent-rich herbal extracts: A trend in herbal medicine development

รองศาสตราจารย์ ภก.ดร.ภาคภูมิ พาณิชยูปการนันท์

คณะเภสัชศาสตร์ มหาวิทยาลัยสงขลานครินทร์

Standardization of Thai herbal medicine

ผู้ช่วยศาสตราจารย์ ภก.ดร.จินดาพร ภูริพัฒนาวงษ์

คณะเภสัชศาสตร์ มหาวิทยาลัยสงขลานครินทร์

Standardized extract of *Centella asiatica* : Success & Failure

รองศาสตราจารย์ ภญ.ดร.มยุรี ตันติสิระ

คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

14.15-14.45 พัก:- อาหารว่าง

14.45-16.00 **Session 8: Metabolic syndrome: its importance and management**

(ผู้ดำเนินการอภิปราย: รองศาสตราจารย์ นพ.วีรวัฒน์ มหัทธนตระกูล มหาวิทยาลัยสงขลานครินทร์)

Definition of metabolic syndrome and impact on CVD

รองศาตราจารย์ นพ.สุภมัย สุนทรพันธ์

คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์

Metabolic syndrome: how to handle?

รองศาตราจารย์ พญ.รัตนา ลีลาวัฒนา

คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์

16.00-16.05 ประกาศและมอบรางวัลการนำเสนอผลงานวิจัย

16.05-16.30 นำเสนอผลงานวิจัยโดยผู้ชนะเลิศ

16.30 พิธีปิดการประชุมโดยนายกสมาคมฯ

วันเสาร์ที่ 19 มีนาคม 2554

9.00-12.00 Workshop: ความร่วมมือทางวิชาการระหว่างสถาบันในด้านงานวิจัย และการเรียนการสอนระดับบัณฑิตศึกษา

Chiravat Sadavongvivad Memorial Lecture

Antioxidants and free radicals in health, life, disease and death

Barry Halliwell

Department of Biochemistry, Yong Loo Lin School of Medicine
National University of Singapore

Reactive (oxygen) species are generated continually in the human body, both for useful purposes and by "accidents of chemistry". They are significant contributors to age-related diseases and perhaps to the ageing process itself, e.g. they contribute to cancer and neurodegeneration [Halliwell B (2007) Oxidative stress and cancer: have we moved forward? *Biochem J.* 401:1-11; Halliwell B (2006) Oxidative stress and neurodegeneration; where are we now? *J. Neurochem.* 97:1634-58]. Nevertheless, reactive species have beneficial effects in killing invading organisms and facilitating signal transduction, especially in coordinating the inflammatory response. Indeed, several epidemiological studies have found little protective effect of antioxidants against disease development, whereas dietary fruits and vegetables appear more beneficial in health maintenance and disease prevention, in at least some studies. Many constituents could contribute to these effects, including antioxidants and (seemingly paradoxically) pro-oxidants, exerting effects within the gastrointestinal tract and perhaps systemically after absorption. The care needed to establish the true effects of antioxidants and pro-oxidants in cell culture [Halliwell B (2008) Are polyphenols antioxidants or pro-oxidants? What do we learn from cell culture and in vivo studies? *Arch. Biochem. Biophys*. 476:107-112] and in vivo [Halliwell and Lee (2010) Using isoprostanes as biomarkers of oxidative stress: some rarely considered issues. *Antioxid Redox Signal.* DOI: 10.1089/ars.2009.2934] will be illustrated by recent data using "biomarkers" of oxidative damage. The 3Ps of biomarkers (potential, promise, pitfalls) will be briefly described.

Session 1: Emerging data of Targeted Therapies in Hemato-Oncology Cancer

How to overcome unmet medical need for neuroendocrine tumor?

Patrapim Sunpaweravong, MD

Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University

Neuroendocrine tumors (NET) represent a heterogeneous group of neoplasm with various clinical characteristics and prognosis. However, most patients with NET are able to have a long term survival and favorable clinical outcomes with multidisciplinary management approaches. Early diagnosis of NET is not able to be achieved straight forwardly due to the non-specific symptoms that the patients have experienced. No standard screening markers and diagnostic procedures have been recommended for NET. Pathological classification of NET has been updated recently and makes the diagnosis of this neoplasm more clinically appropriated. Regarding multidisciplinary treatment approach of NET, effective modalities should be discussed and applied for patients individually. Surgery, external radiotherapy, and ablative procedures should be considered for localized lesions whereas metastatic diseases are treated with systemic therapy. Chemotherapy is effective in poorly-differentiated and highly–proliferative tumors. Advances in utilizing somatostatin analogs and targeted therapy agents (mTOR inhibitors, multi-targeted tyrosine kinase inhibitory) targeting potential molecular pathways involving NET proliferation have been reported and will be reviewed.

Luncheon symposium 1

Aescin: pharmacological mechanisms involved in the treatment of trauma- or CVI-associated oedema

Lucio Cavicchioli

Director, International Medical Marketing, Rottapharm Madaus Group

Chronic venous insufficiency (CVI) is a common disease, with increasing prevalence in the general population and particularly affecting women during pregnancy and throughout their post-menopausal life. CVI is usually primarily considered a physical and haemodynamic disorder, where increased haemostatic pressure in legs (due to standing or sitting over long periods) is associated to presence of varicosis and some degree of thrombosis; the resulting difficulty in closing venous valves affects the circulation, leading to chronic hypoxia of the vascular structures. Oedema of surrounding tissues (and the related risk of difficult-to-heal leg ulcers) represents the consequence of the hypoxia-induced microvascular damage. Primary pharmacological therapy is usually focused on larger venous structures, to cure or prevent thrombophlebitis, and is mostly associated with mechanical compression therapy to reduce oedema formation. This gold standard approach, however, seems not to take into account the underlying pathological condition of microvessels, whose lesioned endothelial structures -severely damaged by the hypoxia- contribute to maintain a self-sustaining unfavourable local microenvironment. Opening of venular gaps leads to an outflow of blood and plasma components to the surrounding interstitial tissues and forms the microscopic correlate to the oedema observed clinically. Thrombogenic factors, e.g. tissue factors, induce interstitial inflammation and thrombosis, which spread to the venular lumen, possibly via the open gaps, reducing or cutting off perfusion. This inflammation may maintain the opening of the venular gaps, thus resulting in a chronic pathologic condition. Some authors have even focused on the smaller vessels and their endothelium, as opposed to venous valves, as the starting cause for CVI. Most likely, a combination of the “macro” and “micro” therapy would represent the most complete curative approach. Particularly in view of their anti-inflammatory and anti-oedematous properties at microcirculation level, pharmacological preparations of highly purified Aescin (extracted from horse-chestnut seeds) have been studied in both preclinical models of CVI and in patients with the disease. Recent data suggest that escin may prevent and/or reduce oedema by preventing hypoxia-induced disruption of endothelial junctions, thus contributing to a physiological restoration of normal local microcirculation.

Session 3: Update on antimicrobials

Update on antimicrobial agents in clinical use

Pisuit Siripaitoon, M.D.

Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University

"super bug, no drug"was shown as a heading title on many leading articles in the United State of America reflecting the critically unfavorable situation among the infectious diseases in that believed the most modernized country especially the medical science. Infectious disease is still addressed as the second leading cause of death in the USA. as well as causing a big economic loss each year. Developing anti-microbial agent resistant is well known worldwide spread with the globalization and occurring in various microbes causing various illnesses including bacterium, virus, fungi and even protozoan.

In Thailand, many species of bacterium had developed almost complete resistant to the commonly available antimicrobial agents especially the hospital acquired strains. The carbapenem-resistant Acinetobacter baumanii and Pseudomonas aeruginosa are the leading problematic organisms in many hospital while the commonly found enteropathologic bacterias, Escherichia coli and Klebsiella pneumonia, are resistant to the third generation cephalosporins which commonly used for. Staphylococci acquired during hospitalization are mostly resist to methicillin.

The more complex treatments for the rapidly increasing cancer diseases have been intervened, the more patients suffering to the invasive fungal infections leading to the needs of newer antifungal agents that cause more expense to the payer.

Thirty years after the treatment of human immune deficiency virus (HIV) infection have been introduced million of people can live longer with the suppressed virus. However, many if them have been suffering the long-term antivirus-drug related toxicities leading to poorer adherence to those agents and finally developed resistant to not only the former used antivirus drugs but also the others in the same class.

The influenza virus causing many death in the past few years. Anti-virus agent is one of the most trusted solution at the beginning; therefore, resistant to oseltamivir has been demonstrated very short after use.

The best solution for those worsening situation do not exist, there is no very soon coming perfect powerful antimicrobial agents for such multi-drug or pan-drug resistant bacteria. The easiest way is searching for the old anti-microbial agent that has not been used for so long, for example, the use of colistin for the treatment of multi-drug resistant A. baumanii infections. The application of the pharmacokinetic and pharmacodynamics knowledge to daily practice making more suitable prescribed dosing as well as using drug monitoring to achieve the best target drug level.

Introduction of newer mechanism of anti-HIV agents give patient the chance to re-suppress the viral load as well as lower the commonly found metabolic complications which associated to the long term use of many anti-HIV agents.

The newer anti-fungal agents, echinocandins and azoles, help us to avoid commonly found nephrotoxicity from the backbone systemic antifungal agent, the amphotericin B, as well as shortening the hospital stay with enteral form azoles.

In the future, the new more powerful anti-microbial agents are still needed, till that reach we have to preserve those available agents by prescribing restriction and careful dosing as well as the infectious control.

Session 4: Pharmacogenomics of adverse drug reaction

Adverse drug reaction in Thailand "Steven-Johnson syndrome/ Toxic epidermal necrolysis"

ภญ. วิมล สุวรรณเกษาวงษ์

หัวหน้าศูนย์เฝ้าระวังความปลอดภัยด้านผลิตภัณฑ์สุขภาพ สำนักงานคณะกรรมการอาหารและยา

บทนำ

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) เป็นภาวะผื่นแพ้ผิวหนังที่รุนแรงจากฐานข้อมูลของศูนย์เฝ้าระวังความปลอดภัยด้านผลิตภัณฑ์สุขภาพ สำนักงานคณะกรรมการอาหารและยา (Thai Vigibase) ซึ่งรวบรวมรายงานอาการไม่พึงประสงค์จากการใช้ยา (adverse drug reactions: ADRs) ที่เกิดขึ้นในประเทศไทย พบว่า SJS/TEN เป็นADRs ที่ส่งผลผู้ป่วยเสียชีวิต มากที่สุด เมื่อเปรียบเทียบกับADRs ชนิดอื่น ๆ

วัตุประสงค์

เพื่อค้นหาลักษณะผู้ป่วยผลลัพธ์ที่เกิดขึ้นและรายการยาที่สงสัยว่าสัมพันธ์กับการเกิดที่เกิด SJS/TEN

วิธีการศึกษา

คัดเลือกรายงานการเกิด SJS/TEN (ATC code 0042, 0013) ที่บันทึกลงในฐานข้อมูล Thai Vigibase ระหว่าง ปี 2527-2553 มาวิเคราะห์ด้วยสถิติเชิงพรรณา

ผลการศึกษา

ในระหว่าง ปี 2527-2553 มีรายงานการเกิด SJS/TEN รวม 8,982 ฉบับจากสถานพยาบาลทั่วประเทศ 760 แห่งที่บันทึกในฐานข้อมูล Thai Vigibase พบเกิดในผู้ป่วยเพศชายและหญิง (ร้อยละ50) และทุกกลุ่มอายุ (ร้อยละ 10-20) ในสัดส่วนที่ใกล้เคียงกัน ผู้ป่วยมากกว่าครึ่งต้องเข้ารักษาตัวในโรงพยาบาล ผู้ป่วยร้อยละ3.2 ต้องเสียชีวิตจากอาการดังกล่าว ยาที่สงสัยว่าสัมพันธ์กับการเกิด SJS/TEN มาก 5 อันดับแรก ได้แก่ co-trimoxazole, allopurinol, carbamazepine, nevirapine containing products, phenytoin ตามลำดับ

สรุป

รายงานการเกิด SJS/TEN ในประเทศไทย ไม่พบความแตกต่างทั้งเพศและอายุ แต่มีความรุนแรงที่ส่งผลให้ผู้ป่วยเกินกว่าครึ่งต้องเข้ารักษาตัวในโรงพยาบาล และบางรายต้องเสียชีวิต ยาที่สงสัยที่ได้รับรายงาน ส่วนใหญ่เป็นยาที่มีหลักฐานชัดเจนว่าทำให้เกิด SJS/TEN ได้ ยาบางรายการมีรายงานว่าสัมพันธ์กับพันธุกรรมที่มีในคนไทย เพื่อป้องกันการเกิด SJS/TEN มาตรการลดปัจจัยเสี่ยงควรต้องได้รับการพิจารณาดำเนินการ

Prevention of adverse drug reactions by pharmacogenomics

Wichittra Tassaneeyakul

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Adverse drug reactions (ADR) are common problems associated with drug therapy. There are two major types of ADR including predictable ADR (e.g. side effects, toxicity) and idiosyncratic ADR (e.g. intolerance, drug hypersensitivity). Examples of predictable ADR are bleeding from warfarin and myelosupression from thioguaine drugs while drug hypersensitivity is well known example of idiosyncratic ADR. The most common hypersensitivity reactions involve cutaneous adverse drug reactions in which its clinical manifestations are heterogeneous ranging from mild-to-severe life-threatening forms. The severe cutaneous adverse drug reactions (SCAR) include Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and hypersensitivity syndrome (HSS).

Recent studies have shown that patients who carried CYP2C9 variants and certain haplotypes of VKORC1 gene required lower dose of warfarin. In addition, patients who carried TPMT variants may at a higher risk of myelosupression-induced by thioguanine drugs. Moreover, strong associations between certain HLA alleles and susceptibility to drug hypersensitivity have been demonstrated. These genetic associations can be drug specific (e.g. *HLA-B*1502* being associated with carbamazepine-induced SJS/TEN, *HLA-B*5701* with abacavir hypersensitivity, HLA-B*5801 with allopurinol-induced SCAR and *HLA-B*3505* with nevirapine-induced cutaneous drug reactions) and can also be phenotype-specific (e.g. *HLA-B*1502* is associated solely with SJS/TEN, and not with either maculopapular eruption or HSS induced by carbamazepine) as well as can also be ethnicity specific (e.g. carbamazepine-SJS/TEN associated with *HLA-B*1502* is seen in Han Chinese and south-east Asians but not in Caucasians or Japanese). Screening of these genes will help physicians to identify patients who are at a higher risk of these ADR.

To date, the US Food and Drug Administration has approved modifications of about 60 drug labels to include pharmacogenetics information. In addition, product labeling of some pharmaceutical products that are commercially available in Thailand such as Tegretol® (carbamazepine), Imuran® (azathiopurine) and Puri-Nethol® (6-mercatporine) contain some pharmacogenomic information.

Session 5: Circadian rhythm and depression: Pharmacology of melatonergic antidepressant agomelatine, an update

Circadian rhythm and depression: Pharmacology of melatonergic antidepressant, agomelatine, an update

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Circadian rhythm is roughly of 24-hour cycle in terms of biochemical, physiological and behavioral processes of the human body functions. The putative body function controlled by circadian rhythm is a 24-hour sleep-wake cycle. (1) Others body functions which demonstrated circadian rhythm vary during day and night are body temperature, work performance and hormonal secretion. The human circadian rhythm is functioning basically triggered by internal factors and influenced by external physical stimuli. To date, a well known Suprachiasmatic nucleus (SCN), acting as a master clock controls the peripheral system throughout the body by means of melatonin as major neurotransmitters. Subsequent binding at two types of melatonin receptors (MT) at the SCN, both MT1 subtype and MT2 subtype, the circadian rhythm is switched on to which circadian amplitude and phase developed. (2) There are clear evidences that depressive patients encounter various symptoms and signs related to circadian rhythm dysfunction such as worsen depressed mood in the morning, intensifying sleep problem such as waking in the middle of the night and further sleep deprivation can somehow reduce symptoms of depression, however only in a shorter period. Thereby, there is a possibility that abnormal circadian rhythm may be one of the causes of the depressive disorder. (3, 4)

Depressive disorder is a heterogeneous disorder. Since currently, available antidepressants have offered only limited benefits especially with respect to response of treatment only 40 to 60 %. These antidepressants have earlier been classed based on their pharmacological action, at least three types of neurotransmitters such as Serotonin (5-HT), Norepinephrine (NE) and Dopamine (DA). Theoretically, there is no single antidepressant suit to all depressed patients. Moreover, there is no clear-cut parameter or biological marker to indicate whether such antidepressant is suitable for such depressed patients. (5-8)

Agomelatine, a new class antidepressant exerts its pharmacological action via both melatonergic and serotoninergic systems. Agomelatine endows selective binding properties at the SCN. Agomelatine exhibits both agonistic activity at the MT1 and MT2 and antagonistic activity at the 5HT2c. Agomelatine improves both circadian rhythm function and antidepressant efficacy in depressive patients demonstrated in series of randomized clinical trials, both placebo-controlled and head-to-head comparison trials against Serotonin Selective Re-uptake inhibitors (SSRIs) and Serotonin Noradrenaline Re-uptake inhibitors

(SNRI). Agomelatine is an anti-depressant which provides many advantages over SSRIs and SNRIs in terms of less troublesome side effects such as GI disturbance, less anti-cholinergic side effects such as dry mouth and palpitation, no overt sedation and devoid of anti-depressant induced sexual dysfunction. (6, 8-12)

Keyword: circadian rhythm, depression, agomenlatine

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Session 6: Medicinal plant utilization: costs, risk and rewards

Medicinal plant utilization: Cost, risk and rewards

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Indigenous flora of tropical countries are abundant of compounds with pharmacological activities which could be transformed into therapeutic agents and personal care products. The normal sequence for development of pharmaceuticals by this approach usually begins with the identification of active lead molecules, detailed biological assays, and formulation of dosage forms in that order, and followed by several phases of clinical studies designed to established safety, efficacy and pharmacokinetic profile of the new drugs.

The availability of modern scientific methods for the cultivation, selection, manufacture and clinical evaluation of herbal remedies has made it increasingly feasible to transform traditional medicine from an almost invisible trade into a modern industrial enterprise capable of making significant contribution to both health care delivery and the economic growth of developing countries.

In order to fully exploit the enormous potential that medicinal plants hold, it is necessary to understand the major factors that drive medicinal plant trade. The first is the proper management of genetic resources so that they can be used in a sustainable manner and for the benefit of greater majority of the population. The second factor is the appreciation that an adequate technological infrastructure is necessary for the conversion of crude plant materials to standardized, effective and safe dosage forms. It is not enough to acquire the scientific know-how without building a supporting technological infrastructure. The third factor is an intimate knowledge of the market place and the ability to create commercial value from what may appear as purely academic or scientific results. The fourth factor is establishment of effective and appropriate regulation that will govern the production and marketing of medicinal plants.

Scientists in developing countries must therefore accept the added role of being the intermediary player between technological development and market needs. This means appreciation of the requirements of his/her role as a translator and promoter of technology to the market place on the one hand and at the same time introduce commercial values to the laboratory. In this new role, the scientist should posses certain qualities and skills, namely, the ability to translate technology into products, the incorporation of marketing and scientific orientations in key decisions, the technical and product development experience in the target markets and the ability to build teams and facilitate brainstorming sessions. In addition, excellent communication skills are vital to coordinate all levels of activity to ensure the successful end results.

Luncheon symposium 2: Recent advance and future trend in cancer treatment

Recent advance and future trend in cancer treatment

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Advance in cancer treatment has continually been developed in the past few decades. The most promising paradigm shifting in cancer therapy is the progress of tailored medicinal approach. A number of novel molecular or genetic pathways involving in tumor proliferation, invasion, and metastasis have been extensively studied and clinically applied for targeting potential pathways or molecules. Multiple agents have been approved as standard therapeutic drugs to improve survival for patients in various cancer types, including tyrosine kinase inhibitors, monoclonal antibodies, and others. However, non-hematologic toxicity profiles related to these novel agents need to be monitored in patients receiving molecularly targeted therapy urging up-to-date knowledge seeking in caring healthcare personnel. This personalized therapeutic approach tends to be used in almost all cancer in the near future.

