出國報告（出國類別：其他）

參加「第九屆中藥全球化聯盟年會

CGCM (The 9th Annual Meeting Of the Consortium for Globalization of Chinese Medicine)」

出國報告

服務機關：行政院衛生署中醫藥委員會

姓名職稱：黃林煌主任委員

派赴國家：香港

出國期間：99年8月22 日至8月24日

報告日期：99年9月28日

公務出國報告提要

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出國報告名稱：參加「第九屆中藥全球化聯盟年會」

頁數 11 含附件：■是□否

出國計畫主辦機關/聯絡人/電話

中醫藥委員會 主任秘書室 委任技士 洪翠英 02-25872828 轉 222

出國人員姓名/服務機關/單位/職稱/電話

黃林煌 中醫藥委員會 主任委員室 主任委員 02-25994326

出國類別：□1 考察□2 進修□3 研究□4 實習■5 其他

出國期間：99 年 8 月 22 日至 8 月 24 日

出國地區：香港

報告日期：99年9月28日

分類號／目：J1／中醫 J0／綜合

關鍵詞：中醫藥、學術研討會

內容摘要：(二百至三百字)

CGCM 全稱是The Consortium for Globalization of Chinese Medicine，台灣是創會會員之一，CGCM 其首要目的就是建立起中醫藥國際化共識，今年已經是第九屆舉辦，主要是由香港浸會大學(HONG KONG BAPTIST UNIVERSITY)所承辦，香港浸會大學設有中醫藥學院，對於中醫藥相當重視，對於中醫藥之教育與研究已經有許多經驗，這次會議辦的很成功，有來自全球10多個國家參與，共有500多篇研究論文發表，CGCM帶領中醫藥走向國際化看起來越來越成功。由於CGCM其首要目的就是建立起中醫藥國際化共識，雖然談的是"中醫藥"但是爲了國際化、全球化，所以會議全程都是以英文爲主要語言，大會邀請許多國際學者及各國中醫藥及傳統醫學負責人參與，學術會議是大會主軸，雖然參加會議人士以華人之學者及學生爲主，但是發表專題演講以來自國際學者爲主，共有來自德國、英國、美國、加拿大、澳洲、法國、香港、澳門、奧地利、韓國、新加坡、馬來西亞、日本、葡萄牙，及台灣等十五個國家學者發表論文及演講，共有16個主題，在香港國際會議廳，從8月23日到8月25日三天舉行，大會特別邀請來自美國NIH 主觀營養食品及中醫藥主任Dr. Paul M Coates，擔任Regulation affair主持人，來自德國TCM中心主任的Dr.Wolfgang Schwartz負責針灸部分的主持人，此外來自英國、香港、台灣及中國大陸許多學者專家都參加本次盛會。

本文電子檔已上傳至公務出國報告資訊網（http://report.gsn.gov.tw）

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摘　　要

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壹、目的

CGCM 全稱是The Consortium for Globalization of Chinese Medicine，台灣是創會會員之一，CGCM 其首要目的就是建立起中醫藥國際化共識，他是由中央研究院鄭永齊院士所號召創立的，今年已經是第九屆舉辦，主要是由香港浸會大學(HONG KONG BAPTIST UNIVERSITY)所承辦，香港浸會大學設有中醫藥學院，對於中醫藥相當重視，對於中醫藥之教育與研究已經有許多經驗，這次會議辦的很成功，有來自全球10多個國家參與，共有500多篇研究論文發表，CGCM帶領中醫藥走向國際化看起來越來越成功。在國內陽明大學是CGCM草創時重要的成員之一，幾年前陽明大學也曾經舉辦過，本次該校主要由藥理研究所、傳統醫藥研究所及生化所參與。

由於CGCM其首要目的就是建立起中醫藥國際化共識，雖然談的是"中醫藥"但是爲了國際化、全球化，所以會議全程都是以英文爲主要語言，大會邀請許多國際學者及各國中醫藥及傳統醫學負責人參與，學術會議是大會主軸，雖然參加會議人士以華人之學者及學生爲主，但是發表專題演講以來自國際學者爲主，共有來自德國、英國、美國、加拿大、澳洲、法國、香港、澳門、奧地利、韓國、新加坡、馬來西亞、日本、葡萄牙，及台灣等十五個國家學者發表論文及演講，共有16個主題，在香港國際會議廳，從8月23日到8月25日三天舉行，大會特別邀請來自美國NIH 主管營養食品及中醫藥主任Dr. Paul M Coates，擔任Regulation affair主持人，來自德國TCM中心主任的Dr.Wolfgang Schwartz負責針灸部分的主持人，此外來自英國、香港、台灣及中國大陸許多學者專家都參加本次盛會。

傳統醫學國際化是必須走的路，透過學術研究的國際交流，最爲普遍與直接，國際學術會議常在歐美等已開發國家舉辦，越來越多相關會議也會在華人地區舉辦，以英文爲主要語言的中醫藥國際研討會不多，CGCM算是最有規模，也越辦越好，希望在相關之學校方面能多鼓勵，給年輕學者及同道有機會多與各國學者接觸交流。

跟中國大陸與香港比起來，看起來他們進步真的很快，尤其是中國大陸，這

次會議幾乎近一半的成員來自大陸，許多年輕面孔，在會上很是踴躍，積極主動學習，但願台灣能有更多年輕優秀學生或學者參與。

中醫藥臨床試驗值得發展，尤其是中醫藥扶正觀念與癌症預防或降低癌症西藥治療期間的併發症，副作用不舒服的改善，這都是中醫藥可以努力的地方，但願這方面將來有所突破。

貳、過程

此次開幕式是由香港浸會大學(HONG KONG BAPTIST UNIVERSITY)校長 Liang Liu 教授及CGCM會長中央研究院鄭永齊院士共同主持，Liu校長做了專題演講，他提到本次會議主辦過程，也提到再相想港中醫藥發展之情形，因爲香港浸會大學設有中醫藥學院，該校也是傳統中醫藥培養基地，他對此也做了些說明，他也代表主辦單位歡迎大家參加，CGCM會長中央研究院鄭永齊院士感謝大家之參與，也表示這次大會市CGCM成立以來最成功、參加人數最多、發表論文最豐富的一次大會，希望這幾天會成功完滿；會議是8/23-8/25 三天舉行，事實上大會很細心在8/22晚上就安排了welcome cocktail.陽明大學相關參與人員與國立中國醫藥研究所黃怡超所長及該所許多同仁及中醫藥委員會主任委員黃林煌醫師一起參與大會雞尾酒會，認識各國許多學者。台灣是CGCM 發起國之一，台灣分會會長是彭汪院士，另外台灣中醫藥的大家長，主管中醫藥的中醫藥委員會的主任委員黃林煌主委，主管中醫藥研究的國立中國醫藥研究所的黃怡超所長也帶著國立中國醫藥研究所四位研究員一同參加並發表論文，另外大學有來自陽明大學藥理所、傳醫所，長庚大學、中國醫藥大學、高雄醫藥大學，中央研究院、台灣大學，醫院如台北市立聯合醫院、榮民總醫院、台北長庚、高雄長庚、中興大學、中國附設醫院都派員參加，在大會發表超過50篇論文。

此次本人亦主持regulatory Affairs場次，國立中國醫藥研究所及陽明大學傳醫所黃怡超教授主持Internation collaborations，長庚大學傳統中醫藥研究所張恆鴻教授主持中醫診斷與評估的討論會，整體來看台灣參與相當踴躍，除了學者，業界如杏輝公司也積極參與，另外也看到幾位年輕的研究生參與發表論文，這真的很好，讓年輕一代參與國際會議，才能一代接一代。

8/23 開幕式外，有兩個議程分別是International collaborations 及 Education 分別由上海同濟大學彭副校長及英國Register 大學中醫研究所 Dr Mon-Fong Mei 所主持，來自台灣的國立中國醫藥研究所黃怡超所長也是國際

合作議程的主持人之一，下午的場次共有四場分別是Industry and Academic Collaboration，主要是希望產業與學界在中醫藥共同合作，另一個場次這是各國對於中醫藥管理的部分，本人也參與這個會議，也擔任共同主持人，第三個場次則是Biological and Mechanism Study 1 (Cancer) 主事談到中醫藥對於癌症的相關探討，主個部分許多人都很有興趣，參加的人相當多，許多內容也都很精采，另一個主題是Bioinformatics and Database 1 及 Quality Control 這兩個主題主要是從資料分析來看中醫藥的相關發展，整天下來會議真的很精采，來自於各國專家學者都很充實的參加第一天的議程，晚上是大會精心安排的晚宴。

8/24上下午各有三個場次，上午場次分別是Biological Activities and Mechanism Study II 主要是討論代謝疾病、老化以及神經疾病等與中醫藥相關探討，另一個場次則是討論中醫藥clinical Trial與安全性之評估，中國大陸有些研究在會場發表，但是仍有些改善的空間，第三個場次則是Herbal Resources I 主要是談到中醫藥與中草藥品質如何管控的研究；下午也有三個場次分別是Biological Activities and Mechanism Study III 主要是討論 中藥西藥並用的交互作用，另一個場次則是討論中醫藥癌症相關的clinical Trial，第三個場次針灸相關臨床研究。

8/25上午個有兩個場次，第一場次是討論天然物及其活性，另一個場次則是討論中醫藥OMIC蛋白質體的相關研究，雖然是最後一天，但是參加這個場次的專家學者仍然很多，來自台大的Ya-Ching Shen 才剛從機場趕來參加並主持討論天然物及其活性，真是令人感動，接著是閉幕會議，會議由CGCM會長鄭永齊院士主持，他感謝大家的參與，也感謝香港浸會大學江大會辦的如此成功，接著各場次主持人代表個場次座綜合及結論報告，最後是進行討論，並決定明年會議將在上海舉行，然後依序是奧地利、澳洲及北京舉行，看起來本次會議相當成功。