Session 7: Medicinal plants: research & development for the community

Active constituent-rich herbal extracts: A trend in herbal medicine development

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Many conventional drugs or their precursors are derived from plants. However, there is a difference between administering a pure isolated chemical and the same chemical in a plant matrix. Whether this "chemical complexity" is advantageous, it is still a matter of some debate. Wills et al (2000) are of the view that synergy is an important concept in medicinal plant use [1]. In the context of chemical complexity it applies if the pharmacological effect of a chemical mixture is greater than the arithmetic sum of the effects of individual components. This needs to be taken into account when considering the preparation of active constituent-rich extracts.

The extraction and fractionation processes are important steps for the preparation of an active constituent-enriched extract. Suitable extraction methods, as well as the choice of solvents for extraction, are capable of increasing the yield of active constituent in the extract.

Rhinacanthus nasutus, a small shrub of Acanthaceae family, has long been used in Thai traditional medicine for treatment of tinea versicolor, ringworm, pruritic rash, abscess pain, and skin diseases. It has been reported that rhinacanthin-C, rhinacanthin-D and rhinacanthin-N isolated from *R. nasutus* possessed antifungal, antibacterial, antiviral, anti-inflammatory, anti-allergic and cytotoxic activities [2-8].

A reversed-phase HPLC has been established for the simultaneous determination of rhinacanthin-C, rhinacanthin-D and rhinacanthin-N in *R. nasutus* leaves [2]. The method involves the use of a TSK-gel ODS-80Ts column (5 μm, 4.6 x 150 mm) with the mixture of methanol and 5% aqueous acetic acid (80:20, v/v) as the mobile phase. All three compounds were eluted within 20 minutes with satisfactory resolution. The parameters of linearity, repeatability, accuracy and specificity of the method were evaluated. The recovery of the method was 94.3 - 100.9% and good linearity (correlation coefficient $\geq$ 0.9999) was obtained for all rhinacanthins. A high degree of specificity as well as repeatability and reproducibility (R.S.D. values less than 5%) were also achieved. The limit of detection and quantification of all rhinacanthins were 0.75 and 3.0 μg/ml, respectively. On the basis of the HPLC analysis, rhinacanthin-C was a major naphthoquinone, the content of which was 1.9% w/w, while rhinacanthin-D (0.16% w/w) and rhinacanthin-N (0.07% w/w) were minor naphthoquinones of *R. nasutus* leaf extract.

A few different extraction solvents were tried to maximise the rhinacanthin content in *R. nasutus* leaf extract. Among the solvents that were used for extraction, methanol gave the highest yield of the crude extract. The obtained extract using methanol gives a rather low total content of rhinacanthins, despite giving the highest yield of crude extract (18.4% w/w of dried leaves). In contrast, ethyl acetate gave the lowest yield of crude extract, but with the highest content of total rhinacanthins (33.0% w/w of dried extract) [2]. This indicates that ethyl acetate is a suitable extraction solvent.

Rhinacanthins are anionic compounds that can be enriched by anion exchange resins. It was found that Amberlite IRA-67 column was capable of improving the rhinacanthin content in the obtained semi-purified extract. The content of total rhinacanthins in the rhinacanthin-rich *R. nasutus* extract was increased to 77.5% w/w compared to 37.4% w/w in the crude extract from ethyl acetate extraction. The interfering compounds, including chlorophyll and other pigments, were also markedly excluded. The weakly basic anion exchanger, Amberlite IRA-67 is therefore suitable for preparation of *R. nasutus* leaf extract [2].

Rhinacanthin-rich *Rhinacanthus nasutus* extract was therefore prepared and standardized to contain total rhinacantins not less than 70% w/w. The antifungal activity of the rhinacanthin-rich *R. nasutus* extract against *Trichrophyton rubrum, T. mentagrophytes* and *Microsporum gypseum* was evaluated and compared with those of the ethyl acetate crude extract and pure standard rhinacanthins [2]. The results showed that antifungal activity of the rhinacanthin-rich *R. nasutus* extract (MIC 7.5, 31.2 and 125 µg/l, respectively) was better than that of the ethyl acetate crude extract (MIC 31.2, 62.5 and 500 µg/l, respectively). The antifungal activity of the rhinacanthin-rich *R. nasutus* extract was equal to that of rhinacanthin-C.

In addition, antimicrobial activity evaluation of the rhinacanthin-rich *R. nasutus* extract and rhinacanthin-C against *Streptococcus mutans*, *Propionibacterium acnes*, *Staphylococcus aureus* and *S. epidermidis* revealed that both of them exhibited antimicrobial activity against *S. mutans*, *P. acnes*, *S. aureus* and *S. epidermidis* [3]. The extract exhibited potent bactericidal activity against Gram-positive anaerobic bacteria including *S. mutans* and *P. acnes* with MBC values of 4 and 32 µg/ml, respectively. The extract also showed moderate bactericidal activity against Gram-positive facultative anaerobic bacteria including *S. aureus* and *S. epidermidis* with the MBC values of 256 and 512 µg/ml, respectively. The antibacterial activity of the rhinacanthin-rich *R. nasutus* extract was also almost equal to that of rhinacanthin-C. This may be due to a synergistic effect of all the three rhinacanthins on antifungal activity.

Thus, the prepared rhinacanthin-rich *R. nasutus* extract is suitable for the development of a suitable topical application antimicrobial cream. According to the satisfactory antimicrobial activity of the rhinacanthin-rich *R. nasutus* extracts, the extracts used in further studies should be standardized to a total rhinacanthin content of not less than 70% w/w.

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Standardization of Thai herbal medicine

ผู้ช่วยศาสตราจารย์ ดร.จินดาพร ภูริพัฒนาวงษ์

ภาควิชาเภสัชเวท และเภสัชพฤกษศาสตร์ คณะเภสัชศาสตร์ มหาวิทยาลัยสงขลานครินทร์

การควบคุมมาตรฐานของสมุนไพรไทย อยู่ภายใต้การกำกับ และดูแลของสำนักงานคณะกรรมการอาหารและยา กระทรวงสาธารณสุข โดยมาตรฐานของสมุนไพรที่จัดทำขึ้นเพื่อส่งเสริมศักยภาพในการผลิต และการใช้สมุนไพรในยาสำเร็จรูปทั้งแผนปัจจุบัน และแผนโบราณ การที่สมุนไพรยังไม่เป็นที่ยอมรับ อาจเนื่องมาจากขาดข้อมูลทางวิทยาศาสตร์ที่จะมารับรอง หรือยืนยันผลของสมุนไพรนั้น และยังไม่มีมาตรฐานที่จะมากำหนดถึงคุณภาพของสมุนไพรในการนำมาผลิตยา

การกำหนดคุณภาพของสมุนไพร หรือยาสมุนไพรจะเป็นการสร้างความน่าเชื่อถือ ความมั่นใจให้กับผู้บริโภคในการผลิตภัณฑ์ ข้อกำหนดของสมุนไพร หรือยาสมุนไพรก็เช่นเดียวกับยาแผนปัจจุบันคือจะระบุไว้เป็น Monograph และจัดพิมพ์เป็นเภสัชตำรับของยาสมุนไพรไทย (Thai Herbal Pharmacopoeia) สำหรับหัวข้อใน Monograph จะประกอบไปด้วย

Nomenclature
Definition
Description
- morphology of plants
- organoleptic characters
- macroscopical characters
- microscopical characters

Packaging and storage
Identification
- chemical tests
- chromatographic examination

Test
- Foreign matter
- Loss on drying or Water
- Ash etc.

Assay
Test for contaminants
- Microbial limit
- Pesticide residues

Category and Dose

ขมิ้นชัน (KHAMIN CHAN)

Curcumae Longae Rhizoma; Curcumae Domesticae Rhizoma
Turmeric

Synonyms Curcuma; Yellow Root; Indian Saffron

Category Stomachic; carminative; pharmaceutic aid (colouring agent); astringent.

Turmeric is the dried rhizome of *Curcuma longa* Linn. (*C. domestica* Valeton), DMSc Herbarium Nos. 31, 1410, 1458 (Family Zingiberaceae).

Constituents Turmeric yields about 7 per cent of a yellow volatile oil containing turmerone and zingiberene as major constituents and many other sesquiterpenes and monoterpenes; yellow colouring matter including curcumin or diferuloylmethane (1.8 to 5.4 per cent), desmethoxycurcumin, and bisdesmethoxycurcumin.

Description of the plant A perennial herb with a thick, ellipsoid-ovate rhizome, orange inside, giving rise to short blunt daughter rhizomes called fingers, leafy shoots to 1 m tall bearing 6 to 10 leaves. Leaves: simple, glabrous; lamina, elliptic, oblong-elliptic or lanceolate; 30 to 45 cm long and 10 to 15 cm wide; base narrow; apex acuminate; petiole as long as lamina (rather abruptly broadened to leaf sheath, forming a pseudostem). Inflorescence: scape from the apex of the rhizome; peduncle 15 cm long or more, spike 10 to 15 cm long and 5 to 7 cm in diameter; bract, white or white with green, 5 to 6 cm long, each subtending flowers; bracteoles thin, pale green and tinged with pink, elliptic to ovate, up to 3.5 cm long; flowers as long as the bracts; calyx whitish tubular, unilateral split, unequally toothed; corolla white, tubular at base, upper half cup-shaped with 3 unequal lobes inserted on edge of cup lip. Lateral staminode petaloid, oblong, folder under the dorsal petal; staminode and lip creamy-white with yellow median band; filament united to another about the middle of the pollen sac, spurred at base; ovary trilocular. Fruit: globose to ellipsoid capsule; seed arillate (Fig. 1).

Description

Macroscopical Dried rhizome occurs as an ovate, oblong or pear-shaped of round turmeric; cylindrical and often short-branched of long turmeric; the round about half as broad as long, the long 2 to 5 cm long and 1 to 2 cm thick; externally yellowish to yellowish brown, with root scars and annulations, the latter from the scars of leaf bases; fracture horny; internally orange-yellow to orange, waxy, showing a cortex separated from a central cylinder (about twice as broad as cortex) by a distinct endodermis; in both cortex and central cylinder, scattered bundles are seen.

Microscopical Transverse section of the rhizome shows epidermis consisting of a layer of rectangular cells; covering trichomes, unicellular, up to 280 μm long. Hypodermis composed of 3 to 6 layers in the mature rhizome, but absent in the younger. Cork, 4 to 6 layers of rectangular cells. Cortex composed of thin-walled parenchymatous cells containing numerous starch grains, yellowish oil droplets and yellow colouring matter occasionally seen; starch grains, simple, flattened, rounded to oval or irregular in outline, very faint transverse striations could be seen in some granules. Endodermis, a layer of thin-walled cells. Stele, thin-walled parenchymatous cells containing numerous starch grains, yellowish oil droplets and yellow colouring matter. Fibrovascular bundles, non-

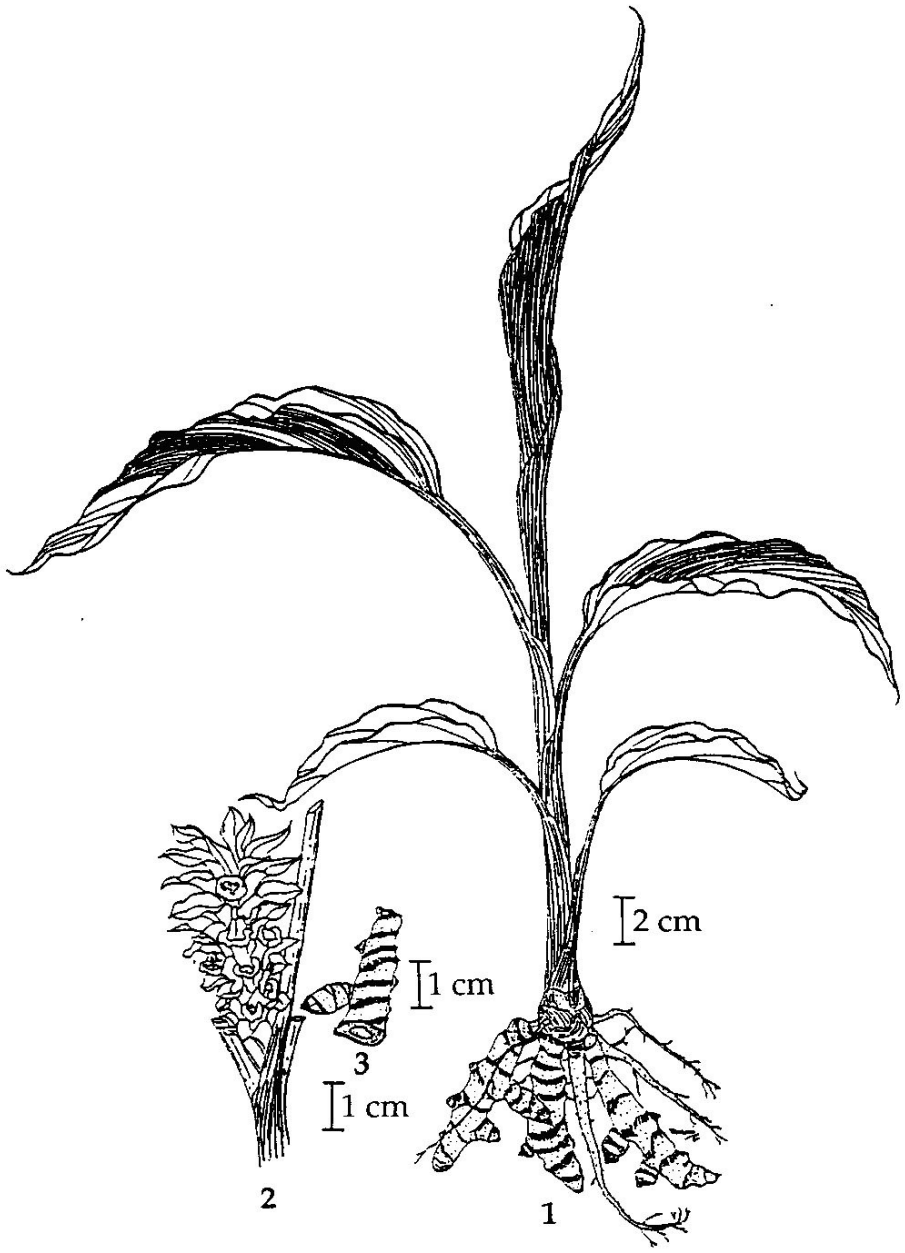


Fig. 1 *Curcuma longa* Linn.

1. whole plant
2. inflorescence
3. rhizome

40 THP I

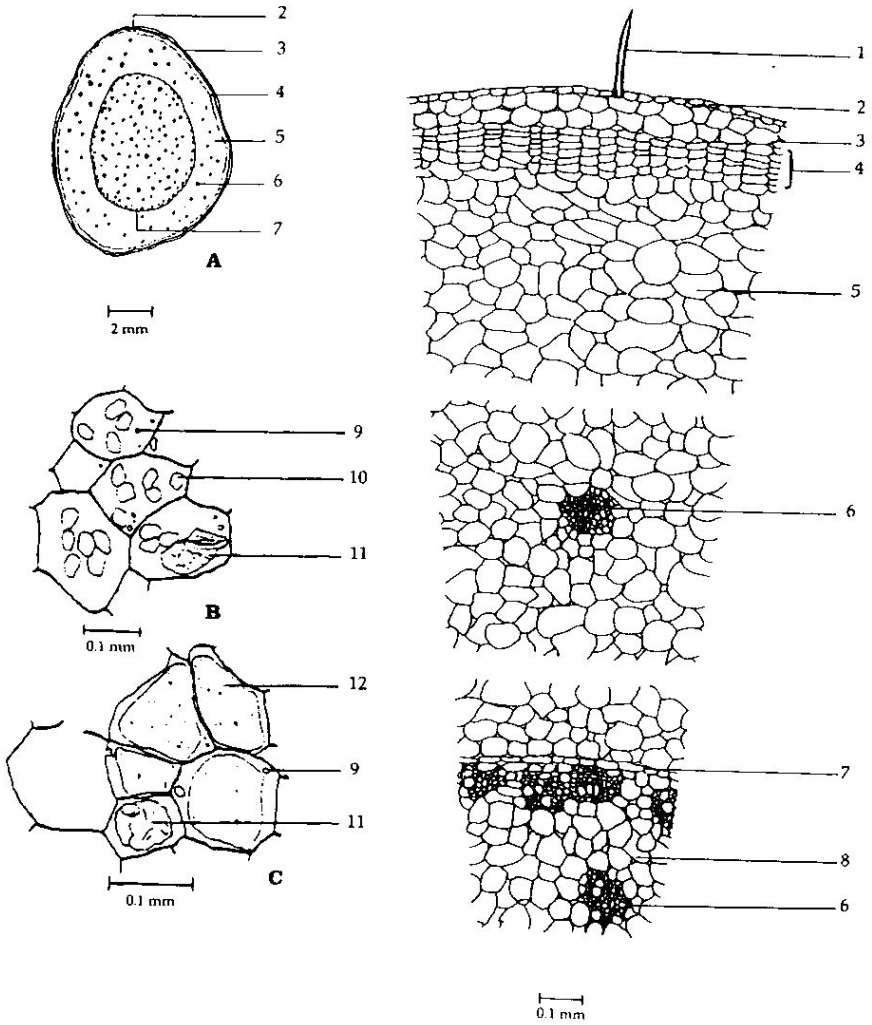


Fig. 2a Transverse Section of the Rhizome of *Curcuma longa* Linn.

A. diagram of transverse section

B. parenchyma of untreated rhizome

C. parenchyma of steam-treated rhizome

1. unicellular covering trichome
2. epidermis
3. hypodermis
4. cork layers
5. cortical parenchyma containing starch granules
6. vascular bundles
7. endodermis
8. stele parenchyma containing starch granules
9. oil droplet
10. starch granule
11. orange-yellow colouring matter
12. yellow gelatinized starch mass

THP I 41

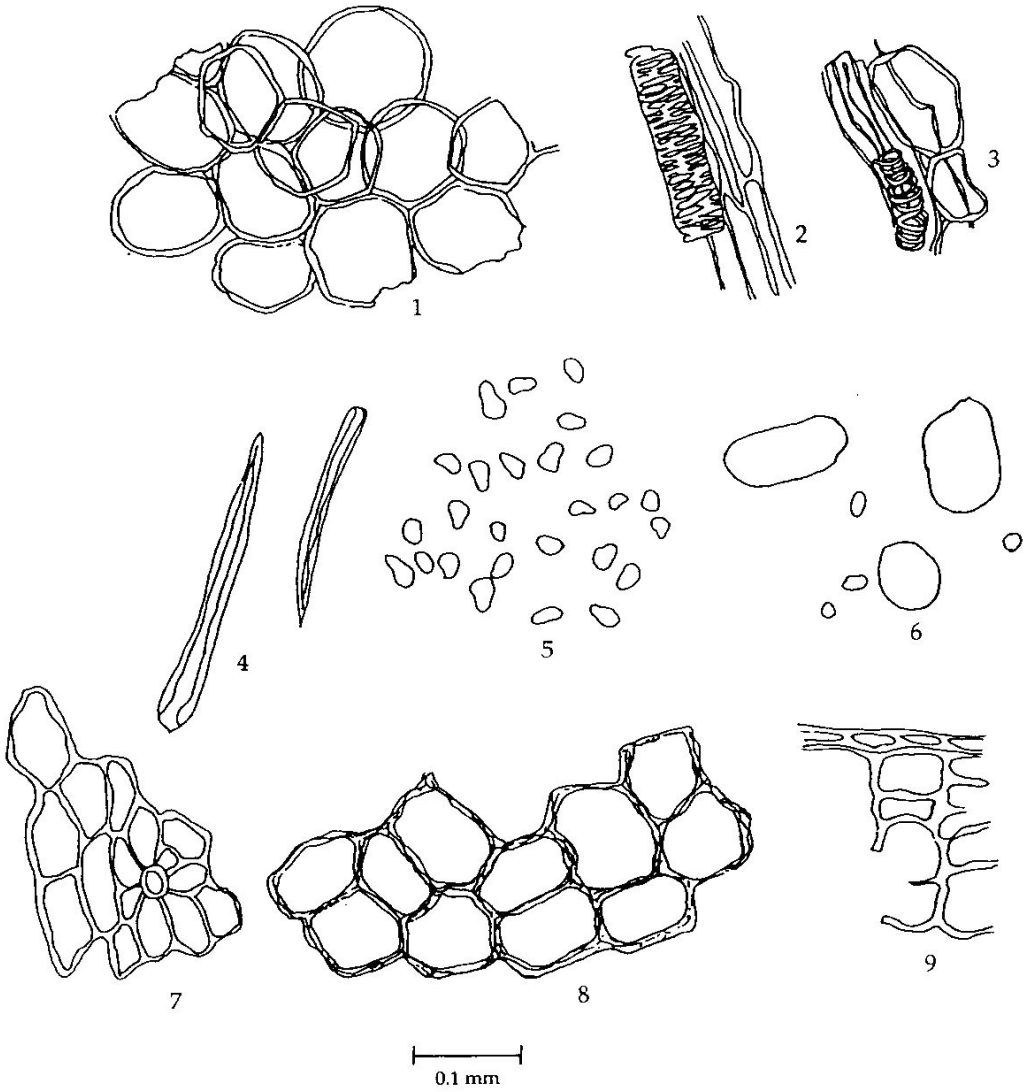
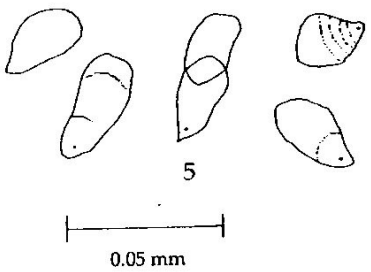


Fig. 2b Powdered Drug of the Rhizome of *Curcuma longa* Linn.

1. parenchyma
2. reticulate vessel
3. spiral vessel
4. unicellular trichomes
5. starch granules
6. altered starch grains
7. epidermis in surface view
8. cork in surface view
9. epidermis and hypodermis in sectional view



lignified walled cells, scattered in cortex and stele; vessels, spiral, scalariform and reticulate (Fig. 2a).

Turmeric in powder possesses the diagnostic microscopical characters of the unground drug (Fig. 2b).

Packaging and storage Turmeric should be kept in tightly closed containers, protected from light, in a cool and dry place.

Identification

A. Extract 10 g of the sample, in powder, with 2 ml of *acetic anhydride*, add a few drops of *sulfuric acid* and observe under ultraviolet light (366 nm): the solution shows blood-red colour.

B. Carry out the test as described in the "Thin-layer Chromatography" (Appendix 3.1), using *silica gel G* as the coating substance and a mixture of 49 volumes of *benzene*, 49 volumes of *chloroform* and 2 volumes of *ethanol* as the mobile phase but allowing the solvent front to ascend 17 cm above the line of application. Apply separately to the plate, 5 µl of each of the following two solutions. Prepare solution (A) by placing 1 g of the sample, in powder, in a stoppered test-tube, adding 3 ml of *methanol* and shaking for a while. Set aside for 1 hour and filter. For solution (B) dissolve 1 mg of *curcumin* in 1 ml of *methanol*. After removal of the plate from the chromatographic chamber, allow it to dry in air, and examine under ultraviolet light (366 nm), locating the spots. The chromatogram obtained with solution (A) shows a yellow-brown spot (hR_f value 28 to 34), corresponding to the curcumin spot from solution (B). Other two yellow-brown spots correspond in hR_f values to the spot numbers 2 and 3. Several spots of higher and lower hR_f values are observed (Table 1); see also Fig. V (Appendix 3.1H). Spray the plate with a 10 per cent w/v solution of *phosphomolybdic acid* in *ethanol* and heat at 105° for 5 minutes; the spot due to curcumin is orange-brown. The spots due to those of numbers 2, 3, 10, 14 and 15 in Table 1 are orange, orange-brown, blue, blue, and blue, respectively. Other spots of different colours are observed (Table 1); see also Fig. V (Appendix 3.1H).

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Table 1 hR_f Values of Components in Methanolic Extract of the Rhizome of *Curcuma longa* Linn.

Spot*	hR_f Value	Detection with	
		UV366 (colour)	*Phosphomolybdic Acid* (colour)
1	5-8	light brown	brown
2	11-15	yellow-brown	orange
3	17-20	yellow-brown	orange-brown
4	21-24	blue-green	blue
5	28-34	yellow-brown	orange-brown
6	35-38	blue-green	blue
7	39-42	yellow	light yellow
8	44-46	–	blue
9	48-51	–	blue
10	52-53	–	blue
11	57-60	–	blue
12	62-66	–	blue
13	71-74	–	blue
14	80-85	–	blue
15	87-90	–	blue

* 1, 4, 6-9, 11-13 = unknown
2 = bisdesmethoxycurcumin
3 = desmethoxycurcumin
5 = *curcumin*
10 = curcumol
14 = *dl*-turmerone
15 = ar-curcumene (ar = aromatic)

Water Not more than 10.0 per cent v/w (Azeotropic Distillation Method, Appendix 4.12).

Foreign matter Not more than 2.0 per cent w/w (Appendix 7.2).

Acid-insoluble ash Not more than 1.0 per cent w/w (Appendix 7.6).

Total ash Not more than 8.0 per cent w/w (Appendix 7.7).

Ethanol-soluble extractive Not less than 10.0 per cent w/w (Appendix 7.12).

Water-soluble extractive Not less than 9.0 per cent w/w (Appendix 7.12).

Volatile oil Not less than 6.0 per cent v/w (Appendix 7.3H). Use 10 g in *No.180 powder*, accurately weighed. Use 100 ml of *water* as the distillation liquid and a 500-ml round-bottomed flask. Distil at a rate of 2 to 3 ml per minute for 5 hours. Use 2.0 ml of *xylene* in the graduated tube. Calculate the content of volatile oil with reference to the anhydrous substance.

Curcuminoids content Not less than 5.0 per cent w/w of curcuminoids, calculated as curcumin, when determined by the following method.

Standard curcumin solution Dissolve about 2 mg of *curcumin*, accurately weighed, in sufficient *methanol* to produce 5.0 ml.

Standard curcumin curve Transfer into five 10-ml volumetric flasks, 20, 40, 50, 60, and 80 µl, respectively, of *Standard curcumin solution*, dilute to volume with *methanol*, and mix. Measure the absorbances of the standard solutions relative to the blank at 420 nm (Appendix 2.2). Plot the readings and draw the curve of best fit.

Procedure Transfer about 300 mg of Turmeric, in powder and accurately weighed, into a 10-ml volumetric flask, add *tetrahydrofuran* to volume and mix. Set aside at room temperature for 24 hours with frequent shaking. Dilute 1.0 ml of the clear supernatant liquid with *methanol* to produce 25.0 ml. Transfer 1.0 ml of this solution into a 50-ml volumetric flask, dilute to volume with *methanol* and mix well. Measure the absorbance of the sample solution, and by reference to the Standard curcumin curve, calculate the content of curcuminoids as curcumin in the sample.

Dose 3 to 9 g.

Standardized extract of *Centella asiatica* : Success & Failure

รองศาสตราจารย์.ภญ.ดร.มยุรี ตันติสิระ

ภาควิชาเภสัชวิทยาและสรีรวิทยา คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

ในขณะที่การใช้สมุนไพรแบบดั้งเดิมก็ยังเป็นสิ่งที่ดำรงอยู่ในหลาย ๆประเทศ ทั้งในลักษณะของภูมิปัญญาท้องถิ่นหรือในลักษณะที่เป็นศาสตร์ซึ่งมีการเรียนการสอนอย่างเป็นระบบสืบเนื่องกันมาโดยตลอด สมุนไพรก็เป็นแหล่งที่มาที่สำคัญอย่างหนึ่งของยารักษาโรคของการแพทย์แผนปัจจุบัน ความพยายามที่จะพิสูจน์คุณค่าของสมุนไพรในปริบทของโลกวิทยาศาสตร์ได้ก่อให้เกิดผลงานวิจัยมากมายในวารสารทางวิชาการทั่วโลก ประเทศไทยเองก็ได้เริ่มมีการวิจัยสมุนไพรเพื่อพัฒนาไปใช้เป็นยามาช้านาน แต่มียาจากสมุนไพรน้อยชนิดมากที่ได้รับการพัฒนาจนเป็นสารสกัดมาตรฐานซึ่งก็คือสารสกัดที่ผู้ผลิตสามารถควบคุมปริมาณสารสำคัญในสารสกัดให้เป็นไปตามมาตรฐานที่กำหนดไว้เสมอ จึงสามารถระบุขนาดใช้ที่แน่นอน และสามารถอ้างอิงข้อมูลระหว่างงานวิจัยซึ่งมีวิธีการวิจัยที่หลากหลาย จึงได้รับการยอมรับเป็นอย่างดีจากประชาคมผู้นิยมการแพทย์ทางเลือก ดังเช่น สารสกัดมาตรฐานจากใบแป๊ะก้วยที่มีชื่อว่า EGb 761 ดังนั้นในปีพ.ศ. 2545 ซึ่งเป็นปีที่รัฐบาลได้เริ่มให้การสนับสนุนโครงการวิจัยเชิงบูรณาการ คณะผู้วิจัยจากคณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย จึงได้ร่วมกันเสนอชุดโครงการวิจัยเรื่องการวิจัยและพัฒนาสารสกัดมาตรฐานบัวบกเพื่อนำไปใช้ในอุตสาหกรรมยาและเครื่องสำอางค์ ซึ่งเป็นโครงการ 3 ปี ได้รับเงินทุนสนับสนุนประมาณ 16 ล้าน โดยมีวัตถุประสงค์หลักคือพัฒนาสารสกัดมาตรฐานบัวบกที่มีฤทธิ์สมานแผลและมีฤทธิ์แก้ไขภาวะบกพร่องของการเรียนรู้และความจำ คณะผู้วิจัยได้ประสบความสำเร็จเป็นอย่างดีในการเตรียมสารสกัดมาตรฐานบัวบก (ซึ่งต่อมาได้รับการตั้งชื่อว่า ECa 233) ซึ่งมีลักษณะเป็นผงละเอียดสีขาวนวล มีส่วนประกอบของไตรเทอร์พีนอยด์ไม่ต่ำกว่า 80 % และมีอัตราส่วนระหว่างมาเดคัสโซซายด์กับเอเชียติโคซายด์อยู่ระหว่าง 1.50 ± 0.5 และมีความคงตัวไม่ต่ำกว่า 2 ปี ECa 233 แสดงฤทธิ์แก้ไขภาวะบกพร่องของการเรียนรู้และความจำ และมีฤทธิ์สมานแผลในโมเดลสัตว์ทดลองหลายโมเดล รวมทั้งมีข้อมูลการทดสอบพิษวิทยาที่แสดงถึงความปลอดภัยในระดับสูง จึงได้มีการนำเอา ECa 233 ไปเตรียมเป็นยาป้ายปาก และทดสอบกับผู้ป่วยแผลร้อนใน ซึ่งพบว่า ยาป้ายปากที่มี 0.05 % ECa 233 สามารถลดความเจ็บปวดและเร่งการหายของแผลร้อนในได้เท่าเทียมกับยาป้ายปากที่มี 0.10 % ของไตรแอมซิโนโลน ซึ่งเป็นยาที่นิยมใช้กันอยู่ในปัจจุบัน

จากความสำเร็จของ ECa 233 ตั้งแต่วิธีการเตรียมเป็นสารสกัดมาตรฐาน จนถึงการเตรียมเป็นยาป้ายปากเป็นงานวิจัยที่ได้มีภาคเอกชนได้มาติดต่อผ่านสถาบันทรัพย์สินทางปัญญาจุฬาลงกรณ์มหาวิทยาลัยขอรับการถ่ายทอดเทคโนโลยีเพื่อนำไปใช้ผลิตหรือใช้ข้อมูลในเชิงพาณิชย์แล้วทั้งสองกรณี

ประกอบกับผลการทดสอบคัดกรองเบื้องต้นที่พบว่าสารสกัดหยาบบัวบกมีฤทธิ์ต้านชักในโมเดลของหนูเมาส์ที่ถูกเหนี่ยวนำให้ชักด้วยไฟฟ้า คณะผู้วิจัยจึงมุ่งที่จะทำการวิจัยเพื่อเตรียมสารสกัดมาตรฐานบัวบกที่มีฤทธิ์ต้านชักโดยใช้กลยุทธ์การวิจัยเช่นเดิม คือ activity-guided isolation ซึ่งหลังจากที่ใช้เวลาทำงานด้วยกันระหว่างนักวิจัยทั้งสองสาขาคือเภสัชวิทยากับเคมีของผลิตภัณฑ์ธรรมชาติเป็นเวลา 2 ปี คณะผู้วิจัยก็ไม่สามารถจะตอบได้ว่า สารใดเป็นสารที่มีการออกฤทธิ์ต้านชักที่ดี โดดเด่นแตกต่างจากสารอื่น ๆโดยชัดเจน จนสามารถนำไปเป็น bioactive marker ของสารสกัดมาตรฐานได้ นอกจากนั้นในขนาดที่สูงขึ้นสารบางตัวซึ่งมีฤทธิ์ต้านชักก็อาจแสดงฤทธิ์ช่วยส่งเสริมให้ชักได้ คณะผู้วิจัยจึงต้องขอยุติโครงการดังกล่าว

Session 8: Metabolic syndrome: its importance and management

Definition of metabolic syndrome and impact on cardiovascular disease

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Metabolic syndrome is the cluster of several cardiometabolic risk factors, including abdominal obesity, hyperglycemia, dyslipidemia and elevated blood pressure that are likely to be linked to insulin resistance. Since 1998, at least three organizations have proposed criteria for the clinical diagnosis of metabolic syndrome. There is general consensus regarding the main components of the metabolic syndrome but different definitions require different cut points and have different mandatory inclusion criteria. Several prospective cohort studies found an association between the metabolic syndrome and cardiovascular disease. However, there are many limitations that need to be recognized. First, Impact of the different components of the metabolic syndrome on cardiovascular events was different. Therefore, the metabolic syndrome with different components showed a different risk of cardiovascular disease. Second, there are at least 4 different methods for measuring waist circumference. Up to now, there is no standard method for measuring waist circumference. Third, when analysis was done by gender, significant association between the metabolic syndrome and cardiovascular disease was found to exist only in male. Fourth, the ability of metabolic syndrome to predict cardiovascular events was different among ethnics. The Electricity Generating Authority of Thailand (EGAT) study, only one prospective cohort of metabolic syndrome in Thailand, had several limitations. It surveyed only middle class, well-educated, urban individuals. The major causes of death in this study were cancer and accident. Since 80% of the study population was male, analysis was done only in male. Finally, other conditions have been found to be associated with insulin resistance and cardiovascular disease, such as low serum testosterone levels, high serum ferritin levels, low ankle-brachial index, masked hypertension and non-alcoholic fatty liver disease. Some of these conditions have been found to be a better predictor of cardiovascular disease than the metabolic syndrome. In conclusion, the metabolic syndrome was generally used as a predictor of cardiovascular disease. Since there are many limitations and scanty studies in the Thai populations, large prospective cohort studies in Thailand are still needed.

Key words: metabolic syndrome, cardiovascular disease

Metabolic syndrome: How to handle?

รองศาตราจารย์ พญ.รัตนา ลีลาวัฒนา

สาขาวิชาโรคเมตาโบลิสม ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์

กลุ่มอาการเมตาโบลิก (metabolic syndrome, MS) เป็นกลุ่มปัจจัยเสี่ยงต่อการเกิดภาวะหลอดเลือดแดงแข็งที่พบในผู้ป่วยคนเดียวกัน ปัจจัยเสี่ยงดังกล่าวได้แก่ ภาวะดื้ออินสุลิน (หรือจนมีความผิดปกติของการคุมน้ำตาลในเลือด) ความดันโลหิตสูง อ้วน (หรือลงพุง) ไขมันผิดปกติ (Low HDL-c และหรือ high triglyceride) และการพบโปรตีนในปัสสาวะ พยาธิกำเนิดของ MS เชื่อว่าเกิดจากการสะสมไขมันในช่องท้อง (visceral fat) ซึ่งนำไปสู่ภาวะดื้ออินสุลิน (insulin resistance)

การรักษาภาวะ MS ในปัจจุบัน เน้นการใช้การปรับเปลี่ยนพฤติกรรม (lifestyle modification) ซึ่งเป้าหมายหลักคือการลดน้ำหนักในผู้ที่มีน้ำหนักเกิน อย่างไรก็ตาม แม้ว่าการปรับเปลี่ยนพฤติกรรมจนน้ำหนักลดได้นั้น สามารถลดปัจจัยเสี่ยงต่างๆ รวมถึงภาวะดื้ออินสุลิน แต่การเปลี่ยนแปลงพฤติกรรมเป็นเรื่องที่ไม่ง่าย ทำให้ต้องพยายามหาวิธีการอื่นๆ เช่น ยาที่มีฤทธิ์ลดการดื้ออินสุลิน ฤทธิ์ลดปริมาณไขมันในช่องท้อง ยาที่มีฤทธิ์ลดการสลายไขมัน ตลอดจนยาที่มีฤทธิ์ต่อสมองส่วนกลางทำให้น้ำหนักลด หรือการผ่าตัดเอาไขมันออก การบรรยายครานี้จึงเป็นการทบทวนการรักษาภาวะ MS ด้วยวิธีการต่างๆ ซึ่งพบว่าแม้ว่าการรักษาตามพยาธิสรีระ พยาธิกำเนิด ที่พบว่าส่งผลต่อการเกิด MS แต่ยังไม่มีวิธีใดที่ยืนยันความปลอดภัย หรือมีหลักฐานเชิงประจักษ์ที่ศึกษาจนถึงผลระดับ clinical event ว่าช่วยผู้ที่มี MS ได้

สำหรับผู้ที่มีภาวะ MS การดูแลรักษาที่ได้ผลและปลอดภัยที่สุดคือการปรับเปลี่ยนพฤติกรรม

Key words: metabolic syndrome, treatment, lifestyle, insulin resistance, visceral fat

P01

Acute and chronic effects of aspirin on gastric ulceration in rats

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Aspirin is the most popular drug in the world. High-dose aspirin was commonly prescribed in the past as an anti-inflammatory drug in several inflammatory diseases. Nowadays, it is usually prescribed in low dose to prevent blood clotting in patients with high cardiovascular risk. A common adverse effect of patients taking either high-dose or low-dose aspirin is gastric ulcer. This study aimed to identify the characteristic differences between acute high-dose and chronic low-dose aspirin on the gastric ulceration in male Wistar rats. In addition, the myeloperoxidase activity of the gastric mucosa was also investigated to evaluate the effects of drugs on neutrophil infiltration. The animals were divided into 3 groups. A high-dose (200 mg/kg) aspirin was given once to the first group, and the gastric ulcer measurement was performed 6 hours later. The second group was given aspirin at a low dose (25 mg/kg) once daily for 28 days and the third group being served as the control was given deionized water. Ulcer lesions were evaluated at 24 hours after the last dose. The results indicate that aspirin at both acute high dose and chronic low dose can cause gastric lesions, although at the high dose can produce more pronounced ulceration. In addition, some characteristic differences of gastric lesions between the two dosages of aspirin were observed. Acute high-dose aspirin caused gastric lesions both in glandular and pyloric parts while chronic low-dose aspirin caused gastric lesions only in glandular part. The severity of gastric ulceration, indicated by the "ulcer index", does not seem to be with neutrophil infiltration. This could probably be partly due to the anti-inflammatory activity of aspirin which can alter the function of neutrophil especially at a high dose.

Keywords: aspirin, gastric ulcer, myeloperoxidase activity.