下午大會很精心安排香港進會大學中醫藥學院的參觀及訪問，讓本次大會話下美麗的句點。大家相約明年再相見。

參、心得

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與國立中國醫藥研究所黃怡超所長及該所許多同仁及本人一起參與大會雞尾酒會，認識各國許多學者。台灣是 CGCM 發起國之一，台灣分會會長是彭汪院士，另外主管中醫藥研究的國立中國醫藥研究所的黃怡超所長也帶著國立中國醫藥研究所四位研究員一同參加並發表論文，另外大學有來自陽明大學藥理所、傳醫所，長庚大學、中國醫藥大學、高雄醫藥大學，中央研究院、台灣大學，醫院如台北市立聯合醫院、榮民總醫院、台北長庚、高雄長庚、中興大學、中國附設醫院都派員參加，在大會發表超過 50 篇論文。

本人主持regulatory Affairs場次，國立中國醫藥研究所及陽明大學傳醫所黃怡超教授主持Internation collaborations，長庚大學傳統中醫藥研究所張恆鴻教授主持中醫診斷與評估的討論會，整體來看台灣參與相當踴躍，除了學者，業界如杏輝公司也積極參與，另外也看到幾位年輕的研究生參與發表論文，這真的很好，讓年輕一代參與國際會議，才能一代接一代。

這次參與 CGCM 會議要感謝藥理所林滿玉所長的精心規劃，藥理所的廖志飛教授傳統醫藥研究所陳方佩老師及許中華醫師代表陽明大學出席，除了我們三位之外傳醫所碩士班研究生連純瑩也與會並發表論文，這次個人共發表三篇論文分別是 Auricular acupuncture in obese women: A randomized controlled trial. ， Effect of green tea extract on obese women: a randomized, double-blind, placebo-controlled clinical trial. 及 Evaluation of effect Auricular Stimulation on Obese Women: A Randomized, Controlled Trial. 主要是這兩年來所從事的耳針刺激與綠茶提煉物，治療肥胖的臨床療效評估研究。整體而言本校參與還算熱烈，希望將來有更多同仁參與會議，或發表論文，尤其更希望校方能鼓勵研究生參與，能更深入直接了解中醫藥國際化的趨勢。

肆、建議

傳統醫學國際化是必須走的路，透過學術研究的國際交流，最爲普遍與直接，國際學術會議常在歐美等已開發國家舉辦，越來越多相關會議也會在華人地區舉辦，以英文爲主要語言的中醫藥國際研討會不多，CGCM算是最有規模，也越辦越好，希望校方能鼓勵，本校年輕學者及同道有機會多與各國學者接觸交流。

跟中國大陸與香港比起來，看起來他們進步真的很快，尤其是中國大陸，這次會議幾乎近一半的成員來自大陸，許多年輕面孔，在會上很是踴躍，積極主動學習，但願台灣能有更多年輕優秀學生或學者參與。

中醫藥臨床試驗值得發展，尤其是中醫藥扶正觀念與癌症預防或降低癌症西藥治療期間的併發症，副作用不舒服的改善，這都是中醫藥可以努力的地方，但願這方面將來有所突破。

伍、誌謝

誠摯的感謝署長給予機會及本會同仁協助得以順利成行，並向各位專家請益及彼此間之經驗交流甚爲寶貴，使本次行程獲益良多，令人難忘，謹此致上由衷謝忱！

陸、附錄

參加「第九屆中藥全球化聯盟年會 CGCM (The 9th Annual Meeting Of the Consortium for Globalization of Chinese Medicine)」大會手冊

ABSTRACTS

Hong Kong Convention & Exhibition Centre, Hong Kong

August 23-25, 2010

中药全球化联盟
CONSORTIUM FOR GLOBALIZATION OF CHINESE MEDICINE

香港浸會大學
HONG KONG BAPTIST UNIVERSITY

School of 中醫藥學院
Chinese Medicine

Abstract List for the 9th CGCM Meeting

Acupuncture

No.	Title	Institute	Region	Corresponding Author
001	Teleacupuncture Bridges Science and Practice	TCM Research Center Graz	Austria	Gerhard LITSCHER
002	Clinical Observation on 40 Cases of Eczema Treating by Integrated Herbal Medicine and Acupuncture	China Academy of Chinese Medical Science	Beijing	Miranda FUNG
003	Comparing the Efficacy of Traditional Fire-cupping and Vacuum-cupping	China Academy of Chinese Medical Science	Beijing	Tao HUANG
004	Experimental Study of Effect of Electro-Bian Stone on the Local Blood Perfusion of the Back of the Crus	China Academy of Chinese Medical Science	Beijing	Yu-Qin ZHANG
005	Research Advancement on Epilepsy Treatment by Acupuncture	China Academy of Chinese Medical Science	Beijing	Bing ZHU
006	Revealing Acupuncture Meridian-like System by Reactive Oxygen Species Visualization	Fuzhou University	Fujian	Ping-fan RAO
007	Cellular Mechanisms in Acupuncture Points and Effected Sites	German-Chinese Research Foundation of TCM	Germany	Wolfgang SCHWARZ
008	Electroacupuncture Attenuates Epileptic Seizures	German-Chinese Research Foundation of TCM	Germany	Ying XIA
009	Internal Validity vs External Validity: Paradox in Acupuncture Clinical Trial Studies	Hong Kong Baptist University	Hong Kong	Shi-Ping ZHANG
010	Acupuncture in the Treatment of Knee Osteoarthritis: A Meta-analysis	Hong Kong Baptist University	Hong Kong	Min XU
011	Acupuncture in the Treatment of Low Back Pain: A Meta-analysis	Hong Kong Baptist University	Hong Kong	Min XU
012	Clinical Observations on Laser Acupuncture in Simple Obesity Therapy	Chang Gung Memorial Hospital - Kaohsiung Medical Center	Kaohsiung	Wen-Long HU
013	Technology Innovation of Acupuncture in the World: An Empirical Study Based on Patents	University of Macau	Macau	Yi-Tao WANG
014	Introducing Double-Blinding in Acupuncture Research	University of Porto	Portugal	Henry Johannes GRETEN
015	Low Power Laser Irradiation on Cytochrome c Release and the Opening of TRPV Channel in RBL-2H3 Cells	Fudan University	Shanghai	Ji-Yao CHEN

016	An Engineering Cybernetics Approach to Acupuncture and TCM – Yin-Yang Wuxin Dynamics and Ear Acupoint Electronics Device	Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences	Shanghai	Su-Shing CHEN
017	Effect of Acupuncture on CD4+CD25+ Regulatory T Cells in Tumor-bearing Mice	Shanghai University of Traditional Chinese Medicine	Shanghai	Jian PEI
018	Study on the Characteristics of Infrared Spectrums of Moxibustion	Shanghai University of Traditional Chinese Medicine	Shanghai	Xue-Yong SHEN
019	Influence of Acupuncture on Heroin Addicts' Bias of Attention	Shanghai University of Traditional Chinese Medicine	Shanghai	Ping XU
020	Laser Acupuncture in Patients with Idiopathic Carpal Tunnel Syndrome - a Pilot Study	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
021	The Evaluation of Risk Factor in Needle Sickness	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
022	A Neurovascular Transmission Model of Nitric Oxide for Acupuncture	National Research Institute of Chinese Medicine	Taipei	Sheng-Hsiung HSIAO
023	Auricular Acupuncture in Obese Women: A Randomized Controlled Trial	National Yang-Ming University	Taipei	Chung-Hua HSU
024	Evaluation of Effect of Auricular Stimulation on Obese Women: A Randomized, Controlled Clinical Trial	National Yang-Ming University	Taipei	Chung-Hua HSU
025	Scalp Acupuncture Based on Dynamic Qi Detection Instead of Using Standard Location Might Help Improving Parasthesia	Chang Gung Memorial Hospital - Taoyuan Center	Taoyuan	Ko-Hung LEE
026	What Do Acupuncturists Do – Fertility Related Practice in the UK?	Thames Valley University	UK	Nicola ROBINSON
027	The Integration of Traditional Chinese Medicine into the Health Care System of the Republic of The Philippines	University of Oxford	UK	Paul KADETZ
028	To Unveil the Effect of Acupuncture as a Treatment for Chronic Low Back Pain - A Pilot fMRI Study	Yale University	USA	Shu-Ming WANG

Bioinformatics and Database I (Classification Diseases & Herbal Database)

No.	Title	Institute	Region	Corresponding Author
029	Novel Two-stage Analytic Approach in Extraction of Strong Herb - Herb Interactions in TCM Clinical Treatment of Insomnia	The University of Sydney	Australia	Josiah POON
030	Development Prospect of Chinese Medicine Digitization Projects	Hong Kong Baptist University	Hong Kong	Hu-Biao CHEN

031	Establishment of A Dynamic Ethnomedicinal Database Based on Encyclopedia of Medicinal Plants	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
032	"Poisonous Drugs" and "Sweet Drugs" - Analysis of the Culture of Drug Classification in the "Yellow Emperor's Internal Classic"	The University of Hong Kong	Hong Kong	Lei LI
033	The Pathophysiology of "Heat"/Calor	University of Porto	Portugal	Henry Johannes GRETEN
034	SAPHRON TCM Database: Bioinformatic Approaches and its Application for Drug Discovery	Shanghai Innovative Research Center of Traditional Chinese Medicine	Shanghai	William Wei-Guo JIA
035	Bioinformatics Services Derived from Chinese Herbal Databases - Linking Eastern Medicine with Western Medicine	Tongji University	Shanghai	Zhi-Wei CAO

Bioinformatics and Database II (Application of "Omics" in TCM Research)