P02

Distribution and patterns of polymorphisms of *Plasmodium vivax* dihydrofolate reductase *(Pvdhfr)* and dihydropteroate synthase (*Pvdhps*) in malaria endemic areas of Thailand

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Malaria is the most important public health problems in several countries. In Thailand, co-infections of *Plasmodium vivax* and *P. falciparum* are common. The prevalence and patterns of mutations of *Pvdhfr* and *Pvdhps* were investigated in a total of thirty-six blood samples collected 9from patients with *P. vivax* infection who attended the malaria clinics in Mae-hongson (n= 9), Ranong (n= 12), Pattani (n= 5), Yala (n=6) and Narathiwat (n= 4) provinces during 2009 and 2010. SNP-haplotypes at positions 13, 33, 57, 58, 61, 117 and 173 of *Pvdhfr* and positions 383 and 553 of the *Pvdhps* were examined by nested PCR-RFLP. . All isolates carried mutations at codons 58 (58R) and 117 (117N, 117T). 17 isolates carried mutations at codons 61 (61M). Mutation at codon 57 consisted of two types, 57I and 57L. For *Pvdhps,* the most prevalent alleles were the mutant 383G (94.4%) and the wild-type A383/A553 (5.5%) alleles. The most common *Pvdhfr* alleles were triple mutants 58R/61M/117N (51.6%), 57I/58R/117T (32.3%), 57L/58R/117T (13.0%), and 57L/58R/117T (3.2%); four isolate carried double mutants 58R/117N/T; only one isolate carried quadruple mutation (57I/58R/61M/117T). The most prevalent combination allele was a triple *Pvdhfr* mutant allele 58R/61M/117N combined with a single mutant *Pvdhps* allele 383G. Two isolates carried wild-type alleles of both genes. The results demonstrated that all *P. vivax* isolates in Thailand carried mutant combination of *Pvdhfr* and *Pvdhps*. The development of new alternative antifolates drugs that are effective against SP-resistant *P. vivax* is required.

Keywords: malaria, *Plasmodium vivax*, *Plasmodium vivax dihydrofolate reductase (Pvdhfr)* and *dihydropteroate synthase (Pvdhps)*, PCR-RFLP, sulphadoxine-pyrimethamine (SP).

P03

The study of *UGT1A1* polymorphism in neonate at Songkhla Hospital

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Bilirubin UDP-glucuronosyltransferase or *UGT1A1* gene encodes UGT1A1 enzyme which is responsible for endogenous (bilirubin, steroids, bile acid *etc*.) and xenobiotics glucuronidation to eliminate from the body. Neonatal hyperbilirubinemia (CN1, CN2 and Gilbert's syndrome) and drug toxicity, especially irinotecan caused by *UGT1A1* mutation. *UGT1A1* polymorphism in Asian has been detected such as G71R (mostly found in Japanese), P229Q, F83L, Y486D and TAA$(TA)_7$ (mostly found in Caucasians). For Thai people, no information has been established. In this study, we aimed to study the *UGT1A1* polymorphism in neonate at Songkhla hospital. The 189 cord blood samples were collected and genomic DNA was extracted, then UGT1A1 exon1 and TATA box region were amplified by PCR. DNA sequencing was performing to detect the mutation. The questionnaires about neonate and family were performed before and after birth. We found 4 known mutations, two in the promoter region [(TAA$(TA)_7$ and -64G>C)] and two in the coding region (G71R and P229Q). The orders of variant allele frequency were TAA$(TA)_7$ (0.2037)[6/6= 0.6455, 6/7= 0.3016, 7/7= 0.0529], -64G>C (0.0291)[G/G= 0.9524, G/C= 0.037, C/C= 0.0106], G71R (0.0608)[G/G= 0.8889, G/A= 0.1005, A/A= 0.0106] and P229Q (0.0106)[C/C= 0.9788, C/A= 0.0212]. We found 100 jaundice neonates (55 Male and 45 female) and G71R was the highest relationship with hyperbilirubinemia and prolonged jaundice. We conclude that jaundice after birth may use to be the marker for *UGT1A1* mutation.

Keywords: *UGT1A1*, *UGT1A1* polymorphism

P04

The effect of standardized extract of *Centella asiatica* ECa233 on hemin-induced LDL Oxidation

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Oxidation reaction of low density lipoprotein (LDL) plays a pivotal role in atherogenesis. Hemin (protoporphyrin IX- Fe^{2+}) is oxidative mediator found in plasma of thalassemia patient. *Centella asiatica* have been shown to be antioxidants. The aim of this study was to determine the effect of standardized extract of *Centella asiatica* ECa233 and asiatic acid on hemin-induced LDL oxidation (he-oxLDL). LDL was pre-incubated with either ECa233 or asiatic acid for 30 minutes, and then oxidation was initiated by incubation with hemin for 24 hours. The degree of LDL oxidation was determined by measurement of thiobarbituric acid reactive substances (TBARs) and the relative electrophoretic mobility (REM). The TBARs levels and the REM values were increased in he-oxLDL. However, ECa233 and asiatic acid (20-80 μg/ml) were slightly decreased both TBARs level and the REM value at 24 hr incubation, indicating that ECa233 and asiatic acid could protect LDL oxidation induced by 24 hr- incubation of hemin, though to a lesser extent those of □-tocopherol.

Keywords: *Centella asiatica*, LDL oxidation, hemin, TBARs, α-tocopherol

P05

Proteome analysis of microglial secretion induced by Aβ

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Microglia become activated when exposed to amyloid beta peptides (Aβ), a major component of amyloid plaque, one of neuropathological hallmarks in Alzheimer's disease (AD). Key molecules known to be secreted by activated microglia are proinflammatory cytokines, chemokines and reactive oxygen species (ROS). The aim of this study was to identify novel proteins (as compared to the unstimulated control) that were secreted by microglial cells following Aβ stimulation. Here, we reported that microglia stimulated by Aβ for 12 h secreted several proteins, which could be classified by their functions, regulation of gene expression, metabolism, cell communication/signal transduction, protease inhibitor, immune response and protein binding. Many of these proteins, for example biliverdin reductase A, huntingtin interacting protein-2, nascent polypeptide-associated complex, have recently been reported to associate with neurodegenerative processes in AD. Thus, this protein profile may further our understanding of the role of microglia in AD pathogenesis.

Keywords: Alzheimer's disease, Amyloid peptide, Activated microglia, Proteomics

P06

Screening of microbial-derived products for antimalarial activity

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Multidrug resistant *Plasmodium falciparum* is a problem in tropical and subtropical regions particularly Thailand. The aim of study was to evaluate the *in vitro* antimalarial activity of five microbial-derived products against *Plasmodium falciparum* 3D7 (chloroquine-sensitive) and K1 (chloroquine resistant) clones. The microbial derived products were extracted and investigated for their antimalarial activity. Product number 28 was the only extract which exhibited promising antimalarial activity with IC_{50} value (50% and inhibition concentration 50%) of 0.3835 AU/ml against both clones. Further studies should be performed to investigate the *in vitro* antimalarial activity of this product in *P. falciparum* isolates collected from different malaria endemic areas of Thailand, including its activity in animal model.

Keywords: Microbial-derived product, *Plasmodium falciparum*, antimalarial activity

P07

Microglias stimulated by LPS secrete cofilin-1

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Microglia is resident cells of the brain. Upon activation (e.g. neurodegenerative and neuroinfectious conditions), microglia become activated. Activated microglia are capable of phagocytosis, secrete pro-inflammatory cytokines, chemokines, ROS and other inflammatory mediators. Recent evidences have provided a link between microglia, inflammation and neurodegeneration. As part of the brain's innate immune system, microglia express several types of pattern recognition receptors (PRRs), including toll-like receptor (TLR) 4, which primarily recognizes bacterial cell-wall lipopolysaccharide (LPS). To give an insight into the earliest stage of microgial response to bacterial brain infection, proteins secreted by LPS-stimulated microglial cells at 6 h were examined using two-dimensional gel electrophoresis (2-DE). As compared to that of the unstimulated control, differentially expressed proteins were determined and identified by LC/MS/MS. In addition to known inflammatory cytokines and chemokines, here we reported for the first time that LPS induced secretion of cofilin-1 from microglia. Although the significance of cofilin-1 secretion as part of microglial early response to bacterial infection is not known, it is possible that these cofilins may implicate the roles of microglia in brain Na^+-K^+ homeostasis and neuronal remodeling during bacterial infection.

Keywords: Microglia, TLR-4, Brain infection

P08

Association between *in vitro* sensitivity of *Plasmodium vivax* isolates and polymorphisms of dihydrofolate reductase (*Pvdhfr*) and dihydropteroate synthase (*Pvdhps*)

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In Thailand, the proportion of *Plasmodium vivax* infection currently becomes equal to *P. falciparum*. The study was performed to investigate the association between the polymorphisms of *P. vivax* dihydrofolate redutase (*Pvdhfr*) and *P. vivax* dihydropteroate synthase (*Pvdhps*) and *in vitro* sensitivity of *P. vivax* isolates in Thailand to chloroquine and WR99210 (the experimental inhibitor of *dhfr* enzyme). A total of 32 *P. vivax* isolates were collected from Mae Sot District, Tak Province, the malaria endemic area of Thailand with highest annual malaria incidence. *In vitro* sensitivity test was performed by schizont maturation inhibition test and mutations of *Pvdhfr* and *Pvdhps* were detected by polymerase chain reaction- restriction fragment length polymorphism (PCR-RFLP). Median (95% CI) values for IC_{50} (drug concentration which produces parasite's growth inhibition by 50%) of chloroquine and WR99210 were 134.7 (1.17-264.99) and 139.95 (0.21-523.08) nM, respectively. Mutant alleles of *Pvdhfr* were observed in 20 isolates; 15, 2, 2 and 1 isolates carried 57I/58R/117T, 58R/61M/117N, 57L/58R/117T and 57L/58R/117R, respectively. Nineteen, and 1 isolates carried a single 383G and wild-type A383 of *Pvdhps*, respectively. There was no association between *in vitro* sensitivity of *P. vivax* isolates and mutations of *Pvdhfr* and *Pvdhps.*

Keywords: *Plasmodium vivax*, In vitro sensitivity, Chloroquine, WR99210, Plasmodium vivax dihydrofolate reductase (Pvdhfr), dihydropteroate synthase (Pvdhps) and PCR-RFLP

P09

Regulation of cholesterol transporter protein by black pepper and piperine

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Black pepper extract *(Piper nigrum L.)* and piperine, the active compound of black pepper, were previously shown to block the uptake and absorption of cholesterol into Caco-2 cells. The present study was then aimed to determine the effect of black pepper extract and piperine on the expression of certain proteins functioning in the regulation of cholesterol transport in Caco-2 cells. The expression of proteins was determined by western blotting. The results showed that there was no change in the expression of ABCG5, ABCG8 and ACAT2 in cells treated with black pepper extract and piperine. The expression of cholesterol transporter, NPC1L1, in membrane fraction of Caco-2 cells was lower than that of control. This reduction was not observed in whole cell lysate. The disappearance of NPC1L1 in the membrane fraction may indicate that black pepper extract and piperine could regulate the translocation of NPC1L1 between cell membrane and cytoplasmic compartment.

Keywords: Cholesterol, Black pepper, Piperine, NPC1L1.

P10

Effect of vitamin C on aortic elasticity of mice after cadmium exposure

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Cadmium (Cd) is a toxic heavy metal that is associated with cardiovascular diseases, especially hypertension. Cd-induced toxicity appears to be mediated via oxidative stress. This study was aimed to investigate the effect of vitamin C on aortic elasticity of mice with Cd–induced hypertension. Male ICR mice were received $CdCl_2$ (100 mg/L) in their drinking water whereas normal controls received deionized water. The other two groups of animals treated with $CdCl_2$ were concurrently administered with vitamin C at doses of 50 and 100 mg/kg/day for eight weeks. It was found that Cd administration elevated arterial blood pressure, increased oxidative stress and decreased aortic elasticity. Vitamin C dose-dependently decreased blood pressure and oxidative stress. Moreover, vitamin C at dose of 100 mg/kg/day largely improved aortic stiffness. These findings provide the evidence for the role of antioxidant vitamin C in alleviation of oxidative stress and blood pressure reduction of mice with sub-chronic exposure to CdCl*2*.

Keyword: cadmium, hypertension, elastic properties, oxidative stress

P11

Identification of potential biomarkers in plasma of cholangiocarcinoma patients by using gel-LC-MS/MS

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Cholangiocarcinoma (CAA), a cancer of bile ducts is the cause of severe health problems especially in the northeastern part of Thailand. At present, there is no effective diagnosis or specific biomarkers that can detect the early stage or prognosis of CCA. The aim of the study was to identify new specific biomarkers for CCA using GEL-LC-MS/MS technique. The proteins (30 μg/well) from plasma samples of healthy subjects and patients with CCA were resolved by 12.5% SDS-PAGE and detected by silver staining. Each gel sample lane was cut and single fragments of proteins with molecular weights of less than 14 kDa were digested with trypsin and subjected to LC-MS/MS analysis. The obtained LC-MS/MS data were analyzed by DeCyder™, Mascot™ and MeV™ softwares (t-test, α=0.05) to discriminate significantly expressed proteins from plasma samples of CCA patients from healthy subjects. Six proteins were identified, namely selenocysteine insertion sequence-binding protein 2, class A basic helix-loop-helix protein 15, C-type lectin-like receptor-2, HBF-3, contactin-2 precursor, and hypothetical protein LOC9813. Real-time PCR and Western blot analyses and real-time RT-PCR will be performed to confirm the differentially expressed mRNA and proteins in both samples. Analysis of higher molecular weight proteins in plasma samples from both groups is under way to identify additional potential biomarkers. Efficiency (sensitivity, specificity) of these proteins to be exploited as potential biomarkers for diagnosis of CCA will also be evaluated by ELISA and/or Western blot analysis.

Keywords: Biomarker, Cholangiocarcinoma, GEL-LC-MS/MS.

P12

Associations of *CYP2C9*, *CYP2C19* genetic variants and non-genetic variants with phenytoin blood concentrations in Thai epileptic patients

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Purpose: This study aims to investigate the association of genetic variants in *CYP2C9, CYP2C19* and *ABCB1* genes along with non-genetic variants with phenytoin steady state blood concentrations in Thai patients with epilepsy. *Method*: One hundred and eight Thai epileptic patients on phenytoin maintenance therapy were included in this study. Four candidate SNPs including *CYP2C9*3*(c.1075A>C), *CYP2C19*2* (c.681G>A), *CYP2C19*3*(c.636G>A), and ATP binding cassette subfamily B (*ABCB1* c.3435C>T) were genotyped. Stepwise multiple linear regression statistics was used to identify the association of phenytoin steady state blood concentrations with genetic and non-genetic variants. *Results*: A stepwise multiple linear regression model revealed significant association of phenytoin blood concentrations with the presence of *CYP2C9*3* or *CYP2C19*2* allele, gender and body weight. The model explain 25.5% of the variability in phenytoin blood concentrations per dose (R^2=0.255, *P*=0.028). *Conclusion*: This study suggests that genetic variants in *CYP2C9* and *CYP2C19* together with non-genetic variants (i.e. gender and body weight) influence variability in phenytoin steady state blood concentrations in Thai patients with epilepsy. This finding could be to use to evaluate the efficacy of phenytoin in treating epileptic patients.

Keywords: *CYP2C9, CYP2C19*, non-genetic variants, phenytoin blood concentrations, Thai epileptic patients

P13

Screening of antimalarial activities of Thai medicinal plants

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Malaria remains one of the most serious causes of mortality and morbidity in the world. The problem of multidrug resistant *Plasmodium falciparum* has been aggravating particularly in Southeast Asia. Therefore, development of new potential antimalarial drugs is urgently required. In the present study, we assessed the *in vitro* antimalarial activity of the ethanolic extracts of the thirty Thai medicinal plants/herbal formulations against chloroquine (CQ)-resistant (K1) and CQ-sensitive (3D7) clones of *P. falciparum.* Seventeen ethanolic extracts showed promising antimalarial activity against both clones with parasite survival of less than 50% at the concentration of 50 µg/ml. The extracts from the eight plants (DiMEt, DrLEt, KaGEt, MyFEt, PiCEt, PlIEt, BJK1R and GaMEt) were found to possess potent antimalarial activity with IC_{50} of less than 10 µg/ml for both K1 and 3D7 clones.

Keywords: *Plasmodium falciparum*, Thai herbal medicine, drug resistance

P14

Association between *pfatp6* and *pfmdr1* polymorphisms and treatment response to artesunate-mefloquine combination regimen in patients with acute uncomplicated *Plasmodium falciparum* malaria in Thailand

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The aim of the study was to investigate the association between genetic polymorphisms of multi-drug resistance 1 (*pfmdr1)* and sarco/endoplasmic reticulum Ca^{2+}-ATPase (*pfatp6*) of *Plasmodium falciparum*, and *in vitro* sensitivity in 226 *P. falciparum* isolates. Polymorphism of *pfatp6* at codons R37K, G639D, S769N and I898I, and of *pfmdr1* at codons N86Y, N1042D, D1246Y were analyzed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Copy numbers of *pfatp6* and *pfmdr1* gene of all isolates were analyzed by quantitative real time-polymerase chain reaction (qRT-PCR). Marked decline in sensitivity to artesunate (mean $\pm$ SD IC_{50} 3.66$\pm$0.46 nM) was observed in nine isolates. All carried wild-type alleles of *pfatp6* and *pfmdr1*; only one isolate carried mutation at codon 1042. Analysis of *pfmdr1* copy number showed a single gene copy in 74 out of 102 isolates, whereas 12, 5, 8 and 3 isolates carried 2, 3, 4, and $\geq$ 5 gene copies, respectively. All of the 14 isolates selected based on clinical response to artesunate and mefloquine combination carried only a single copy of the *pfatp6* gene. Interestingly, the increase of *pfmdr1* copy number was markedly present in isolates collected from all (13/13 cases) patients with treatment failure. No association between SNP and amplification of *pfatp6* gene and *in vitro* sensitivity of *P. falciparum* isolates to artesunate and mefloquine was found.

Keywords: *Plasmodium falciparum*, *pfmdr1, pfatp6*, single-nucleotide polymorphism, gene amplification, artemisinin, drug resistance, PCR-RFLP

P15

Situation of pharmacogenetic test in Thailand: Case study of phenotyping and genotyping of Thiopurine S-methyltransferase

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Thiopurine S-Methyltransferase (TPMT) is an enzyme that used for detoxification of thiopurine drugs such as azathioprine, 6-MP and 6-thioguanine. Several studies have shown strong associations between *TPMT* deficiency and myelotoxicity. Recently, several thiopurine drugs have been relabeling in USA as well as Thailand to include the information about TPMT genetic polymorphism and higher risk of myelotoxicity in patients who have TPMT deficiency.

The Pharmacogenetic Unit has been established in Department of Pharmacology, Faculty of Medicine, Khon Kaen University since 2008 in order to provide the pharmacogenetic services for Srinagarind Hospital and other hospitals in Thailand. This unit provide several pharmacogenetic tests including phenotyping and genotyping of TPMT, genotyping of *CYP2C9*, *VKORC1* as well as *HLA-B*1502*, *HLA-B*5801*.

According to TPMT genetic polymorphism, phenotyping is determined based on enzymatic assay of TPMT in erythrocytes while genotyping is based on real-time polymerase chain reaction. Since 2008, 48 samples have been sent to the unit for phenotyping and genotyping. Most of them were request from pediatricians. Results revealed that 85.5% were homozygous *TPMT*1/*1*, 12.5% were heterozygous **1/*3* and 2% were homozygous **3/*3*. For phenotyping, 14% of samples have TPMT activity below 27.5 nmol 6-MTG g^{-1}Hb h^{-1}. The prevalence of *TPMT* polymorphism was similar to the previous data reported in healthy Thai volunteers. Less order of TPMT pharmacogentic tests may result from the fact that general practice doctors and pharmacists are not familiar with this new pharmacogenetic test. Therefore, knowledge in pharmacogenetics should be provided not only for the medical and pharmacy students but also for health care practioners.

P16

Genetic deletion of NAD(P)H: Quinone oxidoreductase-1 (NQO1) as a strategy to enhance chemosensitivity of cholangiocarcinoma cells

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Cholangiocarcinoma (CCA) is an intrahepatic bile duct carcinoma with highly chemoresistant rate and poor prognosis. Evidently, increase of intracellular defense mechanisms is one of the major cellular factors that can contribute to chemo- resistance of several tumors. NAD(P)H: quinone oxidoreductase-1 (NQO1) is an enzyme playing a critical role in cellular defense against reactive oxygen species, protecting cells from chemical-induced toxicity. The aim of this study was to evaluate the role of NQO1 in sensitizing CCA cells to anticancer drugs using small interfering RNA against human NQO1 (NQO1-siRNA) as a tool. First, we demonstrated that in our system, NQO1-siRNA efficiently suppressed the expression of NQO1 in KKU-100 cells, the high NQO1-expressing CCA cells, at both mRNA and protein levels without toxic effect to cells as demonstrated by no change of the basal apoptotic cell death rate of the cells at 48 h post-transfection. The KKU-100 cells transfected with NQO1-siRNA showed more than 80% decrease in NQO1 mRNA expression when compared with control. Consistently, the NQO1 enzyme activity in siRNA-transfected cells was dramatically decreased more than 60% compared to the control. The effects of NQO1-siRNA on chemosensitivity of KKU-100 cells to anticancer drugs were then further examined. The results showed that KKU-100 transfected with NQO1-siRNA significantly improved the sensitivity to all anticancer drugs investigated include 5-fluorouracil, doxorubicin, and gemcitabine. Combination of NQO1-siRNA and anticancer drugs also significantly augmented antiproliferation and cell death. Taken together, NOQ1 is important in sensitizing CCA cells to anticancer drugs and modulation of NQO-1 expression substantially improved the cytotoxicity effect of anticancer drugs. Thus, NQO1 silencing might be a valuable chemotherapeutic strategy for CCA. This work was supported by the Commission for Higher Education.

Keywords: Cholangiocarcinoma (CCA); NAD(P)H-quinone oxidoreductase-1 (NQO1); NQO1 siRNA; Chemosensitivity.

P17

Bovine serum albumin enhances CYP1A2-mediated phenacetin O-deethylation formation by binding to polyunsaturated fatty acids

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The addition of bovine serum albumin (BSA) to incubations has been shown to enhance activities of certain cytochrome P450 (CYP) activities including 2C8 and 2C9 mainly via a reduction of the K_m values without an effect on V_{max}. It has been demonstrated that the intrinsic clearances of CYP2C8 and CYP2C9 substrates that were calculated from microsomal incubations in the presence of BSA improved the prediction of *in vivo* hepatic clearance. This effect arises from albumin binding to inhibitory polyunsaturated fatty acids (PUFAs) released during the course of incubation. The universality of the BSA effect on other CYP isoforms, however, is currently unknown. Since CYP1A2 is one of the enzymes responsible for the metabolism of several drugs, it is therefore interesting to elucidate the effect of BSA on the *in vitro* kinetics of CYP1A2-catalysed phenacetin O-deethylation. In the absence and presence of BSA (2% w/v), data for phenacetin O-deethylation formation by human liver microsomes (HLM) and recombinant CYP1A2 (rCYP1A2) respective exhibited two enzymes and single enzyme Michaelis-Menten kinetics. BSA statistically decreased mean K_m for phenacetin O-deethylation by HLM and rCYP1A2 with a minor effect on mean V_{max}, resulting in statistically increment of intrinsic clearance. A mixture of oleic, linoleic, and arachidonic acid caused an increase in K_m without an effect on V_{max} for phenacetin O-deethylation by rCYP1A2. The addition of 2% BSA to the incubation reversed this inhibitory effect of fatty acid mixture.

Keywords: albumin effect, cytochrome P450 1A2, phenacetin, phenacetin O-deethylation, polyunsaturated fatty acid.

Acknowledgements: This study was supported by grants from The Thailand Research Fund through The Royal Golden Jubilee Ph.D. scholarship (to NW and WT) and Faculty of Medicine, Khon Kaen University, Thailand

P18

Cytotoxic, anti-oxidant, apoptosis and multi-drug resistant gene inducing activities of *Zingiber officinale* Roscoe

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The aim of the study was to investigate cytotoxicity, anti-oxidant, apoptosis and multi-drug resistant gene inducing activities of the crude ethanolic extract of ginger (*Zingiber officinale* Roscoe) against cholangiocarcinoma (CCA). Cytotoxic activity against CCA cell line (CL-6) was assessed by calcein-AM and Hoechst 33342 assay and its anti-oxidant activity was evaluated by DPPH assay. Median IC_{50} values for cytotoxicity and anti-oxidant activities were 10.95, 53.15 and 27.86 μg/ml, respectively. Investigation of the apoptotic activity was performed by DNA fragmentation assay and inductions of genes that may be involved in resistance of CCA to anticancer drugs (MDR-1, MRP-1, MRP-2 and MRP-3) were characterized by real-time PCR. More than ten DNA fragments were visualized and up to 7-9 fold up-regulation of MDR-1 and MRP-3 genes were observed following exposure to ethanolic extract of ginger. Results from *in vitro* studies indicate promising anticancer activity of the crude ethanolic extract of ginger against CCA. Nevertheless, MDR1 and MRP3 may be involved in conferring resistance of CCA to the ginger extract.

Keywords: cholangiocarcinoma, cytotoxicity, The ethanolic extract of ginger

P19

Phenethyl isothiocynate inhibits cholangiocarcinoma cells by disruption of the mitochondrial transmembrane potential

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Phenylethyl isothiocyanate (PEITC) is recognized as a cancer chemopreventive agent from cruciferous vegetables. Previous studies showed that PEITC can induce a large proportion of cholangiocarcinoma cells (CCA) to undergo apoptosis. To better understand the anticancer mechanism of isothiocyanates, we examined the effects of PEITC on CCA cell lines in comparison with normal liver cell line. Treatment of liver Chang cells and CCA, KKU-100 cells with PEITC caused a rapid increase of superoxide formation as assayed by dihydroethidium fluorescent staining. To determine if superoxide was indeed an initial signal responsible for inducing apoptotic cell death, PEITC was introduced in combination with Tempol, a superoxide dismutase mimic and *N*-acetylcysteine (NAC). We found that combination of PEITC with NAC could suppress superoxide, prevent GSH depletion, induce the loss of mitochondrial transmembrane potential ($\Delta\psi_m$), and inhibit PEITC-induced cell death. On the other hand, co-treatment of PEITC with Tempol, although, could suppressed reactive oxygen species (ROS) generation but could not preserve GSH levels and loss of $\Delta\psi_m$ and, eventually could not protect cell death. This suggests ROS generation is more likely to be a secondary effect of PEITC mediated dysfunction of the mitochondria. Altogether, the present study, we demonstrated that PEITC-induced cancer cell killing was associated with change in the GSH redox system and induced loss of $\Delta\psi_m$.

This work was supported by grant-in aid from Khon Kaen University and from Faculty of Medicine. Ornanong Tusskorn is supported by the Commission for Higher Education.

Keywords: Phenylethyl isothiocyanate; Cholangiocarcinoma; Mitochondrial transmembrane potential ; 4-hydroxy-TEMPO; N-acetylcysteine

P20

Hypocholesterolemic effect of sericin and its effect on liver protein expression

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A cholesterol lowering effect of sericin was investigated both in vivo and in vitro. Rats were dosed with cholesterol with and without sericin for 17 days. The result shows that total serum cholesterol and non-HDL levels were reduced in rats fed high-cholesterol diet with all three tested doses of sericin (10, 100, and 1000 mg/kg/day). The expression of certain liver proteins isolated from rats supplemented with sericin was determined. This study suggests that hypocholesterolemic effect of sericin may be involved with down-regulation of microsomal triglyceride transfer protein (MTP), the protein involved in VLDL assembly and cholesterol 7α-hydroxylase (CYP7A1), the protein removed cholesterol from the body by biosynthetic pathway producing bile acids.

Keywords: Hypocholesterolemic effect; MTP ; CYP7A1; sericin; silk protein

P21

Analgesic efficacy of diclofenac and ibuprofen in patients with pain after third molar surgery

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This study aimed to collect the information on the efficacy, onset of action, and duration of action of a single dose of 100 mg of diclofenac compared to 400 mg of ibuprofen for pain relief in patients after impacted third molar surgery. This randomized double-blind clinical trial was performed in sixty Laotian patients undergoing lower third molar removal. Patients were divided into two groups and randomly assigned to treat with either 100 mg of diclofenac or 400mg of ibuprofen. Patients rated their pain intensity (PI) by using visual analog scale (VAS) for 12 h. They started to take medication when they had at least moderate to severe pain. The onset of action was determined by means of a 2-stopwatch method. The duration of action was determined by the time that patients requested the rescue medication. The onset of analgesia for meaningful pain relief (MPR) for ibuprofen (64 ± 26.1minutes) was faster than diclofenac (83 ± 21.1minutes) ($p<.05$). The duration of analgesia for diclofenac and ibuprofen were 406 ± 54.19 minutes and 422 ±44.3 minutes respectively. There were no statistically significant differences in duration of analgesia between diclofenac and ibuprofen groups ($p>.05$). Patients reported no significant differences in analgesic efficacy between 100 mg of diclofenac and 400 mg of ibuprofen. The duration and pain relief of 100 mg of diclofenac and 400 mg of ibuprofen to control pain after impacted third molar surgery were found to be comparable. The onset of analgesia for ibuprofen was faster than diclofenac.

Keywords: Pain, Diclofenac, Ibuprofen, Third Molar Surgery

P22

Mercury in saliva of subjects with amalgam restorations

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The adverse effect of mercury from amalgam restoration is today a matter of debate in several countries. The aim of this study was to evaluate the mercury concentrations in saliva in patients who have had amalgam restorations compared with non-amalgam restoration subjects. The saliva was obtained from twenty-three subjects who had amalgam restorations, and fourteen subjects without amalgam restorations. We used cold vapor atomic absorption spectrometry to quantify mercury concentrations in saliva. The saliva mercury concentrations in the amalgam group and non-amalgam group were 0.37±0.18 micrograms/liter and 0.47±0.23 micrograms/liter respectively. There was no statistically significant difference in the saliva mercury concentrations between the groups (t-test P>.05). Statistical analysis showed a low non- significant negative correlation between saliva mercury concentrations and the number of amalgam restorations (Pearson Correlation r = -0.20, P>.05). Mercury in the saliva of subjects who had amalgam restorations was not higher than those of non-amalgam restoration subjects. No significant difference could be found in the saliva mercury levels between subjects with and without amalgam restoration. Mercury in saliva did not correlate with the amount of amalgam restorations.

Keywords: Mercury, Saliva, Amalgam Restoration

P23

Inhibition of human CYP1A2 activity by Thai medicinal plants with promising activities against cholangiocarcinoma

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Traditional medicine is commonly used as an alternative treatment for cancer. Several Thai traditional folklores have been shown to possess anticancer activities in various human cancerous cell lines with some promising candidates. The cytochrome P450 (CYP) superfamily of enzymes play crucial roles in the metabolism of drugs and thus have a significant impact on the occurrence of drug-drug interactions. Herbal preparations consist of multiple and often unidentified biological constituents. There is a greater possibility that drug-drug interactions could occur between a complex herbal product and administration of single drug than during the co-administration of two individual drugs. The aim of the present study was to investigate the propensity to inhibit CYP1A2-mediated hepatic drug metabolism *in vitro*, of four crude ethanolic extracts of Thai medicinal plants with promising anticancer activity against cholangiocarcinoma, *i.e.,* extracts of *Atractylodes lancea*, *Zingiber officinal*, *Piper chaba* and *Pra-Sa-Prao-Yhai* formulation, using human liver microsomes. The ethanolic extracts from Pra-Sa-Prao-Yhai herbal formulation inhibited CYP1A2 activities in dose dependent manner with potent activity similarly to that of□ □-napthoflavaone (selective inhibitor of CYP1A2), with IC_{50} (concentration causing 50% inhibition of enzyme activity) of 0.03 □g/ml. Results showed that metabolic drug interaction may be of concern for clinical use of Pra-Sa-Prao-Yhai herbal formulation in cholangiocarcinoma.

Keywords: Thai medicinal plants, cholangiocarcinoma, Cytochrome P4501A2, herb-drug interaction

P24

Downregulation of glutamate transporter expression by lopinavir and its implication in excitotoxicity

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The efficient penetration of antiretroviral drugs to central nervous system (CNS) is associated with greater reduction of HIV viral replication in cerebrospinal fluid (CSF). However, HIV-infected patients who receive combination antiretroviral therapy regimens with high CNS penetration show poorer neurocognitive performance compared to patients with less CNS penetration regimens. Chronic administration of ritonavir-boosted lopinavir impaired neurocognitive function in mice. Excitatory amino acid transporter 2 (EAAT2) is an essential glutamate transporter in the brain. The reduced expression and dysfunction of EAAT2 has been linked to learning and memory impairment and various neurologic disorders including HIV-associated dementia. Herein, we hypothesize that lopinavir, a protease inhibitor with high CNS penetration; exert CNS toxicity through its effects on glutamate transporters expressed on astrocytes. Primary human astrocytes exposed to lopinavir at concentrations equivalent to median CSF concentrations showed reductions in EAAT2 transcript and protein expression measured by real time RT-PCR and immunoblotting. Acute application of lopinavir did not affect cytosolic calcium flux [Ca_i] in Fluo-8-loaded primary human astrocytes while chronic exposure of lopinavir increased both spontaneous and glutamate-evoked transient rises in [Ca_i], indicative of increased excitability. Lopinavir did not alter gene expression of EAAT1 and neutral amino acid transporter ASCT1 in primary human astrocytes. In summary, our results indicate that exposure of lopinavir might disrupt astrocyte ability to regulate glutamate levels in the brain. Excess glutamate can increase excitability of astrocytes and neurons, leading to excitotoxicity and neurocognitive impairment.

Keywords: protease inhibitor, astrocyte, EAAT2, calcium influx, excitotoxicity

P25

Antioxidant activity and phenolic contents of Thai white mulberry (*Morus alba* L.) and butterfly Pea (*Clitoria ternatea* L.) Teas

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In this study, two commercially available herbal teas: white mulberry (*Morus alba* L.) and butterfly pea (*Clitoria ternatea* L.) teas were evaluated for their polyphenolic content, and antioxidant activity. Antioxidant activity of aqueous tea infusions derived from five brands of two herbal teas was evaluated using three anti-oxidative methods: the 2, 2'-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging method, the ferrous ion chelating ability, and soybean lipoxygenase inhibition assay. The polyphenol component of herbal tea infusions, key to their healthful qualities, was determined as Gallic acid equivalents (GAE). In addition, anthocyanin content in butterfly pea tea was measured by pH-different method. The low variations in the contents of total polyphenols were observed among tea infusion from different brands of white mulberry tea and butterfly pea tea. Whereas, the high variations in the contents of total anthocyanin was found among infusions from different brands of butterfly pea tea and this may be related to the color intensity of butterfly pea flowers. White mulberry tea infusion showed stronger antioxidant activity, while butterfly pea infusion showed weaker antioxidant activity using two methods (DPPH scavenging method and ferrous ion chelating method). However, both tea infusions showed high and relatively similar antioxidant activity using soybean lipoxygenase inhibition method. Moreover, the amount of total polyphenols found in white mulberry tea was 1.7 times higher than butterfly pea tea. A correlation was observed between DPPH scavenging activity, ferrous ion chelating activity and the total polyphenols contents. Therefore, both herbal teas can be considered to be a good source of water-soluble antioxidants and phenolic compounds.

Keywords: white mulberry (*Morus alba)* tea, Butterfly pea *(Clitoria ternatea)* tea, Antioxidant, Total polyphenols.

P26

Toxicity of silver nanoparticles in A549 cells

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Introduction: Silver nanoparticles (AgNPs) are presently incorporated in textiles, cosmetics, medical devices, personal care and house hold products. Despite increasing production and application of AgNPs, large knowledge gaps regarding their possible toxic effects to human health and environment are awaiting to be elucidated.
Objective: To determine toxic effects of silver nanoparticles in terms of mitochondrial-related cytotoxicity and change of cell cycle in human lung carcinoma (A549) cells.
Materials and Methods: A549 cells were cultured in F-12K media containing 10% FBS and incubated in 95% humidified atmosphere and 5% CO_2 at 37°C. AgNPs suspended in the MilliQ water were treated to the cells at final concentrations of 25, 50, 100 and 200 µg/mL for 24 and 48 h. Cytotoxicity was determined by MTT assay. The cell cycle was determined by FACS analysis.
Results: The results demonstrated that AgNPs not only affected cell viability, as indicated by decrease of mitochondrial function, but also disturbed normal cell cycle of A549 cells in time- and concentration-dependent manner.
Discussion and Conclusion: The results from this study suggest potential cytotoxic effects of AgNPs in A549 cells.

Keywords: Silver, Nanoparticles, Toxicity, Cell cycle, A549

P27

*HLA-B*15:02* allele is not a genetic marker for Steven Johnson syndrome and toxic epidermal necrolysis induced by phenytoin.

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Steven Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous adverse drug reactions (SCAR) which associated with several aromatic antiepileptic drugs (AEDs) including carbamazepine (CBZ), phenytoin (PHT), phenobarbital (PNB) and lamotrigine (LMG). Cross reactivity of SCAR among these AEDs has been reported. Recently, a strong association between CBZ-induced SJS or TEN has been described with *HLA-B*15:02* in Han Chinese and Thais as well as other Asian populations. Although an association of *HLA-B*15:02* and PHT-induced SJS/TEN has been noted in Thai and Chinese patients, the number of patients in these studies were too small to draw any definite conclusion. A case-control study was therefore carried out in order to determine relationship between *HLA-B*15:02* and SJS/TEN induced by PHT in a Thai population. In this study, 25 patients who have been diagnosed as PHT-induced SJS/TEN and 74 patients who were tolerant to PHT were enrolled as cases and controls. Peripheral blood or buccal swab samples were collected for genomic DNA extraction. The presence of *HLA-B*15:02* in these patients were analyzed using a PG1502 DNA detection kit.

Among the PHT-induced SJS/TEN patients, 20.00 % carried the *HLA-B*15:02* while 14.86 % of the PHT -tolerant controls carried this allele. The prevalence *HLA-B*15:02* in the cases and controls was not significantly different among the case and the control groups suggest that *HLA-B*15:02* may not be a valid genetic marker for screening Thai patients who at higher risk of PHT-induced SJS/TEN.

Keywords: *HLA-B*15:02*, phenytoin, Steven Johnson syndrome and toxic epidermal necrolysis

P28

Antioxidant and antiglycation activities of anthocyanin-enriched red grape skin extract

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This study was to determine antiglycation and antioxidant effect of anthocyanin-enriched red grape skin extract (RGSE). The phytochemical analysis revealed that the total anthocyanin content of RGSE was 36.733 ± 0.8 mg cyanidins-3-glucoside/g dried extract. The results show that RGSE significantly inhibited the formation of advanced glycation end products (AGEs), decreased the content of N^{ε}-(carboxymethyl) lysine (CML) and increased free thiol group of fructose-modified BSA in concentration-dependent manner. In addition, RGSE was the effective DPPH (1,1-diphenyl 2-picrylhydrazyl) radical scavenger with IC_{50} value of 0.024 ± 0.001 mg/ml. Taken together, the results from this study show that RGSE had antiglycation and antioxidant activities, which may be beneficial for prevention of diabetic complications.

Keywords: red grape skin extract, anthocyanin, antioxidant, glycation

P29

Bacopa monnieri increases superficial cerebral blood flow

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Bacopa monniera (Brahmi) is a plant well known in Ayuravedic and Thai traditional medicine for memory enhancing (1, 2). Presently, its mechanism of action regarding the effect on blood flow to the brain is still not known. Accordingly, we investigated the actions of Brahmi ethanolic extract on systemic blood pressure and superficial cerebral blood flow and compared this to *Ginkgo biloba* (ginkgo) extract and donepezil, a standard drug for Alzheimer's disease. In the current study, rats were orally administered with either vehicle, Brahmi extract (40 mg/kg BW), ginkgo extract (60 mg/kg BW) or donepezil (1 mg/kg BW) daily for 2 months. These are dose regimes previously reported to improve memory performance tests (2). Systolic blood pressure was measured in conscious, restrained rats every month using a tail cuff method. Finally, each rat was anaesthetized and blood flow in the superficial parietal cortex was measured using the laser Doppler flow method. We found that the 2-month administration of Brahmi, ginkgo or donepezil had no effect on systolic blood pressure nor heart rate. Interestingly, superficial cerebral blood flow was increased in the rats treated with Brahmi (3002$\pm$108 PU, n=6, p=0.004), ginkgo (3110$\pm$206 PU, n=6, p=0.01), or donepezil (2834$\pm$144 PU, n=6, p=0.03) compared with the control group (2337$\pm$125 PU, n=5). These results indicate that one of the memory enhancing mechanisms of actions of Brahmi, ginkgo and donepezil may be to increase of neocortical blood flow.