No.	Title	Institute	Region	Corresponding Author
036	Analysing Complex Interactions in TCM Data	The University of Sydney	Australia	Martin MCGRANE
037	Functional Networks for Salvia Miltiorrhiza and Panax Notoginseng in Combination Explored with Text Mining and Bioinformatical Approach	China Academy of Chinese Medical Sciences	Beijing	Ai-ping LU
038	Analysis of Ginkgo Biloba L. Leaf Ttranscriptome Using a "Next Generation" Sequencing Technology Based on 454 GS FLX Titanium Platform	Chinese Academy of Medical Sciences & Peking Union Medical College	Beijing	Shi-Lin CHEN
039	Transcriptome Analysis for Camptotheca Acuminata Young Leaves for Discovering Putative Genes Relative to Secondary Metabolism	Chinese Academy of Medical Sciences & Peking Union Medical College	Beijing	Shi-Lin CHEN
040	Proteomic Profile of Primary Isolated Rat Mesangial Cells in High Glucose Culture Condition and the Decreased Expression of PSMA6 in Renal Cortex of Diabetic Rats	China-Japan Friendship Hospital	Beijing	Ping LI
041	Reversal of Hypoxia Response by Danshen-Gegen Decoction in Rat Myocardium Cells H9C2	City University of Hong Kong	Hong Kong	Meng-Su YANG
042	Proteomic Profiling of Spinal Cord and Dorsal Root Ganglia: Altered Protein Regulation Following Inflammatory Bowel Diseases Induced by Trinitrobenzene Sulfonic Acid	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN

043	Plasma Proteome Analysis of Anti-cancer and Anti-hyperlipidemia Effects of Triterpenoids from Gynostemma Pentaphyllum in the APCmin/+ Mouse Model	Hong Kong Baptist University	Hong Kong	Wendy Wen-Luan HSIAO
044	Identification of Biomarkers Responsible for Anti-arthritic Effect of Qingfu Guanjieshu Capsule	Hong Kong Baptist University	Hong Kong	Liang LIU
045	HuaLiuFang and its Separated Prescription Drugs Serum Impact on Differentially Expressed the Gene of Uterine Leiomyoma Cells Fibroids	Hong Kong Baptist University	Hong Kong	Wei MENG
046	Proteomic Analysis of Anti-cancer Effects by Tanshinone IIA in Cervical Cancer Cells	Chang Gung Memorial Hospital - Kaohsiung Medical Center	Kaohsiung	Yu-Chiang HUNG
047	Discovery of Potential Biomarkers Associated with Induced Stress in Rats Using Artificial Intelligence Technologies	University of Bradford	UK	Qun SHAO
048	MRMPath: A Web-Based Tool that Identifies Peptide Transitions for LC-MRM-MS Analysis and its Application to Biological Pathways	University of Alabama at Birmingham	USA	Stephen BARNES
049	Immunologic Complexity of Tumor, Spleen and Liver Transcriptional Program in Mice Treated with Chemotherapy and Traditional Chinese Medicine (PHY-906)	Yale University	USA	Yung-Chi CHENG
050	Pathway and Gene Expression Changes in Tumor, Spleen and Liver Tissues in Mouse Treated with PHY906, CPT-11 and their Combination	Yale University	USA	Hong-Yu ZHAO

Biological Activities and Mechanism Study I (Cancer)

No.	Title	Institute	Region	Corresponding Author
051	Inhibitory Effect of Sheng Qi Formula (SQF) Combined with Chemotherapy Drugs on Myeloid-derived Suppressor Cells in the 4T1 Murine Mammary Cancer Model	Guang'an men Hospital, China Academy of Chinese Medical Sciences	Beijing	Jie LI
052	Oxymatrine Diminishes Cancer Stem-like Cells of Breast Cancer MCF-7 Cell Line	Guang'an men Hospital, China Academy of Chinese Medical Sciences	Beijing	Hong-Sheng LIN
053	Rational Design, Synthesis of Isatin Compounds for their Anti-lung Cancer Activity	Institute of Microbiology, Chinese Academy of Sciences	Beijing	Li-Xin ZHANG

054	Enhancement of Cancer Chemotherapy by Phytochemicals – an Approach for the Integration of Traditional Chinese Medicine into Western Medicine	German-Chinese Research Foundation for TCM	Germany	Thomas EFFERTH
055	Inhibition of P-glycoprotein at the Blood Brain Barrier by Phytochemicals Derived from Traditional Chinese Medicine	German-Chinese Research Foundation for TCM	Germany	Thomas EFFERTH
056	Chemical Components with Inhibitory Activities Against Prostate Cancer Cells from Dysosma Versipellis	Jinan University	Guangdong	Ren-Wang JIANG
057	20(S)-Protopanaxadiol, a Metabolite of Ginsenosides, Induces HepG2 Cell Apoptosis and Endoplasmic Reticulum Stress	Hong Kong Baptist University	Hong Kong	Wang-Fun FONG
058	Furanodienone Induces Apoptosis and Inhibits Cell Invasion via Downregulation of Akt Phosphorylation and NF-κB Activation in Human Prostate Cancer Cells	Hong Kong Baptist University	Hong Kong	Wang-Fun FONG
059	Isolation of Active Ingredients with Anti-cancer Activity of Total Triterpenoids Saponins of Gynostemma Pentaphyllum by Cell-based Co-culture Activity-guided Fractionation Assay	Hong Kong Baptist University	Hong Kong	Wendy Wen-Luan HSIAO
060	Pharmacokinetics Study of Triterpenoids Saponinsn with Anti-cancer Activities after Oral Administration of Total Saponins of Gynostemma Pentaphyllum in Mouse Plasma	Hong Kong Baptist University	Hong Kong	Wendy Wen-Luan HSIAO
061	The Triterpenoids Saponins of Gynostemma Pentaphyllum, alone or in Combination with 5-fluorouracil, Exert Anti-cancer Effects in the ApcMin/+ mice and the Colorectal Cancer Cell Lines	Hong Kong Baptist University	Hong Kong	Wendy Wen-Luan HSIAO
062	Compound A, a Novel Ginsenoside Derivative, Induced Apoptosis and S-phase Arrest of Lewis Lung Carcinoma Cells through Activation of MAP Kinases and Suppression of NF-κB Activation	Hong Kong Baptist University	Hong Kong	Liang LIU
063	Ginseng Extract Inhibits in Vitro and in Vivo Growth of Mouse Lewis Lung Carcinoma via Modulation of ERK-p53 and NF-κB Signaling	Hong Kong Baptist University	Hong Kong	Liang LIU
064	Induction of Cell Anergy in Human Jurkat T cells by Matrine through Regulation of MAPK and NFAT Signaling Pathways	Hong Kong Baptist University	Hong Kong	Liang LIU

065	Saikosaponin-d (Ssd) Suppresses the Cancer Cells Growth through Down-regulation of NF-κB Signaling and its Targeted Genes Expression, with Concomitant Induction of Apoptosis in HepG2 Cells	Hong Kong Baptist University	Hong Kong	Liang LIU
066	Screening for Compounds with Anti-cancer Effects from Ginsenosides and their Derivatives	Hong Kong Baptist University	Hong Kong	Liang LIU
067	Suppression of T Lymphocyte Activation by Pseudolaric Acid B through Inhibition of NF-κB Signaling Pathway and p38 Phosphorylation	Hong Kong Baptist University	Hong Kong	Liang LIU
068	Anticancer Effects and Mechanisms of Sesquiterpene Compounds Isolated from Atractylodes Macrocephala in B16 Melanoma Cells	Hong Kong Baptist University	Hong Kong	Zhi-Ling YU
069	Photodynamic Therapy of Pheophorbide a inhibits the Proliferation of Human Breast Cancer cells via Caspase - Dependent and - Independent Apoptotic Pathways in vitro	The Chinese University of Hong Kong	Hong Kong	Kwok-Pui FUNG
070	Investigations on the in vitro Anti-tumor Activities of Rubinoboletus Ballouii	The Chinese University of Hong Kong	Hong Kong	Quan-Bin HAN
071	Induction of Apoptosis and G0/G1 Cell Cycle Arrest by Guttiferone K, Isolated from Garcinia Cowa, on Human Colon Cancer Cells	The Chinese University of Hong Kong	Hong Kong	Ge LIN
072	Reversal of Pgp-mediated Multidrug Resistance by Novel Tenacigenin B Derivatives	The Chinese University of Hong Kong	Hong Kong	Ge LIN
073	Mechanistic study of Bioactive Ingredients of Phellodendron chinense on Human Ovarian Cell Line	The Hong Kong Polytechnic University	Hong Kong	Christine Mui-Ngan YOW
074	Type1 and Type 2 Cell Deaths on Anti-tumor Effect of Berberine in Liver Cancer Cells	The University of Hong Kong	Hong Kong	Yi-Bin FENG
075	Synergistic Effects of Tian-Xian Liquid (TXL) on Anti-tumorigenicity In Vivo	The University of Hong Kong	Hong Kong	Stephen Cho-Wing SZE
076	Anti-metastatic evaluation of Tian-Xian Liquid (TXL) and its Bioactive Fractions in Human Colorectal Cancer Cells and Xenograft Models	The University of Hong Kong	Hong Kong	Yao TONG
077	Ellagic Acid as an Zinc-Chelating Agent to Inhibit Cell Invasion and Angiogenesis	Chang Gung Memorial Hospital - Kaohsiung Medical Center	Kaohsiung	Sheng-Teng HUANG