Keywords: *Bacopa monnieri*, ginkgo, cerebral blood flow, blood pressure

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P30

Preliminary study on pharmacokinetic profiles of standardized extract of *Centella asiatica* ECa 233 in rats

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ECa 233 is a standardized extract of *Centella asiatica* containing mainly madecassoside and asiaticoside. Pharmacological evaluation of ECa 233 in animals demonstrated positive effect on learning and memory deficit induced by β amyloid as well as wound healing effects. The aim of this study was to investigate the pharmacokinetic profiles of ECa 233 after oral administration in rats. Male Sprague-Dawley rat received ECa 233 at the doses of 30 mg/kg by oral administration and blood sample were collected from tail's vein at time 0, 0.5, 1, 2, 4, 6, 8, 10, 12 and 24 hour after administration. Madecassic acid levels in plasma were determined by high performance liquid chromatography (HPLC). The main pharmacokinetic parameters obtained were: *T*max, 1.67+0.33 hour; *C*max, 1.92+0.39 μg/ml; AUC0-24, 6.64+0.97 μg h/ml, respectively.

Keywords: Pharmacokinetics; ECa233, Standardized extract of *Centella asiatica* ; Madecassic acid

P31

Study on *in vitro* antimalarial activity of cyclooxygenase inhibitors against *Plasmodium falciarum*

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Multi-drugs resistance of *Plasmodium falciparum* is a major problem for controlling malaria in Thailand. To deal with this problem, development of novel antimalarial drugs and the use of drug combination have been proposed. The objective of the present study was to assess *in vitro* antimalarial activity of the combination of artesunate and cyclooxygenase inhibitors (aspirin, naproxen and piroxicam), against chloroquine resistant (K1) and chloroquine sensitive (3D7) *P. falciparum*. The test was performed based on fluorescent-based technique. The combination of artesunate and aspirin was observed based on the ratios: 10:0, 7:3, 5:5, 3:7 and 0:10, respectively. The highest final concentrations of artesunate and aspirin used were 50 and 10,000 nM, respectively. Results showed that the concentration that inhibited parasite growth to 50% (IC_{50}) of artesunate against K1 and 3D7 were 2.5 (1.6-3.4) and 2.2 (1.2-3.2) nM, respectively. The IC_{50} values of aspirin, naproxen and piroxicam were greater than 100,000 nM for both strains. The SUM-FIC values of drug combination between artesunate and aspirin against K1 and 3D7 were 0.60 and 0.64, respectively. Results indicated marked synergism of the combination of artesunate and aspirin for both *P. falciparum* strains.

Keywords: *Plasmodium falciparum;* cyclooxygenase (COX) inhibitor, drug resistance

P32

The effects of *Andrographis paniculata* on the pharmacokinetics of midazolam in normal healthy volunteers

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Andrographis paniculata has been widely used for centuries in Asia. Previous *in vitro* studies have shown that *A. paniculata* extracts and its major component, andrographolide, inhibited activity and mRNA expression of human cytochrome P450 3A4 enzyme (CYP3A4). The purpose of this study was to evaluate the effect of *A. paniculata* on the pharmacokinetics of midazolam, a CYP3A4 probe drug. The study was an open-label, randomized, two-phase crossover design. Twelve healthy male volunteers received 4 capsules of 250 mg *A. paniculata* three times a day orally for 7 days. Midazolam plasma concentration time profiles were characterized after a single oral dose of 7.5 mg midazolam on the day before and after *A. paniculata* medication. The results demonstrated that treatment with *A. paniculata* did not change mean pharmacokinetic parameters (C_{max}, T_{max}, $AUC_{0\text{-}12h}$, $AUC_{0\text{-}\infty}$, $T_{1/2}$, Cl/F) of oral midazolam. Thus, no clinically relevant CYP3A4 inhibition after *A. paniculata* in healthy volunteers was suggested.

Keywords: *Andrographis paniculata*, Andrographolide, Midazolam, Pharmacokinetics, Drug interaction

P33

Pharmacokinetics of gabapentin 600 mg tablet in Thai healthy volunteers

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Gabapentin is an antiepileptic drug and structurally similar to γ–aminobutyric acid (GABA) which crosses the blood-brain barrier. Gabapentin is absorbed into the blood by the L-amino acid transport system. An oral bioavailability of gabapentin displays dose-dependent. Plasma concentration of gabapentin are not directly proportional to dose. Therefore, pharmacokinetic of gabapentin is essential for patients who have to receive gabapentin 600 mg. To investigate the pharmacokinetic of gabapentin 600 mg in Thai healthy volunteers**.** The study was performed in 24 Thai male healthy volunteers who received a single oral dose of 600 mg gabapentin tablet. Serial blood samples were collected before and after to 48 hours after drug administration. Plasma gabapentin concentrations were determined by automated High Performance Liquid Chromatography (HPLC) with UV detector after deproteinized with acetonitrile followed by derivatization with 1-fluoro-2,4-dinitrobenzene. The relevant pharmacokinetic parameters were determined. The mean values of pharmacokinetic parameters (mean ± SD) were 3.17 ± 0.80 hrs (1.5 –5.0 hrs) for T_{max}; 4,853.58 ± 1,369.67 ng/ml for C_{max}; 0.11± 0.02 hr^{-1} for K_{el}; 6.62 ± 1.87 hrs (4.89 – 11.41 hrs) for $T_{1/2}$; 47,712.88 ± 12853.61 ng.hr/ml for AUC_{0-t} , 48,713.20 ± 12,909.78 ng.hr/ml for AUC_{0-inf} , 5.24 ± 1.32 L/hr for Cl and 49.28 ± 15.98 L for Vd. The data showed the rate and extent of absorption of gabapentin 600 mg. These data should be use to support the assignment of therapeutic purposes for patients who have to receive gabapentin 600 mg.

Keyword: Gabapentin, Pharmacokinetic

P34

Cytotoxic activity of the ethyl acetate extract from *Glycosmis parva* leaves on human B- lymphoma cells

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This study aimed to investigate cytotoxicity of the ethyl acetate extract from the leaves of *Glycosmis parva* (Criab), a tradition thai herbal medicine, on human B-lymphoma cells or Ramos cells. The extract demonstrated cytotoxic activity against Ramos cells with its IC50 15.68 μg/ml at 24 hours exposure by rezasurin staining assay. It mainly induced apoptosis of these cancer cells after 8 and 16 h of exposure by annexin V-FICT and propidium iodide staining assay. This apoptotic induction activity of the extract was markedly dependent on caspase activation. These results demonstrated that the ethyl acetate extract from leaves of *G. parva* potentially has anti-tumor activity against B- lymphoma cells.

Keywords: *Glycosmis parva*, cytotoxic, apoptosis, cell cycle regulation

P35

Are renal transplant recipients with sirolimus-base regimen with low risk for cardiovascular disease?

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Renal transplant recipients have increased risk of cardiovascular disease (CVD) compared to the general population and other groups of renal disease. In fact, CVD remains the leading cause of death in renal transplantation. Homocysteine is the established CVD risk marker. This study aimed to assess whether renal transplant recipients who received sirolimus (SRL) as their main immunosuppressive therapy had lower risk for CVD as evidenced by a CVD surrogate, homocysteine, compared to those with calcinuerin inhibitor (CNI). Sixty five renal transplant recipients (55 with CNI-based regimen and 10 with SRL-based regimen) and 34 healthy controls were recruited. Plasma homocysteine levels were measured using ARCHITECT® assay. Plasma homocysteine levels were higher in patients (15.43±1.88 μmol/L) compared to those of the controls (10.91±3.67 μmol/L, $p < 0.01$). Plasma homocysteine levels of the CNI-based patients were higher than the SRL-based but this did not reach significance (15.62±8.70 and 14.38±4.47 μmol/L, respectively). These results suggested the higher CVD risk in renal transplant recipients and may support the role of SRL-based regimen in reducing the CVD risk in this group of patients

Keywords: homocysteine, sirolimus, renal transplant recipients.

P36

Molecular characterization of *Plasmodium vivax dihydrofolate reductase (Pvdhfr)* in *Plasmodium vivax* isolates from Thailand

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Malaria is the most important public health problems in several countries. In Thailand, co-infections of *Plasmodium vivax* and *P. falciparum* are common. The prevalence and patterns of mutations of *Pvdhfr* was investigated in a total of 60 blood samples collected from patients with *P. vivax* infection who attended the malaria clinic in Mae Sot, Tak Province in 2009. SNP-haplotypes at amino acid positions 13, 33, 57, 58, 61, 117 and 173 of *Pvdhfr* was examined by nested PCR-RFLP. All parasite isolates carried triple mutant *Pvdhfr* alleles (100%). The most common *Pvdhfr* alleles were 57I/58R/117T (81.7%), 57L/58R/117T (8.3%), 58R/61M/117N (8.3%), and 57I/58R/117T/N (1.7%). Results suggest that all *P. vivax* isolates from Mae sot carried mutant alleles of *Pvdhfr*. The development of new alternative antifolates drugs that are effective against sulfadoxine-pyrimethamine resistant *P. vivax* is required.

Keywords: *Plasmodium vivax*, *Plasmodium vivax dihydrofolate reductase (Pvdhfr)* and antifolate

P37

Study on laxative, antihyperglycemic, and lipid lowering effects of Malva Nut (*Scaphium Lychnophorum* (Hance) Piere.) in rats fed with high fat diet compare with konjac (*Amorphophallus* sp.)

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Dietary fiber has many beneficial effects on human health. Malva nut tree (*Scaphium lychnophorum*) is the indigenous plant of Thailand known as Sumrong. Large amount of mucilaginous substance can be extracted from the fruit. The aim of this study was to investigate the laxative, antihyperglycemic and lipid lowering effects of malva nut in rats fed with high-fat diet compare with konjac. The animals were fed with normal diet, high-fat diet, high-fat diet + malva nut pulp 5% and 10%, high-fat diet + konjac powder 5% and 10%, for 3 months. The results showed that body weight and food intake were not different among all groups. The fecal weight of high-fat diet + malva nut pulp 5%, 10% were significantly increase (68% and 89%, respectively) when compared with high-fat diet group. In all treated rats, their fasting blood glucose, oral glucose tolerance, blood cholesterol, triglyceride, HDL and LDL were not significantly different form high-fat diet group. It is concluded that malva nut has marked laxative effect, but lack of antiobesity, antihyperglycemic and lipid lowering effects.

Keywords: *Scaphium lychnophorum*, laxative, lipid lowering, glucose tolerance

P38

Population pharmacokinetics-pharmacodynamics of mefloquine when used in combination with artesunate as a 3-day combination regimen in the treatment of highly multidrug resistance *Plasmodium falciparum* in Thailand

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Declining in clinical efficacy of artesunate-mefloquine combination for treatment has been documented in areas along the eastern border (Thai-Cambodian) of Thailand. In the present study, we investigated the population pharmacokinetics of MQ when used in combination with artesunate as a three day combination regimen in relation to treatment response in a total of 150 Burmese patients with acute uncomplicated falciparum malaria. The study was conducted at Mae Tao clinic for migrant workers, Tak Province, Thailand. A total of 996 blood samples were collected from 150 (85 males, 65 females) Burmese patients aged over 15 years with acute uncomplicated *Plasmodium falciparum* malaria following a three day combination regimen of artesunate-mefloquine. Whole blood mefloquine concentrations were determined by high performance liquid chromatography (HPLC). The basic pharmacokinetic model, 2 –compartment model for mefloquine absorption and disposition were best fit with mefloquine concentration-time data (NONMEM). Recrudescence was observed in 34 during days 7 and 42; 5 and 5 cases, respectively had reinfection with *P. falciparum* and reappearance of *P. vivax* in their peripheral blood during follow-up. The 42-day efficacy rate of the combination regimen was 72.58%. The pharmacokinetics of mefloquine in patients with sensitive (n=116) and recrudescence (n=34) responses were similar. There appears to be no association between treatment response [parasite clearance time (PCT), fever clearance time (FCT), occurrence of recrudescence] between patients with sensitive and recrudescence responses. This suggests that intrinsic parasite factor, *i.e.,* development of parasite resistance to antimalarial drug, may play important role in determining treatment response of the patients.

Keywords*:* *Plasmodium falciparum*, multi-drug resistance, mefloquine, artesunate, combination therapy, population pharmacokinetics-pharmacodynamics

P39

In vitro antioxidative synergy of Mangosteen crude extracts

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An ethanolic crude extract obtained from the ripe fruit rind of mangosteen (*Garcinia mangostana* L.) (GmEt) possesses antioxidative effect, of which is potentiated when tested in combination with the aqueous crude extract (GmAq). Their synergistic *in vitro* profile is similar to that of the combination between GmEt and the aqueous extract of green tea (GtAq).

Keywords: mangosteen crude extract, *Garcinia mangostana*, antioxidant, synergistic effect

P40

Content of ganoderic acids A and F in Ling Zhi preparations available in Thailand

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Ling Zhi in China, one of the most famous traditional Chinese mushrooms, has been used extensively to preserve human vitality and to promote longevity in eastern Asian countries for thousands of years. There are several commercial Ling Zhi preparations available in various dosage forms such as Ling Zhi extract, spore, tea bag, instant tea, and sliced fruiting bodies. The purpose of this study was to determine and compare the content of ganoderic acids A and F, the potent biologically active compounds, in various Ling Zhi preparations available in Thailand. Seventeen samples of commercial Ling Zhi preparations in various brands and dosage forms were randomly purchased from different stores in Chiang Mai and Bangkok, Thailand. Each Ling Zhi preparation was given the sample code instead of its trade name. In addition, the investigated preparations included the sliced fruiting bodies (MG2FB) and the water extract of fruiting bodies (MG2FB-WE) of MG2-strain Ling Zhi kindly provided from Muang Ngai special agricultural project. The content of ganoderic acids A and F in all Ling Zhi preparations was determined by high performance liquid chromatography (HPLC). The limits of quantification (LOQ) of ganoderic acids A and F were 2.21 and 2.03 μg/mL, respectively. In 19 investigated Ling Zhi preparations, the sample code NPN had the highest content of total ganoderic acids A and F (8723.10 ± 146.53 μg/g), followed by MG2FB-WE (3980.01 ± 28.34 μg/g) and DXN-r (2625.77 ± 26.04 μg/g), respectively. GNO had the lowest content of total ganoderic acids A and F (233.80 ± 33.33 μg/g). Ganoderic acid A was the major compound in most Ling Zhi preparations, except NPN of which ganoderic acid F was the major compound. Neither ganoderic acids A nor F was detected in GEC, DXN-g and BNR. The total content of ganoderic acids in commercially available Ling Zhi preparations was not statistically correlated with their price. The content of ganoderic acids A and F varied considerably among investigated Ling Zhi preparations. It ranged from below the limit of quantification to a remarkably high content.

Keywords: Ganoderic acid A, Ganoderic acid F, Ling Zhi preparations.

P41

Isoflavone contents in Thai and imported soy-based beverages commercially available in Thailand

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Soybeans are the most common source of isoflavones in human food. Isoflavones represent the most common group of phytoestrogens as their structures resembling that of the potent synthetic estrogen diethylstilbestrol. Isoflavones have received considerable attention because of their potential roles in relieving postmenopausal hot flashes as well as prevention and treatment of postmenopausal osteoporosis. The aim of this study was to investigate and compare the contents of isoflavones in the form of β-glycosides (daidzin and genistin) as well as their respective aglycones (daidzein and genistein) in Thai *versus* the imported soy-based beverages commercially available in Thailand. Fifty one brands (34 Thai brands and 17 imported products) of soy-based beverages given the sample code instead of its trade name were analyzed for their isoflavone contents by using high performance liquid chromatography. The average coefficient of intraday and interday assay validation for daidzin, genistin, daidzein and genistein was less than 4.5%. The total isoflavone contents in both soy-based beverages varied substantially from approximately 7-85 mg per serving, and β-glycosides dominated. Although the mean concentrations of aglycones in Thai soy-based beverages were significantly greater than those of imported products, the mean concentrations of β-glycosides and total isoflavone contents per serving (either mg or μmol) between both products did not differ significantly. The average price per serving of imported products was statistically more expensive despite comparable total isoflavone contents. In conclusion, total isoflavone contents in both products varied substantially. The Thai soy-based beverages contained comparable averaged contents of isoflavones per serving compared to the imported products, but were less costly.

Keywords: Isoflavones, daidzin, daidzein, genistin, genistein, soy-based beverages.

P42

Anti-ulcerogenic activity of the water extract from *Malvastrum coromandelianum* (L.) Garcke

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The anti-ulcerogenic activity of the water extract from *Malvastrum coromandelianum* (L.) Garcke (MCE) was investigated in rats by various experimental models, which included indomethacin-, EtOH/HCl-, and restraint water immersion stress-induced gastric lesions. MCE at the doses of 200-800 mg/kg and the reference drug, ranitidine (H_2-receptor antagonist, 100 mg/kg), were used in this study. The results showed that MCE reduced ulcer formation in all models. The efficacy of MCE (800 mg/kg) was comparable to that of ranitidine. Moreover, the efficacy of MCE was superior to that of ranitidine in EtOH/HCl model. The possible mechanisms of anti-ulcerogenic activity of the extract are particularly through the increase of defensive factors and/or the decrease of aggressive factors.

Keywords: *Malvastrum coromandelianum* (L.) Garcke, anti-ulcerogenic activity.

P43

Analgesic Activity from *Stahlianthus involucratus* Rhizomes Ethanol Extract in Animal Models

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Stahlianthus involucratus is one of plants in the Zingiberaceae family that has been used in Chinese traditional medicine for analgesic. However, the scientific evidences about its pharmacological activities have not been reported yet. This study aimed to investigate its analgesic activity. Its rhizomes ethanol extract was administered orally to animals. Animal studies used in this study were acetic acid-induced writhing response in mice and tail-flick test in rats. The SI extracts significantly reduced number of writhes in dose-dependent manner. On the contrary, this extract, only at higher doses (37.5 and 75 mg/kg) slightly increased reaction time. The inhibition of peripheral endogenous substances production and/or activity may be the possible mechanism of action of SI extract. In conclusion, the SI extract showed analgesic activity that may be act via peripherally acting mechanism.

Keywords: Analgesic activity, *Stahlianthus involucratus.*

P44

Inhibition of proinflammatory cytokines and mediators by the hexane extract of *Glycosmis parva* leaves

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Glycosmis parva (Som Cheun) is a Thai medicinal plants used for the treatment of various inflammatory conditions but the action mechanism is uninvestigated. In this study, we evaluated the effect of the hexane extract of *Glycosmis parva* leaves on proinflammatory cytokines and mediators released from the macrophage cells. Murine macrophage, J774A.1 cells stimulated with lipopolysaccharide (LPS) were exposed to different concentration of the extract ranging from 1.56-50 μg/ml. Nitric oxide production was determined using Griess reagents. Measurement of mRNA expression of proinflammatory cytokines (TNF-α, IL-1β and IL-6), inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) were performed by RT-PCR. It was found that the extract inhibited NO production in LPS-stimulated cells in a concentration-dependent manner with its IC_{50} values 11.76 μg/ml. There was no evidence of cytotoxicity to the cells. *Glycosmis parva* extract profoundly inhibited the expression of TNF-α by 91.10, 93.02, 94.27% when its concentration used were 6.25, 12.5 and 25 μg/ml. The inhibition effect of the extract on IL-1β was found only at high concentration (25 μg/ml). It didn't have any effect on IL-6 mRN expression. Furthermore, the extract demonstrated significant inhibitory effect on mRN expression of iNOS and COX-2. The noticeable effect was also found at the high concentration of the extract. (25 μg/ml). The results indicated that the hexane extract from *Glycosmis parva* leaves reduced proinflammatory cytokines and mediators in the macrophage during inflammatory process.