078	Relationship of Cytokine Level with Cancer Cachexia and Therapeutic Effects of Chinese Herbs on Cancer Cachexia Mice	Chang Gung Memorial Hospital - Keelung Center	Keelung	Ching-Hsien CHANG
079	Glycyrol Induces Apoptosis in Human Jurkat T Cell Lymphocytes via the Fas-FasL/caspase-8 Pathway	Seoul National University	Korea	Yeong-Shik KIM
080	Induction of Nucleolin Translocation by Acharan Sulfate in A549 Human Lung Adenocarcinomas	Seoul National University	Korea	Yeong-Shik KIM
081	Platycodin D, a Triterpenoid Saponin from Platycodon Grandiflorum Induces Cell Cycle Arrest and Caspase-mediated Apoptosis in Human Cancer Cell Lines	Seoul National University	Korea	Yeong-Shik KIM
082	The In Vitro Anti-breast Cancer Activity of Furanodiene, a Natural Product Isolated from Ezhu	University of Macau	Macau	Yi-Tao WANG
083	Orient Dredging Regimen Exercise(ODRE) Plays a Role in the Prevention and the Recovery of Cancer Diseases	Tongji University	Shanghai	Xiao-Dong CHENG
084	Induction of G2/M Phase Arrest and Apoptosis by Oridonin in Human Laryngeal Carcinoma Cells	Shenyang Pharmaceutical University	Shenyang	Takashi IKEJIMA
085	Biologics as a New Class of Active Principles in Herbal Medicine	Nanyang Technological University	Singapore	James TAM
086	Mechanism Study of Migration Inhibition on Human Lung Non-small Carcinoma Cell by Extract of Pericarpium Citri reticulatae	China Medical University	Taichung	Wen-Te CHANG
087	The Characteristics of eIF3i in Prostate Cancer Treatment with penta-O-galloyl-β-D-glucose (5GG) Via Proteomic And Western Analysis	National Chung Hsing University	Taichung	Jung-Yie KAO
088	Deoxyelephantopin Suppresses Lung Metastasis of B16 Melanoma in Mice	Academia Sinica	Taipei	Lie-Fen SHYUR
089	Deoxyelephantopin Sensitizes Human Breast Cancer MDA-MB-231 Cells via Activation of Extracellular Signal-Regulated Kinase 1/2 and Inhibition of Signal Transducers and Activators of Transcription Signaling	Academia Sinica	Taipei	Ning-Sun YANG
090	Effect of Moscatilin in Esophageal Cancer	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
091	Aloe-Emodin Reverses Epithelial-to-Mesenchymal Transition in Metastatic Oral Cancer Cells by Targeting Twist	China Medical University	Taipei	Tzong-Der WAY

092	Evaluation on Bioactive Compounds of Six Golden Camellias and Anti-cancer Effects in Breast Cancer Cell Lines	China Medical University	Taipei	Tzong-Der WAY
093	Osthole Suppresses Fatty Acid Synthase Expression in HER2-Overexpressing Breast Cancer Cells through Modulating Akt/mTOR Pathway	China Medical University	Taipei	Tzong-Der WAY
094	(-)-Epigallocatechin Gallate Induces Fas/CD95-mediated Apoptosis through Inhibiting Constitutive and IL-6-induced JAK/STAT3 Signaling in Head and Neck Squamous Cell Carcinoma Cells	China Medical University	Taipei	Tzong-Der WAY
095	NBM-HD-1: A Novel Histone Deacetylase Inhibitor, Semi-Synthesized from a Natural Derivative, with Anticancer Activity Both In Vitro and In Vivo	Taipei Medical University	Taipei	Yu-Cheng KUO

Biological Activities and Mechanism Study II (Metabolic, Neural Diseases & Aging Process)

No.	Title	Institute	Region	Corresponding Author
096	The Inhibitory Activities of Pomegranate on Carbohydrate Digestive Enzymes α-glucosidase and α-amylase	The University of Sydney	Australia	George LI
097	Neuroprotective Effect of Wei Nao Kang (WNK) Mediated by Inhibition of NMDA-dependent Ca2+ Influx	University of Western Sydney	Australia	Dennis CHANG
098	Study on Mechanism of Delaying Vascular Aging of Senile Mice by Chinese Herbs with Tonifying Qi and Activating Blood	China Academy of Chinese Medical Science	Beijing	Jing YANG
099	Amelioration of Diabetic Nephropathy in Otsuka Long-Evans Tokushima Fatty (OLETF) Rats by a Group of Chinese Herbs (Tangshen Formula)	China-Japan Friendship Hospital	Beijing	Ping LI
100	Proteomic Analysis of Protective Mechanism on Type 2 Diabetic Nephropathy Rats by a Group of Chinese Herbs (Tangshen Formula)	China-Japan Friendship Hospital	Beijing	Ping LI
101	American Ginseng (Panax Quinquefolius) Prevents Diabetes Induced Retinal Changes	The University of Western Ontario	Canada	Subrata CHAKRABARTI
102	Ginseng Effects on Intestinal Lipid Secretion and Plasma Clearance in Pcyt2-Deficient Mouse Model for Metabolic Syndrome	University of Guelph	Canada	Marica BAKOVIC
103	Berberine Ameliorates Renal Injury in Experimental Diabetic C57BL/6 Mice Involved in Suppression of SphK-S1P Signaling Pathway	Sun Yat-Sen University	Guangdong	He-Qing HUANG

104	Effects of Berberine on Matrix Accumulation and NF-kappa B Signal Pathway in Alloxan-induced Diabetic Mice with Renal Injury	Sun Yat-Sen University	Guangdong	He-Qing HUANG
105	Effect of Emodin on Cell Proliferation, FN Expression and p38MAPK Pathway in Rat Mesangial Cells Cultured Under High Glucose	Sun Yat-Sen University	Guangdong	He-Qing HUANG
106	Development of High-throughput Yeast-based Activity-guided Screening Assay Targeting HMG-CoA Reductase Activity and Isolation of Active Constituents Inhibit HMG-CoA Reductase Activity from Total Triterpenoids Saponins of Gynostemma Pentaphyllum	Hong Kong Baptist University	Hong Kong	Wendy Wen-Luan HSIAO
107	Catechins and Procyanidins in Extract of Ginkgo Biloba Show Protent Inhibitory Activity against β-Amyloid Peptide Aggregation	Hong Kong Baptist University	Hong Kong	Zhi-Hong JIANG
108	Cellular Lipidomic Study of β-Amyloid-induced Neurotoxicity and Intervention Effects of EGCG in Green Tea by Using UPLC-MS Based Glycerophospholipid Profiling and Multivariate Analysis	Hong Kong Baptist University	Hong Kong	Zhi-Hong JIANG
109	Baicalein Inhibits Aggregation of Amyloidogenic Polypeptides and Prevents Protein Aggregation-induced Neurotoxicity	Hong Kong Baptist University	Hong Kong	Min LI
110	Cryptotanshinone Decrease β-Amyloid Generation by Modulating Amyloid Precursor Protein Processing	Hong Kong Baptist University	Hong Kong	Min LI
111	Astragaloside IV Protects Human Astrocytes in against High Glucose-induced Cell Death by Attenuating ROS Production	Hong Kong Baptist University	Hong Kong	Pui-Kwan WONG
112	Anti-hepatosteatotic Effect and Mechanism of Schisandrin B in Steatotic Cell Models	Hong Kong Baptist University	Hong Kong	Zhi-Ling YU
113	The Ginsenoside Protopanaxatriol Protects Endothelial Cells from Hydrogen Peroxide-induced Cell Injury and Cell Death by Modulating Intracellular Redox Status	Hong Kong Baptist University	Hong Kong	Patrick Ying-Kit YUE
114	The Effect of Chinese Scorpion (Buthus Martensii Karsch) on Neuropathic Pain	Hong Kong Baptist University	Hong Kong	Hong-Qi ZHANG
115	COX-1 and COX-2 Upregulation in Spinal Dorsal Horn after Spinal Nerve Ligation	Hong Kong Baptist University	Hong Kong	Hong-Qi ZHANG

116	Cardiovascular Tonic Herbal Medicine: Danshen And Gegen Decoction	The Chinese University of Hong Kong	Hong Kong	Kwok Pui FUNG
117	Identification of a Compound from the Traditional Chinese Medicine with Antidepressant-like Property	The Hong Kong University of Science and Technology	Hong Kong	Nancy Y. IP
118	Compound A2287 Rescues Primary Neurons against NMDA Excitotoxicity and Reduces Cerebral Infarct in a Rodent Stroke Model	The Hong Kong University of Science and Technology	Hong Kong	Nancy Y. IP
119	Herba Cistanche Induces Mitochondrial Uncoupling and Glutathione Redox Cycling In H9c2 Cardiomyocytes	The Hong Kong University of Science & Technology	Hong Kong	Robert K. M. KO
120	The Holistic Approach of Anti-Aging Lycium Barbarum (Wolfberry) in the Protection against Pathological Factors Related to Alzheimer's Disease	The University of Hong Kong	Hong Kong	Raymond Chuen-Chung CHANG
121	Neuroimmune Responses of Polysacharides from Lycium Barbarum (Wolfberry) in Retina after Experimental Glaucoma	The University of Hong Kong	Hong Kong	Raymond Chuen-Chung CHANG
122	Effects of Buyang Huanwu Decoction on Modulating Cellular Growth Signals and Improving Neural Stem Cells Proliferation and Differentiation for Post-Stroke Treatment	The University of Hong Kong	Hong Kong	Xi CHEN
123	A Non-competitive JAK2 Inhibitor from Ginkgo Biloba	The University of Hong Kong	Hong Kong	Chung-Hang LEUNG & Dik-Lung MA
124	Parallel Activation of Nrf2 and PI3K/Akt Pathways by z-ligustilide Enhances the Survival of Neuronal PC12 Cells under Oxygen and Glucose Deprivation: A Role for Heme Oxygenase-1	The University of Hong Kong	Hong Kong	Jian-Hui RONG
125	Drug Discovery from Herbal Medicine: Where we are? Where we go? - A Lesson from a Classic Formula Study for Post-stroke Treatment	The University of Hong Kong	Hong Kong	Jian-Gang SHEN
126	Facilitation of Male Sexual Behavior by Lycium Barbarum (Wolfberry) Polysaccharide	The University of Hong Kong	Hong Kong	Kwok-Fai SO
127	Effect of Erxian Decoction and its Bioactive Fractions on Lipid Profile of Menopausal Rat Model	The University of Hong Kong	Hong Kong	Yao TONG