Keywords: *Glycosmis parva*, inflammation, TNF-α, IL-1β, IL-6, iNOS, COX-2

P45

Effect of curcuminoids extract capsules on oxidative stress in diabetes mellitus type II

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Oxidative stress plays a major role in the complications of diabetes mellitus. Free radical was greatly increased due to prolonged exposure to hyperglycemia and impairment of oxidant/antioxidant equilibrium. Curcuminoids have been claimed to represent a potent antioxidant properties. The purpose of this study was to investigate the effects of curcuminoids extract capsules on oxidative stress and antioxidant enzyme activities in diabetes mellitus type II. Two hundred diabetes mellitus patients were participated in this study. Patients received two capsules of either curcuminoids extract (250 mg) or placebo capsules three times a day for 6 months. The glutathione (GSH) levels and antioxidant enzymes activities in red blood cell were measured at 0, 3 and 6 month. The results showed that superoxide dismutase (SOD) activity and GSH were significantly increased in curcuminoids group when compare with placebo group (p<0.05). This study demonstrated that supplementation with curcuminoids extract capsules have a potential role in boosting superoxide dismutase activity and total glutathione which are antioxidant-related defenses in diabetes mellitus type II patients.

Keywords: oxidative stress, antioxidant enzyme, diabetes mellitus, curcuminoid

P46

Risk factors for metabolic syndrome independently predict arterial stiffness in chronic kidney disease

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Introduction: Arterial stiffness (AS) is a feature of chronic kidney disease (CKD) and may contribute to increased cardiovascular disease (CVD) in CKD[1]. Metabolic syndrome (MS) is common in CKD[2] but the contribution of MS to AS in CKD is not well-established. We hypothesised that as renal function declines, AS increase, and are independently linked to components of MS, including waist circumference, triglyceride, HDL, blood pressure, and fasting plasma glucose[3].
Method: 115 CKD patients (stage 1 to 5, 47±12yrs; M/F=77/38) and 23 non-renal controls (47±8yrs; M/F=13/10) were recruited. Patients on dialysis, with established CVD, vasculitis or diabetes mellitus were excluded. Subjects underwent carotid-femoral pulse wave velocity (PWV) as a measure of AS. Risk factors for MS were identified according to the National Cholesterol Education Program's Adult Treatment Panel III clinical identification of MS[3].
Results: PWV increased linearly as renal function decreased (r^2=0.08, p<0.01). 18% and 21% of the subjects or MS for risk for MS, respectively. Mean BMI was 28±6 kg/m^2. CF-PWV correlated with the number of the MS risk factors (Figures 1). For each of the risk factors for MS, CF-PWV increased with waist circumference (r^2 = 0.09, p < 0.01), systolic blood pressure (r^2= 0.25, p < 0.01), diastolic blood pressure (r^2= 0.10, p < 0.01), and glucose (r^2 = 0.09, p < 0.01). CF-PWV also increased with triglycerides and inversely correlated to HDL cholesterol but these relationships did not reach significance. Adjusted for renal function, age, smoking status, gender and blood pressure, multiple linear regressions showed that waist circumference was independent determinants of PWV.
Conclusions: In the absence of CVD and diabetes, irrespective of renal function, age, smoking status, and gender, CKD patients with MS have increased AS. Whilst blood pressure remains the strongest determinant of AS, the presence of MS or risk factors for it is also an important determinant of AS in the CKD population. As these are not related to renal function, they provide a target for intervention to improve CVD outcomes at all stages of CKD.

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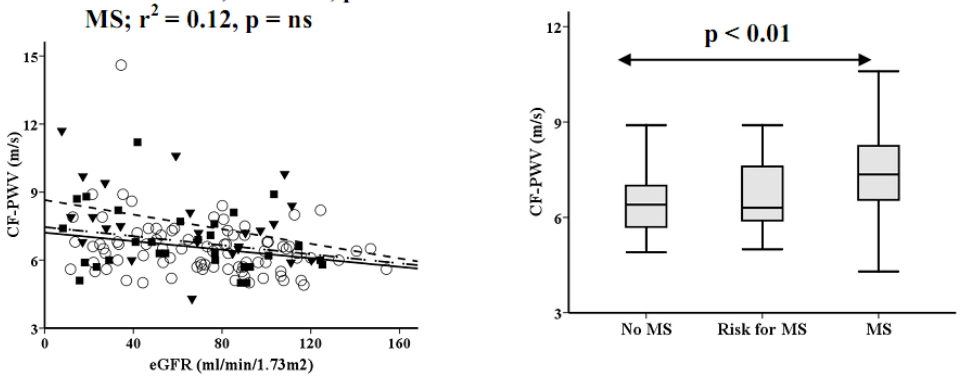
Figure 1 Relationships of the number of MS risk factors to CF-PWV.



Key: No MS (white circle, — fitted line, risk factors = 0-1); Risk for MS (black square, - · - fitted line, risk factors = 2); MS (black triangle, --- fitted line, risk factors ≥ 3). For B, p value is for one-way ANOVA; eGFR: estimated glomerular filtration rate; ns: non-significant.

P47

Effects of phyllanthin and hypophyllanthin on vascular tension of isolated rat aorta

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The purpose of this study was to investigate the modulating effects of phyllanthin and hypophyllanthin on vascular tension, using in the *in vitro* model of isolated rat aorta. Our results indicated that both phyllanthin and hypophyllanthin significantly relaxed the sustained contraction induced by phenylephrine (PE) in a concentration-dependent manner. In addition, endothelial removal had no significant influence on the vasorelaxation responses of the aortic rings toward these two compounds. In comparison to hypophyllanthin, phyllanthin was a more potent vasorelaxant with the apparent EC_{50} values of 55.4 ± 5.5 μM (for the endothelium-denuded rings). Our data also demonstrated that both compounds were able to inhibit the contraction of vascular smooth muscle provoked by either PE (1 μM) or KCl (40 mM). In high K^+ - Ca^{2+} free solution, phyllanthin (100 μM), but not hypophyllanthin, significantly inhibited the contractile responses upon cumulative addition of $CaCl_2$. These findings suggested that phyllanthin and hypophyllanthin could modulate the vascular tension via the endothelium-independent mechanisms. The modulating effect of phyllanthin, in part, was through the inhibition of Ca^{2+} influx to vascular smooth muscle cells.

Keywords: vasorelaxation, phyllanthin, hypophyllanthin

P48

Comparison the efficacy between intranasal corticosteroids mometasone furoate with fluticasone furoate in persistent allergic rhinitis

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Allergic rhinitis (AR) is an extremely common health problem. Patients with AR suffer from both nasal and ocular symptoms. The new intranasal corticosteroids (INCs) mometasone and fluticasone with furoate ester side chain are highly potent with minimal systemic absorption. This study purposed to compare the efficacy, tolerability and safety of mometasone furoate (MF) and fluticasone furoate (FF) in Thai patients with persistent allergic rhinitis (PER). The study was a randomized, open-label and parallel group study. Ninety seven patients with PER and nasal symptoms with or without eye symptoms were enrolled into the study. The patients were randomized into 2 groups receiving 2 sprays/nostril once daily either MF or FF for 4 weeks. Total nasal symptom scores (TNSSs), total ocular symptom scores (TOSSs) and nasal airway resistances (NAR) were assessed at baseline and after 4 weeks of treatment. After 4 weeks treatment, MF and FF produced statistically significant improvement in TNSSs, TOSSs and individual symptoms ($P < 0.0001$). Furthermore, both MF and FF produced a similar significant improvement in total NAR from baseline at 75 Pascal (Pa) ($P = 0.009$ and $P < 0.0001$, respectively) and at 150 Pa ($P = 0.002$ and $P < 0.0001$, respectively). However, the difference between treatments was not statically significant. MF was as effective as FF in relieving nasal symptoms and ocular symptoms and in improving nasal airflow.

Keywords: persistent allergic rhinitis, mometasone furoate, fluticasone furoate, symptom scores, nasal airway resistance.

P49

Effect of the water extract from Mareng-roipad formulation on human leukemic cells

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Mareng-roipad formulation containing more than 40 kinds of dried and powdered plants is a traditional medicine which has been used to treat several cancers for more than a century. Effects of the water extract of this formulation on human acute leukemic T cells (Jurkat cells) were investigated in this study. The water extract had cytotoxic effect on Jurkat cells in a concentration- and time-dependent manner after 48 h exposure by propidium iodide (PI) staining assay with fluorescence flow cytometer. The extract induced Jurkat cell death mainly by apoptotic induction, in a concentration- and time-dependent manner, determining by annexin V-FITC/PI staining assay with fluorescence flow cytometer. Its apoptotic induction activity was partly dependent on caspase activation. A pan-caspase inhibitor z-VAD-FMK could partially inhibit its apoptotic induction activity. The extrinsic pathway through Fas-Fas ligand interaction was involved in the apoptotic induction activity of this extract on Jurkat cells because an inhibitory anti-Fas ligand antibody could inhibit this activity of the extract. The results from this study demonstrate that the water extract of Mareng-roipad formulation can induce human leukemic cell apoptosis involving the death receptor pathway. This traditional medicine formulation may have potential to treat leukemia.

Keywords: Mareng-roipad formulation, apoptosis, Jurkat cells

P50

Inhibitory effect of a water extract from *Stephania venosa* tubers on N-methyl D-aspartate receptor

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Water extract from *Stephania venosa* (*S. venosa*) tubers has a sedative effect in an animal experiment. It has been known that sedative activities may involve antagonism of the N-methyl D-aspartate (NMDA), serotonin (5-HT), or glycine receptors. NMDA receptor is particularly interesting because it is involved in several neuronal dysfunctions. Therefore, this study aimed to evaluate the effects of water extract from *S. venosa* tubers on the NMDA receptor. *Xenopus* oocytes were injected with cRNA mixture of NR1a and NR2B and responses to NMDA were recorded using the two-electrode voltage clamp technique. The extract at 0.1–1000 μg/ml dose-dependently inhibited the NMDA receptor function with an IC_{50} of 200 μg/ml. The inhibitory effect of the extract was reversible when compared to that of the NMDA-channel blocker MK-801. Combinations of the extract and the competitive NMDA receptor antagonist AP-5 showed a more pronounced inhibition than either one alone. Selectivity of the inhibitory effect of the extract was also evaluated. The extract decreased 5-HT receptor function with an upward bell-shaped concentration dependence. The extract at 1–100 μg/ml dose-dependently decreased 5-HT receptor response with an IC_{50} of 3 μg/ml but at 0.1–1 μg/ml the inhibition was gradually increased when the concentration was decreased. The inhibitory effect of the extract on glycine receptors was less potent than the effect on NMDA receptor. These results suggest that the extract reversible inhibited the NMDA receptor by interacting with a binding site rather the site for AP-5. Moreover, the inhibition of the extract was more specific to NMDA receptor than glycine receptor. Possible active compound (s) underlying the inhibitory effect of the extract are discussed.

Keywords: *Stephania venosa* tubers, water extract, *Xenopus* oocytes, NMDA receptor

P51

A simple HPLC method for determination of sulfasalazine in human plasma

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A reversed-phased high-performance liquid chromatographic (HPLC) method with a single step plasma protein precipitation has been developed for determination of sulfasalazine in human plasma. The chromatographic separation was achieved using C18 column (YMC HPLC Column, 250 x 4.6 mm, 5 μm) with an isocratic mobile phase consisting of 0.5 M phosphate buffer (pH 6.8) contain 0.006 M tetrabutyl amonium hydrogen sulfate: acetonitrile (65:35 v/v) at flow rate of 1.0 ml/min. Sulfasalazine and internal standard (phenacetin) were detected by UV detection at 273 nm. Under these chromatography conditions, retention times of phenacetin and sulfasalazine were 7.4 and 9.6 minutes, respectively. This method was validated with respect to specificity, linearity, lower limit of quantification, precision, accuracy, auto-sampler stability and long-term sampler stability. No interference was observed in the chromatograms. Good linearity was achieved with a sulfasalazine calibration curve ranging from 0.4-10 □g/ml. The between-batch and within-batch accuracy and precision were within acceptable range (less than ±15%). After precipitation with acetronitrile, sulfasalazine was stable autosampler at 10 ^{o}C for 6 hours. The stability of sulfasalazine in plasma after storage at -80^{o}C was about 25 days. In conclusion, the developed HPLC method was simple, reliability, and was applicable for pharmacokinetic study of sulfasalazine in human.

Keywords: Reversed-phased high-performance liquid chromatographic (HPLC) method, Sulfasalazine

P52

Effects of the standardized extract of *Centella asiatica* ECa233 on the respiration of mitochondria isolated from rat brain

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The effects of standardized extract of *Centella asiatica* ECa233 on the respiration of mitochondria isolated from rat brain were studied. The rat brain mitochondria were incubated with ECa233 5 concentrations (0.01, 0.1, 1, 10, and 100 mg/ml). High concentration of ECa233 (100 mg/ml) decreased the rate of oxygen consumption by 26 and 30% while using glutamate plus malate and succinate as substrate, respectively. However there was no significant difference in the rate of oxygen consumption of the brain mitochondria incubated with all ECa233 concentrations compared with the control. The finding suggested no toxic effect of ECa233 on mitochondria. The data supported further investigation on the protective effects of ECa233 on brain mitochondria.

Keywords: standardized extract of *Centella asiatica* ECa233, brain mitochondria, oxygen consumption, respiratory control index

P53

Effect of anthraquinone glycosides extracted from *Senna alata* leaves on the contractions of rat isolated gastric fundus

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Anthraquinone glycosides extracted from the leaves of *Senna alata* Linn. (Chum-Het-Thet) were investigated on the motility of rat isolated gastric fundus. The glycosides produced dose-dependently and significantly increase in the force of contraction of the fundus. The contractions were partially inhibited (50-60%) by the muscarinic receptor blocker, atropine (10^{-6} M), and were almost or completely abolished by other receptor blockers, histamine H_1-receptor antagonist, chlorpheniramine (2.56×10^{-4}M), serotonin-receptor antagonist, cyproheptadine (10^{-5} M) and also by a calcium channel blocker, verapamil 10^{-4} M. Thus, it is suggested that the contractile effect of the glycosides involved the activation of muscarinic, histamine and serotonin receptors which caused the contraction by the increase in the intracellular Ca^{2+} which partly due to the influx of extracellular Ca^{2+}. It is likely that the extract might be a useful gastrokinetic agent.

Key words*:* anthraquinone glycoside, *Senna alata*, rat isolated gastic fundus, gastrokinetic, contraction

P54

Protective effects of silk Lutein extract and vitamin E on UV-B induced oxidative stress in retinal pigment epithelial cell damage

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UV-B induced oxidative stress of retinal pigment epithelial cells plays an important role in the development of age-related macular degeneration (AMD). This study was aimed to investigate the protective effect of silk lutein extract (SLE) and vitamin E on UV-B induced retinal epithelial cells damage. Oxidative stress in ARPE-19 cells was evaluated by measuring the level of intracellular reactive oxygen species (ROS) and lipid peroxidation. The results showed that SLE and vitamin E cloud significantly reduce the effect of UV-B on the formation of intracellular ROS and lipid peroxidation, and these two substances however slightly increased cell viability. The combination of SLE and vitamin E exhibits more antioxidative effect than that of individual compound. These data suggest that lutein from silk cocoon and vitamin E exhibit a partial protective effect against UV-B induced oxidative stress.

Keywords: Oxidative stress; Silk lutein extracted; vitamin E; UV-B

P55

Effect of the ethanolic extract of *Passiflora foetida* on conditioned place preference

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In the traditional medicine of many countries, *Passiflora incarnata* was proved to be useful in drug addiction therapy. In this study, we investigated the effect of *Passiflora foetida,* a plant in the same genus, on drug addiction. We evaluated the effect of the ethanolic extract of *P. foetida* (PF) on locomotor activity and conditioned place preference (CPP). The results showed that PF at doses of 25, 50, 100 and 200 mg/kg produced no significant effects on locomotor activity as compared to control animals. The reinforcing effect of PF was tested using CPP paradigm. All doses of PF did not show any significant effects of CPP. These results suggest that PF may be useful in the prevention and treatment of drug addiction.

Keywords: Addiction, *Passiflora foetida*, Morphine, Conditioned Place Preference

P56

Opisthorchis viverrini: Molecular analysis of a gene encoding vitelline B eggshell precursor protein

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Eggshell proteins are essential and highly abundant antigens of trematodes as each adult parasite produces a large number of eggs every day. In this study, an adult stage cDNA library of *Opisthorchis viverrini* was constructed and screened for abundant transcripts using a differential filter hybridization approach. The cDNA prepared from adult stage RNA of the parasite was used as ^{32}P-labeled probe and several hybridizing clones were isolated and had their cDNA inserts sequenced. The deduced amino acid sequence of the obtained cDNA from clone C2A2 showed significant similarity to vitelline B eggshell precursor proteins of other trematodes. This cDNA had a size of 893 bp and encoded a protein of 247 amino acid residues with a calculated molecular mass of 27.6 kDa (OVVPB). BLASTP results showed significant identity values to eggshell precursor proteins from *Clonorchis sinensis* (63%), *Fasciola hepatica* (37%) and *Schistosoma japonicum* (46%). OVVPB contains 17 tyrosine-glycine motifs (-YG-) which are known to be the site for tyrosine oxidation to DOPA in quinone-tanning during eggshell formation. Detection of the gene's transcripts by Northern and RNA *in situ* hybridization showed a 900 nucleotides transcript size and a location in vitelline cells, respectively. In ongoing analyses the OVVPB protein will be characterized for its application in diagnosis and/or vaccine approaches.

Keywords: Eggshell, vitelline, *Opisthorchis viverrini*

P57

Preliminary investigation on the application of ultrasonography as a tool for monitoring the development and progress of cholangiocarcinoma in *Opisthorchis viverrini* /dimethylnitrosamine-induced hamsters

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Cholangiocarcinoma (CCA) is the bile duct cancer which is the most common cancer in Thailand particularly in northeastern region. Effective diagnosis of CCA either in human or animals is not currently available. Diagnostic tool for monitoring the development and progress of CCA in animal models is essential for research and development of new promising chemotherapeutics for CCA. In this study, we preliminarily investigate the application of ultrasonography to monitor the development and progress of CCA in 10 hamsters induced by *Opisthorchis viverrini* (OV)/dimethylnitrosamine (DMN) administration. Control group (10 hamsters) received a mixture of water and Tween-80 during the same period. Ultrasonography was performed once every four weeks starting from week 12 until week 24. Results of histopathological examination (at autopsy) and ultrasonography images of liver and gall bladder were in agreement. Although ultrasonography does directly detect the occurrence of CCA, it reflects the thickening of bile ducts and abnormality of liver tissues. Ultrasonography may be used as a reliable tool to monitor the development and progress of CCA in animal models used in research and development of new promising chemotherapeutics for CCA.

Keywords: Ultrasonography, Cholangiocarcinoma, Diagnosis, Hamster, *Opisthorchis viverrini*, dimethylnitrosamine

P58

Relationships between topiramate concentrations in serum and saliva of Thai epileptic patients

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The objective of this study was to determine the correlation between serum and saliva topiramate concentrations in Thai epileptic patients. The study was conducted in the Department of Medicine Neurology Unit, Epilepsy Clinic, Pramongkutklao Hospital. Patients aged between 15-60 years old and receiving topiramate were included into this study. The correlation equation between serum and saliva topiramate concentrations was constructed from 10 patients, receiving topiramate monotherapy. The blood and saliva samples were collected at the time before the morning dose and at 1, 2, 4, 6 and 8 hours after topiramate ingestion. Topiramate concentrations in blood and saliva samples were measured by turbidimetric immunoassay technique. The results showed that serum and saliva topiramate concentrations were closely correlated with a correlation coefficient of 0.919 ($n=60$, $p<0.001$). The describing equation of this relationship was $Y= 0.962X + 1.197$. The correlations between serum and saliva concentrations were closely correlated with the correlation coefficient of 0.992, 0.929, 0.873, 0.915, 0.933 and 0.993 (all data were from $n=10$, $p<0.001$) at the time point of 0, 1, 2, 4, 6 and 8 hours after topiramate ingestion, respectively. The results of this study support the use of saliva as an alternative to serum for monitoring topiramate therapy. And the most appropriate time of saliva collection is the time before or at least 8 hours after topiramate ingestion.