128	Chrysotoxine, a Novel Bibenzyl Compound Isolated from Dendrobium Species, Inhibits 6-hydroxydopamine Induced Apoptosis in SH-SY5Y Cells via Mitochondria Protection and NF-ĸB Modulation	The University of Hong Kong	Hong Kong	Yan-Bo ZHANG
129	Peony-Glycyrrhiza Decoction (PGD), an Herbal Preparation, Suppresses Synthesis and Secretion of Prolactin in Pituitary Adenoma Cells – Implication for the Treatment of Hyperprolactinemia	The University of Hong Kong	Hong Kong	Zhang-Jin ZHANG
130	Eriocaulon Buergerianum Extract Protects against 6-hydroxydopamine-induced Neuron Death on PC12 Cells In Vitro and Zebrafish In Vivo	University of Macau	Macau	Simon Ming-Yuen LEE
131	Characterization of (+)-praeruptorin A Metabolism in Human Liver Microsomes	University of Macau	Macau	Ru YAN
132	Identification of the Major Urinary and Fecal Metabolites in Rats Dosed with Radix Peucedani Extract by RRLC/ESI-MS	University of Macau	Macau	Ru YAN
133	Dose-Dependent Effects of Betel Nut on Cardiovascular Risk Factors in a Rat Model	Aga Khan University	Pakistan	Mohammad Perwaiz IQBAL
134	Quantitation by UPLC-MS\MS of Endogenous Estrogens and Monoamine Neurotransmitters and its Application on Bioactivities Evaluation of Qing'e Formula	Shanghai R&D Centre for Standardization of Traditional Chinese Medicine	Shanghai	Zi-Jia ZHANG
135	Schwann Cell Migration Induced by Earthworm Extract via Activation of PAs and MMP2/9 Mediated through ERK1/2 and p38	China Medical University	Taichung	Chih-Yang HUANG
136	Lipid Metabolism Of Curcuma Longa on High-hat-diet Induced Obesity Mice with Hepatic Steatosis	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
137	Evaluation for the Impact of Penta-O-galloyl-glucopyranose Isoforms (PGG) on Each Stages of Adipocyte Life Cycle	National Research Institute of Chinese Medicine	Taipei	Hui-Kang LIU
138	Andrographolide Inhibits LPS, IFNγ and Oxygen-glucose Deprivation-induced Microglial Activation through Modulation of PI3K, ERK, and Nuclear Factor-κB Activation	National Research Institute of Chinese Medicine	Taipei	Yuh-Chiang SHEN
139	Tanshinone Ⅱ A Stimulates Endothelial Cell Growth and Angiogenenis by Up-repulating the Levels of Endothelial Nitric Oxide Synthase and Phosphatidylinositol 3-Kinase	JiangHan University	Wuhan	Yong YE

Biological Activities and Mechanism Study III (Mechanism & Drug Interaction)

No.	Title	Institute	Region	Corresponding Author
140	Comparison Study on Cardiac Toxic Reaction of White Prepared Lateral Root of Aconite to Normal rats and Traditional Chinese Medicine Indication Model Rats	China Academy of Chinese Medical Sciences	Beijing	Ai-ping LU
141	The Experimental Study on Hepatic and Renal Toxicity of Rats Induced by Fructus Gardeniae and Pharmacokinetics of Geniposide	China Academy of Chinese Medical Sciences	Beijing	Hong-Jun YANG
142	Hepato-toxicity or Protection? Pattern Recognition for the Paradoxical Effect of a Phytomedicine (Rheum Palmatum L.) to Treat Liver Injury	PLA Institute of Chinese Materia Medica	Beijing	Jia-bo WANG
143	Attenuation of Oxidative and Nitrosative Stress by Pure Constituents of Traditional Chinese Remedies	University of Western Ontario	Canada	Lei ZHANG
144	Inhibitory Effects of Radix isatidis Extract on Attachment of Influenza A and B Virus to MDCK Cells	Fuzhou University	Fujian	Jian-Wu ZHOU
145	Binding and Interaction of Anti-diabetic MRPs to Pancreatic ß-Cell Plasma Membrane	Fuzhou University	Fujian	Jian-Wu ZHOU
146	Emodin Inhibits Current through SARS-associated Coronavirus 3a Protein	German-Chinese Research Foundation of TCM	Germany	Silvia SCHWARZ
147	YiNaoKang's Effect on the AS Based AIS SD Mice's Brain VEGF Expression and Brain Pathological Change	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Yan HUANG
148	Effect of Oral Schisandra Sphenanthera Extract on the Pharmacokinetics of Paclitaxel in Rats	Sun Yat-sen University	Guangdong	Min HUANG
149	Study of Biological Activities and Molecular Mechanism of Herbal Formula (Radix Rehmanniae and Radix Astragali) on Human Skin Fibroblast Cell Line HS27	City University of Hong Kong	Hong Kong	Meng-Su YANG
150	Up-regulation of L-type Calcium Channels in Colonic Smooth Muscle Cells is Involved in Colonic Motility Dysfunction Induced by NMS	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
151	Inhibitory Effect of Magnolol on Colonic Motility is Mediated through Down-regulation of Voltage-dependent L Type Ca2+ Channels of Colonic Smooth Muscle Cells in Rats	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN

152	Magnolol Regulates the Colonic Motility Dysfunction through Inhibiting l-type Calcium Channels in Colonic Smooth Muscle in Neonatal Maternal Separation Rats	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
153	Magnolol Attenuates the Colonic Smooth Muscle Contraction by Decreasing the Activities of MLCK/myosin Light Chain 20 in Colonic Smooth Muscle	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
154	The Analgesic Effect of JCM-16021 on Trinitrobenzene Sulfonic Acid (TNBS)-induced Postinfectious Irritable Bowel Syndrome Rats	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
155	Therapeutic Effect of JCICM-4-07 on Visceral Pain and Diarrhea	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
156	The Role of Nerve Growth Factor in Visceral Hypersensitivity and Irritable Bowel Syndrome	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
157	Excitatory and Inhibitory Amino Acid Changes in Brain of Neonatal Maternal Separation Rats: An In Vivo Microdialysis Study	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
158	Role of MicroRNA-214 in Ginsenoside-Rg1-induced Angiogenesis	Hong Kong Baptist University	Hong Kong	Ricky Ngok-Shun WONG
159	Activation of Canonical Wnt Signaling Pathway in Aortic Vascular Smooth Muscle Cells is Associated with Oxidative Stress Induction in Diabetic Macro-vasculopathy	Hong Kong Baptist University	Hong Kong	Kin-Man YUE
160	GR/PI3K/Akt/eNOS Signaling Plays an Important Role in Cardioprotection of Ginseng Extract RSE in Rats	Hong Kong Baptist University	Hong Kong	Hua ZHOU
161	Ginsenosides Increase Coronary Perfusion Flow in Rat Heart through Activation of PI3K/Akt-eNOS Signaling and Cardiac Energy-Associated Protein Expression	Hong Kong Baptist University	Hong Kong	Hua ZHOU
162	Synergistic Effects of the Combination of Baicalin with Ciprofloxacin and Gentamicin against Methicillin-resistant Staphylococcus Aureus	The Chinese University of Hong Kong	Hong Kong	Ben Chung-Lap CHAN
163	The In Vivo and In Vitro Diabetic Wound Healing Effects of a 2-herb Formula and its Mechanisms of Action	The Chinese University of Hong Kong	Hong Kong	Clara LAU
164	The Anabolic Effect of Green Tea and its Polyphenol, Epigallocatechin on Bone Through the Differentiation of Mesenchymal Stem Cells	The Chinese University of Hong Kong	Hong Kong	Ping-Chung LEUNG

165	Photoinactivation of Hypericin on MDR S Aureus and ESBL-Producing E.Coli Pathogens	The Hong Kong Polytechnic University	Hong Kong	Christine Mui-Ngan YOW
166	The Role of Reactive Oxygen Species in the Hepatoprotective Mechanism of Schisandrin B In Vivo: A Comparative Study with Curcumin and Menadione	The Hong Kong University of Science & Technology	Hong Kong	Robert Kam-Ming KO
167	Phytochemicals Ameliorates Oxidative Stress by Inducing Glutathione Antioxidant Response through ROS Production in H9c2 Cells	The Hong Kong University of Science & Technology	Hong Kong	Robert Kam-Ming KO
168	Antimicrobial Activity of Fructus Mume Extract and its Main Acidity Compounds on Streptococcus Mutans	The University of Hong Kong	Hong Kong	Ricky WONG
169	Novel Mechanisms: Components of Dendrobium Species that Promote Aquaporin-5 (AQP-5) Expression	The University of Hong Kong	Hong Kong	Yan-Bo ZHANG
170	Polysaccharides of Dendrobium Officinale Restore the Abnormal Expression and Distribution of Aquaporin-5 in Sjögren's Syndrome Model	The University of Hong Kong	Hong Kong	Yan-Bo ZHANG
171	Resveratrol Improves Hippocampal Atrophy in Mice with Chronic Fatigue	Kanazawa Medical University	Japan	Junji MORIYA
172	Platycodin D Regulates the Expression of Adipogenic Factors Related to AMPK-AKT Pathway in Adipocytes and Inhibits Fat Accumulation in High Fat Diet-induced Obese Mice	Seoul National University	Korea	Yeong-Shik KIM
173	Anti-inflammatory and Anti-angiogenic Effects of Resveratrol and its Analogs in Human Umbilical Vein Endothelial Cells and Zebrafish	University of Macau	Macau	Simon Ming-Yuen LEE
174	Calycosin From Radix Astragali Promotes Angiogenesis involving Estrogen Receptor and Mitogen-activated Protein Kinase (MAPK) Signaling Pathway in Zebrafish and HUVEC	University of Macau	Macau	Simon Ming-Yuen LEE
175	Indirubin Shows Anti-angiogenic Activity in an In Vivo Zebrafish Model and an In Vitro HUVEC Model	University of Macau	Macau	Simon Ming-Yuen LEE
176	In vitro Study of Indigo Compound Recipe on JAK2 Mutated HEL Cell Line	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Min CHEN
177	Absorption and Metabolism of Flavonoids in Extract of Fructus Aurantii Immaturus	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Yan CHEN
178	Glucuronidation of Wogonin and Other Four Analogical Flavones in Rat Liver Microsomes	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Xiao-bin JIA

179	Study on Processing Mechanism of Epimedium Based on Biological Transformation Combined with Intestinal Absorption Barrier	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Xiao-bin JIA
180	Preparation of Icaritin Liposomes and its Studies on Rat Intestinal Absorption in Situ	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Xiao-bin JIA
181	Effects of Danggui Buxue Tang on HIF-1α and Angiogenesis in Fibrotic Rats	Shanghai University of Traditional Chinese Medicine	Shanghai	Cheng-Hai LIU
182	Effects of Sorafenib on Gelatinase Activities and Hepatic Sinusoidal Endothelial Cell in Cirrhosis Mice	Shanghai University of Traditional Chinese Medicine	Shanghai	Cheng-Hai LIU
183	Effect of Xiaozhang Cataplasm on Ascites and Dose-Effect Relationship in Cirrhotic Mice with Ascites	Shanghai University of Traditional Chinese Medicine	Shanghai	Cheng-Hai LIU
184	Glucuronidation, a New Metabolic Pathway of Pyrrolizidine	Shanghai University of Traditional Chinese Medicine	Shanghai	Zheng-Tao WANG
185	Andrographolide Inhibits the Expression and Function of CYP3A4 in 1α, 25 Dihydroxyvitamin D3 Treated Caco-2 Cells	Shenyang Pharmaceutical University	Shenyang	Feng QIU
186	The Effects of Buyanghuanwutang on Pulmonary Fibrosis Induced by the Bleomycin in Rats	Chengdu University of Traditional Chinese Medicine	Sichuan	Fei WANG
187	The Effect of Xin-San-Guo-Tang Compound Tibetan on Polycythemia induced by Chronic Hypoxia in Rat	Chengdu University of Traditional Chinese Medicine	Sichuan	Wen-Bin WU
188	The Absorption of Mercury Of "Zuo Ta" in the Small Intestinal	Chengdu University of Traditional Chinese Medicine	Sichuan	Yong ZENG
189	Prenylflavones from Epimedium for Breast and Prostate Cancer	National University of Singapore	Singapore	Eu-Leong YONG
190	Effects of Resveratrol on Pressure Overload-induced Cardiac Hypertrophy and Apoptosis in a Rat Abdominal Aortic Constriction Model	China Medical University	Taichung	Chih-Yang HUANG
191	Sesamin Reduces Cardiac Hypertrophy in a Rat Coronary Artery Ligation Model	China Medical University	Taichung	Chih-Yang HUANG
192	Evaluation of Vasorelaxation and Antioxidant Activity of Rhodiola Rosea	China Medical University	Taichung	Daih-Huang KUO
193	Laser-induced Carotid Artery Injury Model in Rat to Study the Effects of Ferulic Acid	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
194	Anti-Inflammation Effects of Andrographolide Attenuates Hepatic Angiogenesis and Fibrogenesis in Thioacetamide-Induced Liver Injury Mice	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG

195	2-Methoxystypandrone Represses RANKL-induced Osteoclastogenesis	National Research Institute of Chinese Medicine	Taipei	Wen-Fei CHIOU
196	Lipucan® Stimulates Glucose Uptake through Enhanced GLUT4 Expression and Translocation	Sinphar Pharm. Co. Ltd	Taipei	Muh-Hwan SU
197	The Importance of the Metabolic Regulation of Critical Dioxygenases in Cancer and Other Chronic Diseases by Botanicals	University of Alabama at Birmingham	USA	Stephen BARNES

Biological Activities and Mechanism Study IV (Immunomodulation)

No.	Title	Institute	Region	Corresponding Author
198	The Yin and Yang Actions of North American Ginseng Root in Modulating the Immune Function of Macrophages	The University of Western Ontario	Canada	Edmund LUI
199	The Study of RNAi System Inhibited the Expression of IL-1RI in Human Rheumatoid Arthritis Fibroblast-like Synovial cell	Guangzhou University of TCM	Guangdong	Jun-Hua ZHUANG
200	Schisandra Sphenanthera Extract (SchE) is a Promising Tacrolimus-Sparing Agent for Renal Transplant Recipients	Sun Yat-sen University	Guangdong	Min HUANG
201	Amelioration Collagen-induced Arthritis in Rats by Sinomemine through Regulation of MMPs, TIMPs, and Cytokines	Hong Kong Baptist University	Hong Kong	Liang LIU
202	A Simplified Method for Quantifying Cell Migration/ Wound Healing in 96-well Plates	Hong Kong Baptist University	Hong Kong	Ricky Ngok-Shun WONG
203	Novel Anti-Inflammatory and Analgesic Effects of Plumbagin through Inhibition of Nuclear Factor-kappa B Activation	Hong Kong Baptist University	Hong Kong	Hua ZHOU
204	Immunomodulatory Activities of Ganoderma Sinense	The Chinese University of Hong Kong	Hong Kong	Clara LAU
205	Investigation of the Immunomodulatory Effects of Radix Astragali Targeting Dendritic Cells	The Hong Kong Polytechnic University	Hong Kong	Daniel Man-Yuen SZE
206	Differential Effects of Radix Paeoniae Rubra on Cytokine and Chemokine Expression Inducible by Mycobacterium	The University of Hong Kong	Hong Kong	Allan SY LAU
207	Recent Progress on Elucidation of Immunomodulating Activity and its Action Mechanism of Kampo (Japanese Herbal) Medicines	Kitasato University	Japan	Haruki YAMADA

208	Bioactivity Guided Evaluation of Sesquiterpenes as an Anti-inflammatory Activity Isolated from Cyperus Rotundus L: Effect of Chemical Structures and Cellular Signaling Pathway	Seoul National University	Korea	Yeong-Shik KIM
209	Suppression of LPS-induced Inflammatory and NF-ĸB Responses in RAW 264.7 Macrophages by Anomalin Isolated from the Root of Saposhnikovia Divaricata	Seoul National University	Korea	Yeong-Shik KIM
210	Novel Labdan Diterpene Derivative Isolated from Leonurus Japonicum as a Function of Anti-inflammatory Activity in LPS-stimulated RAW 264.7 Cells	Seoul National University	Korea	Yeong-Shik KIM
211	Panax Notoginseng Reduces Atherosclerotic Lesions in apoE-deficient Mice and Inhibits TNFa-induced Endothelial Adhesion, Molecular Expression and Monocyte Adhesion	University of Macau	Macau	Simon Ming-Yuen LEE
212	The Effects of Mitragynine on the Expression of COX-1 and COX-2 in LPS-stimulated RAW264.7 Macrophage Cells	Malaysian Institute of Pharmaceuticals and Nutraceuticals	Malaysia	Mohamed Isa ABDUL MAJID
213	Anti-Malarial Drug Artesunate Attenuates Allergic Airway Inflammation and Inhibits Phosphoinositide 3-kinase Pathway in Mouse Asthma Model	National University of Singapore	Singapore	Fred W.S. WONG
214	Identification of the Immunomodulatory Ingredients in Semen Cuscutae	China Medical University	Taichung	Ming-Kuem LIN
215	Carthamus Tinctorius L Attenuates Lipopolysaccharide-Induced Cardiomyocyte Fibrosis Via Down-Regulating the Expressions of uPA, MMP-2, MMP-9	China Medical University	Taichung	Wen-Huang PENG
216	Stimulatory Effect of Echinacea purpurea Extract on Trafficking Activity in Mouse Dendritic Cells: Revealed by Genomic and Proteomic Analyses	Academia Sinica	Taipei	Ning-Sun YANG
217	The Inhibitory Effect of Phytocompound Cytopiloyne on Cytokine Expression and its Signal Transduction Mechanism in Dendritic Cells	Academia Sinica	Taipei	Ning-Sun YANG
218	Anti-inflammatory Effect of Specific Herbal Extracts in Skin and Colon-associated Inflammatory Disease Models	Academia Sinica	Taipei	Ning-Sun YANG
219	Specific Herbal Extract (PE) Suppresses NF-κB-mediated Inflammation in Murine Macrophages and in Mouse Skin	Academia Sinica	Taipei	Ning-Sun YANG

Clinical Trial I (Safety and Other Diseases)

No.	Title	Institute	Region	Corresponding Author
220	The TCM Five-pattern Personality Characteristics of Depressed Patients	China Academy of Chinese Medical Science	Beijing	Xue-Yu LV
221	Risk Factors of Gastrointestinal and Hepatic Adverse Drug Reactions in the Treatment of Rheumatoid Arthritis	China Academy of Chinese Medical Science	Beijing	Miao JIANG
222	Impact of Doctor's Identification on TCM Syndrome (Pattern) Differentiation	China Academy of Chinese Medical Science	Beijing	Meng-Yu LIU
223	Extraarticular Symptoms could Influence ACR Response in the Treatment of Rheumatoid Arthritis with Biomedicine	China Academy of Chinese Medical Science	Beijing	Ai-Ping LU
224	The Effect of Tangshen Formula on Patients with Type 2 diabetic Kidney Disease: a Multicentric Randomized Placebo-Controlled Trial	China-Japan Friendship Hospital	Beijing	Ping LI
225	Excretion of Urinary Glycosaminoglycans in Type 2 Diabetic Nephropathy	China-Japan Friendship Hospital	Beijing	Ping LI
226	Clinical Study on BuShenQiangDuZhiLiu Decoction in the Treatment of Ankylosing Spndylitis	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Yi-Ting HE
227	Review and Comparison of Commonly Used Casual Relationship Standard of Adverse Drug Reactions in TCM Clinical Trials	Guangzhou University of Traditional Chinese Medicine	Guangdong	Xin-Feng GUO
228	Efficacy of a Chinese Herbal Proprietary Medicine (Hemp Seed Pill) for Functional Constipation. A randomized, Double-blind, Placebo Controlled Clinical Trial	Hong Kong Baptist University	Hong Kong	Zhao-Xiang BIAN
229	Systematic Review on the Efficacy and Safety of Herbal Medicines for Vascular Dementia	Hong Kong Baptist University	Hong Kong	Min LI
230	Developmental Toxicity of Chinese Herbs: A Review of Experimental Studies	Hong Kong Baptist University	Hong Kong	Min XU
231	Herbal TMGT decoction in the Treatment of Hypertension: A Meta-analysis	Hong Kong Baptist University	Hong Kong	Min XU
232	Herbal XFZY decoction in the Treatment of Coronary Artery Disease: A Meta-analysis	Hong Kong Baptist University	Hong Kong	Min XU
233	The Safety Assessment of Radix Dipsaci in Embryonic Development of Mice	Hong Kong Baptist University	Hong Kong	Min XU
234	Recent Situation of Manipulation of Osteoarthritis of Knee	Hong Kong Baptist University	Hong Kong	En ZHU