Keywords: topiramate, serum, saliva.

P59

Effect of the ethanolic extract of *Mitragyna speciosa* leaves on conditioned place preference

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Mitragyna speciosa Korth. has long been used in Thai traditional medicine for the treatments of pain, fever, cough, diarrhea, opioid-addiction and for enhancing the labor work efficiency and tolerance. However, there is no clear evidence of the rewarding effect of *M. speciosa* in animal models. Thus, this study was aimed to investigate the rewarding effect of the ethanolic extract of *M. speciosa* leaves (MS) using conditioned place preference (CPP) model in rats. Various doses of MS (50-400 mg/kg, p.o.) show neither stimulating nor sedative effects using locomotor activity test in mice. In CPP test, the same doses of MS also did not showed reinforcing effect compared to vehicle and morphine positive-control groups. The results from this study demonstrated that MS were not found to have stimulating, sedative and rewarding effects.

Keywords: Addiction, *Mitragyna speciosa*, Morphine, Conditioned Place Preference, Kratom

P60

Hypoglycemic effect of standardized *Centella asiatica* extract ECa 233 in streptozotocin-induced diabetic rats

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Centella asiatica (*C.asiatica*), locally known as Bua-bok, is a local Thai herb used as CNS depressant, antibacterial, antiinflammatory, antiproliferant, antiulcer, and wound healing. Recently, the ethanolic and methanolic extracts of *C.asiatica* were found to exert hypoglycemic effect in Alloxan-induced diabetic rats. Thus, this study was designed to examine the hypoglycemic effects of ECa 233, which is a standardized *C.asiatica* extract, on Streptozotocin-induced diabetic rats by measuring body weight , food intake, and levels of plasma glucose at day 0, 7, 10, 14, 21 and 28 days after the intraperitoneal injection of 50 mg/kg B.W. STZ. In contrast to gradually increasing in weight observed in normal rats, diabetic rats receiving orally given distilled water or ECa 233 showed no increment of body weight whereas the food intake had increased from that of day 7 in all groups. Plasma glucose in diabetic group treated with distilled water and ECa 233 at the dose of 10 mg/kg B.W. gradually increased and significantly different from those of their respective day 7 at day 21 and 28. However, anti-hyperglycemic effect of ECa 233 was demonstrated at the dose of 30 and 60 mg/kg. B.W. in which the plasma glucose at the late phase of the experiment did not show significant elevation from their value at day 7. Our findings clearly reveal hypoglycemic effect of ECa 233 in STZ-induced diabetic rats and suggest the possibility to develop the test compound to a food supplement or adjunctive medication for diabetic patients.

Keywords : hypoglycemic effects, the standardized extract of *Centella asiatica* ECa 233, diabetic rats

P61

Effect of water extracts of *Vernonia cinerea* Less. on nicotine withdrawal mice

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Nicotine is considered to be the primary component of tobacco smoke. It exhibits dopamine release in core structure of reward system, ventral tegmental area (VTA) and nucleus accumbens (NAc), and causes tobacco addiction. *Vernonia cinerea* Less. has been reported to have many medicinal properties. Different parts of the plant have different therapeutic values such as analgesic, antipyretic, anti-inflammation, and smoking cessation. The aims of this study were to evaluate effect of *V. cinerea* on nicotine withdrawal mice and to determine the mechanism of action of *V. cinerea* extracts (VE) in alteration of nicotinic and muscarinic receptors protein expression on western blot analysis. We found that VE at high concentration (500 mg/kg) significantly decreased total abstinence signs (TAS) and exhibited no changes in locomotion and anxiety-like behaviors. Moreover, VE had no differences on nicotinic and muscarinic receptor protein expression. These results suggested that VE might be involved with reduction of nicotine withdrawal symptoms in other mechanisms which are not be related to nicotinic and muscarinic receptors.

Keywords: Nicotine, Withdrawal, *Vernonia cinerea* Less., Nicotinic receptor, Muscarinic receptor

P62

Acute oral toxicity of *Aegle marmelos* (L.) Correa ex Roxb. ethanolic extract in rats

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Aegle marmelos (L.) Correa ex Roxb is a tree from the family Rutaceae. Many parts of the plant were designed for different biological activity study such as anti-diarrhea, anti-flatulent and anti-asthma. However the toxicity data of this plant is still unavailable. Acute oral toxicity of *Aegle marmelos* (L.) Correa ex Roxb ethanolic extract was investigated by using OECD guideline No.423, 2001. Both sexes of Wistar rats were oral administered at dose 2,000 and 15,000 mg/kg bw of suspension extracted solution and observed for 14 days. The result showed that no mortality, abnormal toxicity signs and gross pathology in rats were found. Therefore, the oral LD_{50} of the ethanolic extract in rats is higher than 15,000 mg/kg bw.

P63

Phytochemicals and cytotoxicity of *Elephantopus Scaber* Linn. leaves extracts

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Elephantopus scaber Linn. (Asteraceae) is commonly called "Doe-mai-rue-lom" and has been used for medicinal plant. The present study was performed to phytochemical screening and evaluate cytotoxic activity of this herb using MTT assay. The *E scaber* leaves was extracted with 95% ethanol to give yield 8.9 % w/w. It was composed of high antioxidant activity compound, such as chlorogenic acid and luteolin. The ATCC CRL-1474 (dermal human fibroblast:NHFF) and ATCC CRL-6475 (Melanoma cell:B16-F10) were chosen for cosmetic application. The IC_{50} value were 0.33 and 0.20 mg/ml. for 24 hr treatment. It would be interesting to do further study for developing in cosmetic products.

Keywords : *Elephantopus scaber* Linn., cytotoxicity , phytochemical

P64

Anti-stress effect of *Ocimum gratissimum* Linn. ethanolic extract in cold restraint-induced stress rats

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Ocimum gratissimum Linn**.** (*O. gratissimum*) is a native plant grown in Thailand, so called "Ka-prao-chang" or "Yee-ra". The pharmacological properties of the plant have been known as anti-bacterial, laxative, analgesic and muscle relaxant. The anti-stress study of *O. gratissimum* ethanolic extract (OGE) was investigated using cold restraint model in rats. The blood cortisol level was measured for stress status consideration. The result showed that this extract could reduce blood cortisol in rats which under stress. This indicated that OGE has a tendency to use as anti-stress agent.

Keywords: *Ocimum gratissimum* Linn**.**, Anti-stress, Cold restraint stress

P65

The comparison of bioflavonoid compounds and anti-oxidant activity from citrus peels extract

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The ethyl acetate extracts was obtained from fruits peels of *Citrus reticulata* Blanco cv. Sainampueng, *Citrus aurantifolia* Swingle and *Citrus hystrix* DC. The active ingredient was analyzed using thin layer chromatography (TLC) techniques comparing to authentic standard. It contained spots equivalent to some bioflavonoid compounds including rutin, hesperidin, hesperitin, and chlorogenic acid. The crude extract of *C. hystrix* has hesperidin and rutin more than *C. aurantifolia* and *C. reticulate*. While *C. reticulate* has unknown phenolic compound (blue spot) which strong antioxidant, but *C. aurantifolia* and *C. hystrix* are less. The antioxidant activity was evaluated using DPPH assay. The EC_{50} of crude extract of *C. hystrix*, *C. aurantifolia* and *C.reticulata* are 41.74 μg/ml, 157.54 μg/ml and 26.14 μg/ml, respectively. The crude extracts had lower activity than vitamin C and rutin, which have EC_{50} 1.90 μg/ml and 0.03 μg/ml, respectively. From these results showed that ethyl acetate extract from *C.reticulata* peels has high content of some phenolic compound equivalent to bioflavonoid which was high potent antioxidant activity more than *C. hystrix* and *C. aurantifolia*.

Keywords: *Citrus reticulata* Blanco cv. Sainampueng, *Citrus aurantifolia* Swingle, *Citrus hystrix* DC, bioflavonoid compounds

P66

Effects of curcuminoids on lipid peroxidation and antioxidant enzyme in rat microsome and HepG2 cells

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Alcohol consumption enhances reactive oxygen specie (ROS), lipid peroxidation or decreases the level of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) in alcoholic liver disease (ALD). ALD cause oxidative stress. Curcuminoids, a complex compounds derived from turmeric extract, have shown antioxidant activities. The present study was evaluated the effects of curcuminoids against ethanol-induced lipid peroxidation in rat microsomal extraction and cells culture. We found that curcuminoids in the dose dependent manner decrease lipid peroxidation as represented with malondialdehyde (MDA) levels in ethanol induced toxicity HepG2 cells supplemented with various concentrations curcuminoids. In addition, curcuminoids at 500 and 750 mg/kg/day decreased the MDA levels significantly in liver microsomes from the ethanol induced toxicity rats. However, the superoxide dismutase (SOD) enzyme activities did not change in rat microsomal extractions and curcuminoids did not enhance the enzymes activity. Therefore, curcuminoids have a potential property to protect lipid peroxide production in ethanol-stimulated HepG2 cells and in microsomal extraction from ethanol induced toxicity rats.

Keywords: alcoholic liver disease, ethanol, lipid peroxidation, superoxide dismutase, curcuminoids

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ฤทธิ์ของสารสกัดจากหญ้าดอกขาว (*Vernonia cinerea* Less.) ต่อการสร้างไนตริกออกไซด์ ในภาวะตับอักเสบ

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โรคตับเป็นหนึ่งในโรคที่เป็นสาเหตุการตายของประชากรไทยและยังไม่สามารถรักษาให้หายขาด ได้เกิดได้จากหลายสาเหตุ เมื่อเซลล์ตับเกิดการอักเสบจะกระตุ้นให้เกิดการสร้างอนุมูลอิสระรวมถึง ไนตริกออกไซด์ (nitric oxide, NO) ในปริมาณที่มากกว่าปกติส่งผลให้เซลล์เกิดการอักเสบอย่างต่อเนื่อง ในปัจจุบันมีการนำสมุนไพรไทยมาใช้รักษาโรคต่าง ๆมากมาย หญ้าดอกขาว (*Vernonia cinerea* Less.) เป็นพืชสมุนไพรที่มีการศึกษาว่ามีฤทธิ์ยับยั้งการอักเสบได้ดี การศึกษาครั้งนี้จึงมุ่งเน้นศึกษาฤทธิ์ของสารสกัดหญ้าดอกขาวต่อการสร้าง NO และปริมาณเอนไซม์ inducible nitric oxide synthase (iNOS) ในภาวะตับอักเสบโดยให้สารก่อการอักเสบ lipopolysaccharide (LPS)1.0 μg/m, tumor necrosis factor-alpha (TNF-α) 400 ng/ml, interleukin-1 beta (IL-1β) 400 ng/ml ร่วมกับสารสกัดหญ้าดอกขาวในเซลล์ตับ HepG2 ที่ความเข้มข้น 62.5, 125, 250 และ 500 μg/ml เป็นเวลา 24 ชั่วโมง วัดการสร้าง NO ด้วยสารเรืองแสง diaminofluorescein -2 diacetate และตรวจสอบการแสดงออกของเอนไซม์ iNOS ด้วยวิธี immuno blot พบว่า HepG2 ที่ได้รับสารก่อการอักเสบมีการเพิ่มการสร้าง NO และปริมาณเอนไซม์ iNOS เมื่อเปรียบเทียบกับกลุ่มควบคุม ในเซลล์ตับที่เกิดภาวะอักเสบพบว่า สารสกัดหญ้าดอกขาวมีแนวโน้มที่จะผลลดการสร้าง NO และปริมาณเอนไซม์ iNOS เมื่อเปรียบเทียบกับกลุ่มที่ไม่ได้รับสารสกัด อย่างไรก็ตามผลการทดลองไม่แสดงนัยสำคัญทางสถิติ จากผลการศึกษาแสดงในเบื้องต้น สารสกัดหญ้าดอกขาวมีแนวโน้มที่จะลดปริมาณและการสร้าง NO ของเซลล์ตับ HepG2 ที่กระตุ้นให้เกิดการอักเสบได้

คำสำคัญ: Nitric oxide, Anti-inflammation, *Vernonia cinerea* Less., Hepatitis

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Derris scandens Benth extract induces necrosis rather than apoptosis of SW480 colon cancer cells

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The extract from *Derris scandens Benth* was previously shown to have anti-proliferative effect against SW480 colon cancer cells. Therefore, the present study was aim to investigate the mechanism of action of the anti-proliferative effect of *D. scandens* extract. Several apoptotic signaling pathways were determined following *D. scandens* treatment. Caspase-3 activity and the expression of Bax pro-apoptotic and Bcl-2 anti-apoptotic proteins were determined. The result showed that *D. scandens* (5-10 μg/ml) slightly increased caspase-3 activity, as well as up-regulated Bax and down-regulated Bcl-2 proteins of SW480 cells. However, these changes were not statistically significant. *D. scandens* extract significantly induced cell necrosis determined by the release of LDH. These results suggest that *D. scandens* primarily mediate SW480 cell death through necrotic rather than apoptotic process.

Keywords: *Derris scandens Benth*, apoptosis, colon cancer, SW480 cells

P69

Acridone alkaloids from the root of *Citrus reticulata* Blanco

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Chemical investigation of the dichloromethane extract from the root of *Citrus reticulata* Blanco (Rutaceae) resulted in the isolation of four known acridone alkaloids, citracridone-I (1), 5-hydroxynoracronycine (2), citrusinine-I (3) and citbrasine (4). Their structures were elucidated by spectroscopic analyses as well as comparison their spectral data to those reported in the literatures. Their antimicrobial activity was evaluated.

Keywords: *Citrus reticulata* Blanco, acridone alkaloids, antimicrobial

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2.	ดร.สถาพร	พฤฒิพรรลาย	รองประธานอนุกรรมการ
3.	ผศ.ดร.พยงค์	วณิเกียรติ	อนุกรรมการ
4.	รศ.ภญ.ดร.ศรีจันทร์	พรจิราศิลป์	อนุกรรมการ
5.	รศ.ภญ.ดร.วิจิตรา	ทัศนียกุล	อนุกรรมการ
6.	รศ.ภญ.ดร.สุพีชา	วิทยเลิศปัญญา	อนุกรรมการ
7.	รศ.ภญ.มาลินี	วงศ์นาวา	อนุกรรมการ
8.	รศ.นพ.วีรวัฒน์	มหัทธนตระกูล	อนุกรรมการ
9.	ผศ.ภก.ดร.กิจจา	สว่างเจริญ	อนุกรรมการ
10.	ผศ.สมสมร	ชิตตระการ	อนุกรรมการ
11.	ดร.วันดี	อุดมอักษร	อนุกรรมการ
12.	อาจารย์สมชาย	ศรีวิริยะจันทร์	อนุกรรมการ
13.	นางสาวอารีรัตน์	แซ่เจน	อนุกรรมการ
14.	นายประดิษฐ์	สุนทรากร	อนุกรรมการ
15.	นายสมชาย	พิสสุพรรณ์	อนุกรรมการ

อนุกรรมการฝ่ายเอกสารการประชุม

1.	ดร.สถาพร	พฤฒิพรรลาย	ประธานอนุกรรมการ
2.	ผศ.สุภาภรณ์	การเสนารักษ์	รองประธานอนุกรรมการ
3.	รศ.ดร.ลัดดาวัลย์	ผิวทองงาม	อนุกรรมการ
4.	น.ส.อารีรัตน์	แซ่เจน	อนุกรรมการ

อนุกรรมการฝ่ายลงทะเบียนและที่พัก

1.	ผศ. นิสิตา	บำรุงวงศ์	ประธานอนุกรรมการ
2.	รศ.ภญ.มาลินี	วงศ์นาวา	รองประธานอนุกรรมการ
3.	นางสาวอารีรัตน์	แซ่เจน	อนุกรรมการ
4.	นางนิรชา	ยันเยี่ยม	อนุกรรมการ
5.	นายวิลาด	รัญดร	อนุกรรมการ
6.	นายประดิษฐ์	สุนทรากร	อนุกรรมการ
7.	นายสมชาย	พิสสุพรรณ์	อนุกรรมการ

อนุกรรมการฝ่ายเหรัญญิก

1.	ผศ.สุภาภรณ์	การเสนารักษ์	ประธานอนุกรรมการ
2.	ผศ.สมสมร	ชิตตระการ	รองประธานกรรมการ
3.	ผศ.ภญ.ดร.ภัสราภา	โตวิวัฒน์	อนุกรรมการ
4.	นางพาชื่น	สาวิชชโก	อนุกรรมการ

อนุกรรมการฝ่ายหารายได้

1.	รศ.นพ.วีรวัฒน์	มหัทธนตระกูล	ประธานอนุกรรมการ
2.	รศ.ภก.ดร.ชัยชาญ	แสงดี	อนุกรรมการ
3.	ดร.วันดี	อุดมอักษร	อนุกรรมการ
4.	ผศ.สมสมร	ชิตตระการ	อนุกรรมการ
5.	อาจารย์สมชาย	ศรีวิริยะจันทร์	อนุกรรมการ
6.	นางสาวอารีรัตน์	แซ่เจน	อนุกรรมการ

อนุกรรมการฝ่ายพิธีการ สถานที่ และปฏิคม

1.	ผศ.สมสมร	ชิตตระการ	ประธานอนุกรรมการ
2.	ดร.วันดี	อุดมอักษร	รองประธานอนุกรรมการ
3.	ดร.สถาพร	พฤฒิพรรลาย	อนุกรรมการ
4.	นางพาชื่น	สาวิชชโก	อนุกรรมการ
5.	นายวิลาด	รัญดร	อนุกรรมการ
6.	นางนิรชา	ยันเยี่ยม	อนุกรรมการ
7.	นางสาวอารีรัตน์	แซ่เจน	อนุกรรมการ
8.	นางสาวจิระภา	พันธรัตน์	อนุกรรมการ
9.	นายประดิษฐ์	สุนทรากร	อนุกรรมการ
10.	นายสมชาย	พิสสุพรรณ์	อนุกรรมการ

อนุกรรมการฝ่ายประชาสัมพันธ์และประเมินผล

1.	อาจารย์สมชาย	ศรีวิริยะจันทร์	ประธานอนุกรรมการ
2.	ผศ.นิสิตา	บำรุงวงศ์	รองประธานอนุกรรมการ
3.	รศ.ดร.พิศมัย	เหล่าภัทรเกษม	อนุกรรมการ
4.	ผศ.ดร.ปัทมา	ลิ้วานิช	อนุกรรมการ
5.	ผศ.สมสมร	ชิตตระการ	อนุกรรมการ
6.	นางนิรชา	ยันเยี่ยม	อนุกรรมการ
7.	นางสาวอารีรัตน์	แซ่เจน	อนุกรรมการ
8.	นางสาวจิระภา	พันธรัตน์	อนุกรรมการ
9.	นายประดิษฐ์	สุนทรากร	อนุกรรมการ
10.	นายสมชาย	พิสสุพรรณ์	อนุกรรมการ

อนุกรรมการฝ่ายประกวดผลงานวิจัย

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3.	ผศ.ภก.ดร.กิจจา	สว่างเจริญ	อนุกรรมการ
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5.	นางสาวอารีรัตน์	แซ่เจน	อนุกรรมการ

รายนามคณะกรรมการที่ปรึกษาและบริหารสมาคมเภสัชวิทยาแห่งประเทศไทย
วาระประจำปี พ.ศ. 2553-2554

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กิตติกรรมประกาศ

สมาคมเภสัชวิทยาแห่งประเทศไทย

ขอขอบพระคุณ

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วันที่ 17-19 มีนาคม 2554

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ธนาคารกสิกรไทย จำกัด (มหาชน)
บริษัท กิบไทย จำกัด
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บริษัท โคคา-โคลา จำกัด
บริษัท ซาโนฟี่-อเวนตีส (ประเทศไทย)
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บริษัท ทาเคดา (ประเทศไทย) จำกัด
บริษัท ไทยนครพัฒนา จำกัด
บริษัท ธเนศร์พัฒนา จำกัด
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