235	Using Chinese Version of MYMOP in Chinese Medicine Evaluation: Validity, Responsiveness and Minimally Important Change	The Chinese University of Hong Kong	Hong Kong	Vincent CHUNG
236	Evaluation of the Pharmacological Activities of Traditional Chinese Medicine in the Amelioration of Symptoms of Allergic Asthma	The Chinese University of Hong Kong	Hong Kong	Clara LAU
237	Development of Biomarker for the Assessment of Pyrrolizidine Alkaloid-Containing Herbal Medicine Induced Hepatotoxicity	The Chinese University of Hong Kong	Hong Kong	Ge LIN
238	A Double-Blind, Randomized, Placebo-Controlled Trial to Evaluate the Effect of Multi-herb Mixture, NM_KIDS_042 on the Height Growth in Elementary School Children	Kyung Hee University	Korea	Hocheol KIM
239	Studies on the Curative Effects of Wu Xing Jian Gu Exercise to Patients with Osteoporosis	Shanghai University of Traditional Chinese Medicine	Shanghai	Xiao SHI
240	Some Methodological Issues in Clinical Trials for the Treatment of Syndromes in Traditional Chinese Medicine	Nanyang Technological University	Singapore	Hai HONG
241	Comparison of Chinese Herbal Formula and Laxatives for Residents with Chronic Constipation in Long-term Care: A Randomized, Double-blind, Placebo-controlled Trial	China Medical University	Taichung	Yi-Chang SU
242	An Twelve-week, Randomized, Double-blind Study to Evaluate the Efficacy and Tolerability of Danshen (Salvia Miltiorrhiza) as Add-on Therapy in Taiwanese Patients with Essential Hypertension	Chung Shan Medical University	Taichung	James Cheng-Chung WEI
243	Effect of Green Tea Extract on Obese Women: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial	National Yang-Ming University	Taipei	Chung-Hua HSU
244	An Open, Single Arm, Multi-center, 12-Week Phase IV Study to Evaluate the Efficacy and Safety Profiles of Memoregain® in Subjects with Mild to Moderate Vascular Dementia	Sinphar Pharm. Co. Ltd	Taipei	Muh-Hwan SU
245	Treatment of Osteoarthritis with HLXLD: A Translational TCM Study in the US	Harvard Medical School	USA	David Y-W. LEE

Clinical Trial II (Cancer & Liver Inflammation)				
No.	**Title**	**Institute**	**Region**	**Corresponding Author**
246	Clinical Study of Elemene Injection Combined with Radiotherapy in Treatment for Non-small-cell Lung Carcinoma Patients with Brain Metastasis (BM-NSCLC)	Guang'an men Hospital, China Academy of Chinese Medical Sciences	Beijing	Wei HOU
247	Evidence-based Medical Study of TCM on Non Small Cell Lung Cancer	Guang'an men Hospital, China Academy of Chinese Medical Sciences	Beijing	Hong-Sheng LIN
248	A Comparative Study on the Methods of TCM and Western Medicine Therapeutic Evaluation of Advanced Non-small Cell Lung Cancer	Guang'an men Hospital, China Academy of Chinese Medical Sciences	Beijing	Pei-Tong ZHANG
249	The Distribution of Traditional Chinese Medicine Constitution and Prognosis Analysis in Primary Liver Cancer	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Shun-Qin LONG
250	The Retrospective Analysis of TCM Syndrome Types Associated with Adverse Reactions after Chemotherapy who were Advanced Large Intestine Cancer	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Liu-Nig LI
251	Combination of Chinese Herbs with Gefitinib as the First-line Treatment for Patients with Advanced Non-small Cell Lung Cancer	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Wan-Yin WU
252	Clinical Research on External High Frequency Thermotherapy plus TCM Differentiation for Treating Advanced Non-small Cell Lung Cancer	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Wan-Yin WU
253	Effect and Advantage of Orally Taking Chinese Herbal Medicine for Treatment of Lung Cancer	Hong Kong Baptist University	Hong Kong	Liang LIU
254	Correlational Study on the Five Personalities and Breast Cancer	The University of Hong Kong	Hong Kong	Jian-ping CHEN
255	Phase II Clinical Efficacy and Safety of SR-T100 in the Treatment of Actinic Keratosis	G&E Herbal Biotechnology Co.,Ltd	Tainan	Kou-Wha KUO
256	Phase I/II Study of PHY906 Plus Capecitabine (CAP) in Patients with Gemcitabine-refractory Pancreatic Cancer (PC)	Yale University	USA	Muhammad W. SAIF

Education

No.	Title	Institute	Region	Corresponding Author
257	Evolution of an Integrative Oncology Research and Education Program that includes Chinese Medicine within the Department of Oncology at McMaster University	McMaster University	Canada	Stephen SAGAR
258	Introduction to Natural Therapies for Health Preservation in Chinese Medicine	Hong Kong Baptist University	Hong Kong	Yi DANG
259	Internationalization of Chinese Medicine ---- International Education of Chinese Medicine	Hong Kong Baptist University	Hong Kong	Yi DANG
260	Flower Therapy for Health Preservation	Hong Kong Baptist University	Hong Kong	Yi DANG
261	New Area of Chinese Medicine Education --- Launching the Program of Master of Science in Personal Health Management (Chinese Medicine) in China	Hong Kong Baptist University	Hong Kong	Yi DANG
262	Emotionless Holism: Factor and Rasch Analysis of the Chinese Integrative Medicine Attitude Questionnaire	The Chinese University of Hong Kong	Hong Kong	Vincent CHUNG
263	Developing Ontological Search Engine for Global Access Portal of Academic TCM Websites	The Hong Kong Polytechnic University	Hong Kong	Lawrence Wing-Chi CHAN
264	The Research on Human Rights Protection of Chinese Elderly Patients with Alzheimer's: Case Studies	University of Macau	Macau	Chun-Huan LAO
265	First Master Degree of TCM in Europe	University of Porto	Portugal	Henry Johannes GRETEN
266	Comparison of Chinese Medicine Education in Different Countries	China Medical University	Taichung	Yi-Chang SU

Herbal Resources I (Cultivation and Herbal Quality)

No.	Title	Institute	Region	Corresponding Author
267	Amount of Alkaloids in Processed Aconite Roots: Comparison of Specific Hplc Determination of Toxic Aconite Alkaloids with a Titration Method of Total Alkaloids	TCM Research Center Graz	Austria	Rudolf BAUER
268	Phylogeny and Cultivation Origination of Medicinal Plants of Genus Coptis	China Academy of Chinese Medical Sciences	Beijing	Lu-Qi HUANG
269	Introducing Novel Herbal Products in Canada: Safety, Quality, and Efficacy by Controlled Environment Production and Chemical Profiling	University of Guelph	Canada	Praveen SAXENA

270	Quality Evaluation of Radix Polygoni Multiflori and its Dregs by Determination the Contents of Stilbene Glucoside, Emodin and Physcion	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
271	Traditional Experiences and Modern Understanding of Morphological Identification of Chinese Materia Medica	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
272	Molecular Authentication of the Chinese Herb Huajuhong and its Antimicrobial Activity against Pathogenic Microorganisms	The Chinese University of Hong Kong	Hong Kong	Pang-Chui SHAW
273	Study on Quality Specification of Isatis Indigotica	Shanghai University of Traditional Chinese Medicine	Shanghai	Rui WANG
274	Genetic Diversity and Relationship of Fritillaria Thunbergii Landraces and Related Taxa	Tongji University	Shanghai	Zhou CHENG
275	Cloning and Molecular Characterization of Microsomal Oleate Desaturase Gene (FAD2) from Safflower (Carthamus Tinctorius L.)	Sichuan Agricultural University	Sichuan	Wei WU
276	An Observation for the Cultivation of TCM Herbs	Kunming Institute of Botany, Chinese Academy of Sciences	Yunnan	Chong-Ren YANG

Herbal Resources II (Identification and Manufacturing)

No.	Title	Institute	Region	Corresponding Author
277	A gDNA Microarray for Genotyping Danshen (Salvia Miltiorrhiza) and Other Economically-important Salvia Species	RMIT University	Australia	Alexandra Cristina OLARTE GUASCA
278	Study on Extracting Magnolia Officinalis by Using O/W Microemulsion	China Academy of Chinese Medical Science	Beijing	Hua YANG
279	Study on Extracting Angelica Sinensis by Using O/W Microemulsion	China Academy of Chinese Medical Science	Beijing	Hua YANG
280	Screening of Bioactive Components in Cerebrospinal Fluid after Administration of Chinese Medicine	China Academy of Chinese Medical Sciences	Beijing	Peng ZHANG
281	Use of ITS2 Region as the Universal DNA Barcode for Plants and Animals	Chinese Academy of Medical Sciences & Peking Union Medical College	Beijing	Shi-Lin CHEN
282	The Strategies on Medicinal Plant Genome Sequencing Project	Chinese Academy of Medical Sciences & Peking Union Medical College	Beijing	Shi-Lin CHEN

283	Flow Cytometric Analysis of Nuclear DNA Content in Poria cocos	Chinese Academy of Medical Sciences & Peking Union Medical College	Beijing	Shi-Lin CHEN
284	Studies on Macroscopic and Microscopic Identification of Cordyceps Sinensis and its Counterfeits	Hong Kong Baptist University	Hong Kong	Hu-Biao CHEN
285	The Study of Hong Kong Chinese Materia Medica's Concocted Processing Characteristics	Hong Kong Baptist University	Hong Kong	Hu-Biao CHEN
286	Microscopic Study on the Bark of Schefflera Octophylla and Bombax Malabaricum	Hong Kong Baptist University	Hong Kong	Hu-Biao CHEN
287	Differentiation of the Sweet and Bitter Variants of Gynostemma pentaphyllum Based on their Distinct Triterpenoid Saponin Profiles and Ribosomal DNA Sequences	Hong Kong Baptist University	Hong Kong	Wendy Wen-Luan HSIAO
288	A Statistic Analysis for the Development of TCM Products	Hong Kong Baptist University	Hong Kong	Zhijun YANG
289	Authentication of Chinese Materia Medica Decoction Dregs by the Comparison of Morphological and Microscopic Characteristics before and after Decoction	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
290	The Application of Fluorescence Microscopy in the Authentication of Dregs and Processed Products of Chinese Materia Medica	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
291	Identification of Powdered Chinese Materia Medica by Fluorescence Microscopy	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
292	Microscopic Identification of Commonly Used Chinese Materia Medica in Hong Kong	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
293	Market Investigation and History of Spicy and Aromatic Chinese Medicinal Materials	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
294	Macroscopic Identification of Chinese Medicinal Materials in Commerce	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
295	Ethnobotanical Study of 24-Herb Liangcha Used by Cantonese in Lingnan	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
296	Application of Forensically Informative Nucleotide Sequencing (FINS) in the Identification of Traditional Chinese Medicine	The Chinese University of Hong Kong	Hong Kong	Pang-Chui SHAW

297	Research and Development on the Taiwanese Traditional Chinese Medicinal Crop-salvia Miltiorrhiza (Tanshen): Chemical Profiling	Kaohsiung Medical University	Kaohsiung	Fang-Rong CHANG
298	Effect of Polygala Tenuifolia on Penile Erection and Isolation of Two Phenolic Glycosides by HSCCC	Kyung Hee University	Korea	Hocheol KIM
299	Discrimination of Polygonum Mulfiflorum, Cynanchum Wilfordii and Cynanchum Auriculatum by Genetic and Chemical Analysis	National Institute of Food and Drug Safety Evaluation	Korea	Young-Hun SHIM
300	The Preparation and Application of Continuous Two-dimensional Open-tubular Ion Exchange / Reversed Phase Monolithic Column Capillary Electrochromatography System	East China University of Science & Technology	Shanghai	Wei-Bing ZHANG
301	Characterization of the Components from Fuzheng Huayu Decoction in Rat Serum by High-Performance Liquid Chromatography–mass Spectrometry	Shanghai University of Traditional Chinese Medicine	Shanghai	Cheng-Hai LIU
302	Genetic Diversity and Effective Components of Cordyceps Sinensis Populations in China	Tongji University	Shanghai	Zhou CHENG
303	Rapid Identification of the Medicinal Plant Taraxacum mongolicum from its Adulterants by Ribosomal DNA Internal Transcribed Spacer (ITS)-Primed Polymerase Chain Reaction	China Medical University	Taichung	Meng-Shiou LEE

Herbal Resources III (Natural Products and Biological Activities

No.	Title	Institute	Region	Corresponding Author
304	The Effects of Qianlie-Bao Capsule on Animal Mode of Prostatic Hyperplasia and Prostatitis	China Academy of Chinese Medical Science	Beijing	Xiao-Hua HONG
305	Up-regulation of Licochalcone A Biosynthesis and Secretion by Tween 80 in Hairy Root Cultures of Glycyrrhiza Uralensis Fisch	National Engineering Research Center for Crop Molecular Design	Beijing	Jing-Mei LIU
306	Systems Chemistry: Systemic Properties and Energy Management in Bioactive Molecules	Global Institute of Computational Molecular and Materials Science	Canada	Gregory CHASS
307	Hyperglycemic Effects of Mangiferin Hydrastis Granulein in GK Rats with Diabetes Mellitu	Changchun University of Chinese Medicine	Changchun	Zhe LIN

308	A Traditional Chinese Patent Prescription, You-Gui-Wan, can Maintain the Balance of Sex Hormones and Alleviate the Atrophy of Sex Organs in Female Natural Aging Rats	Guangzhou University of Traditional Chinese Medicine	Guangdong	Mu-Rong YE
309	Xanthones from the Stems of Cratoxylum Formosum ssp. Pruniflorum and their RXRα Transcriptional Inhibitive Activities	Institute of Traditional Chinese Medicine and Natural Products, Jinan University	Guangdong	Xin-Sheng YAO
310	In Vitro Study on Kang Bin Du Granule against Swine-origin Influenza A Virus (A/ H1N1)	National Engineering Research Center for Modernization of Traditional Chinese Medicine	Guangdong	Hui CAO
311	Simultaneous Characterization of Hydrolysable Tannins, Naphthalene Derivatives and Flavonoids in Juglans Mandshurica by UPLC Coupled to ESI-Q-TOF-MS	Hong Kong Baptist University	Hong Kong	Hu-Biao CHEN
312	New Acylated Protopanaxadiol-type Ginsenosides from the Root of Panax Ginseng	Hong Kong Baptist University	Hong Kong	Wang-Fun FONG
313	Synthesis and DNA G-quadruplex Binding Activity of Glucosaminoside Derivatives of Epigallocatechin in Green Tea	Hong Kong Baptist University	Hong Kong	Zhi-Hong JIANG
314	Potential Application of Traditional Medicine (TCM) for the Treatment of Methicillin-resistant Staphylococcus Aureus (MRSA) Infections – Bioassay-guided Fractionation of Sophora Flavescens Ait	The Chinese University of Hong Kong	Hong Kong	Ping-Chung LEUNG
315	Effect of the Seed of Nelumbo Nucifera, on Electric Stimulation-induced Penile Erection in Rats	Kyung Hee University	Korea	Hocheol KIM
316	Inhibitory Compounds on LPS-induced NO Production in BV-2 microglial Cells from Abies Koreana	Seoul National University	Korea	Jin-Woong KIM
317	Anti-obesity Effects of Dioscorea Opposita on High-fat Diet-induced Obesity in Mice and in Vitro Assays	Seoul National University	Korea	Jin-Woong KIM
318	Enzymatic Transformation of Platycosides and One-step Separation of Platycodin D by High-speed Counter-current Chromatography	Seoul National University	Korea	Yeong-Shik KIM
319	Platelet Anti-aggregation and Blood Anti-coagulant Effects of Compounds Isolated from Evodiae Fructus	Seoul National University	Korea	Hye Sook YUN-CHOI

320	Different Flavonoids from Hylocereus Undatus Flower	University of Macau	Macau	Qing-Wen ZHANG
321	Preparative Separation of Patchouli Alcohol from Essential Oil of Pogostemon Cablin Using High Performance Centrifugal Partition Chromatography	University of Macau	Macau	Qing-Wen ZHANG
322	The Use of Caenorhabditis Elegans as the Model for Anti-Infective Screening Assay	Malaysian Institute of Pharmaceuticals and Nutraceuticals	Malaysia	Tengku Sifzizul TENGKU MUHAMMAD
323	Analysis of Catalpol Derivatives by Characteristic Neutral Losses Using Liquid Chromatography Combined with Electrospray Ionization Multistage and Time-of-flight Mass Spectrometry	China Pharmaceutical University	Nanjing	Min-Jian QIN
324	Investigation on Material Foundation of Antioxidant and Anti-lung Cancer of Prunella Vulgaris L.	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Liang FENG
325	Current Research Status of Targeting Interference of Leukemia Stem Cell with Components from Natural Products	Jiangsu Provincial Academy of Chinese Medicine	Nanjing	Bin-Feng YANG
326	Lead Screening and Optimization Based on Traditional Chinese Medicine	Yantai University	Shandong	Ke LIU
327	Chemical Constituents of Psidium guajava L. and Verbena officinalis L., and Quality Evaluation of Herba Verbenae	Shanghai R&D Centre for Standardization of Traditional Chinese Medicine	Shanghai	Gui-Xin CHOU
328	Studies on the Chemical Constituents of Gentiana Crassicaulis	Shanghai R&D Centre for Standardization of Traditional Chinese Medicine	Shanghai	Zheng-Tao WANG
329	Yield and Components Comparison of Essential Oils Extracted from Six Citrus Cultivars	Tongji University	Shanghai	Xiao-Ling YANG
330	Hyperglycemic Effects of Mangiferin Hydrastis Granulein in GK Rats with Diabetes Mellitu	Changchun University of Chinese Medicine	Changchun	Zhe LIN
331	Five Kinds of Alkaloids from Rhizoma Coptis Improve Glucose Uptake of 3T3-L1 Cells without Adipogenesis Activity	Chengdu University of Traditional Chinese Medicine	Sichuan	Xianli MENG
332	Inhibition of NADPH Oxidase-produced Oxidative Stress-stimulated JNK/NFkB Signaling by Diallyl Trisufide (DATS) Suppresses High Glucose-induced Cardiomyocyte Apoptosis	China Medical University	Taichung	Wei-Wen KUO

333	Deoxyelephantopin Protects Mice from Lipopolysaccharide/D-Galactosamine - Induced Fulminant Hepatitis through Attenuating LPS, TNF-α, or IL-6 Mediated Signaling Pathways	Academia Sinica	Taipei	Lie-Fen SHYUR
334	Butanol Extract of Gentiana Scabra bge. has Immunomodulatory Effects and Attenuates Pathological Signs in MRL/lpr Mice	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
335	Andrographolide Inhibits iNOS Expression by Down-regulating LPS-induced Activity of NF-ĸB and Enhances Suppressor of Cytokine Signaling 3 in Raw 264.7 Cells	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
336	Benzoxazinoid Glycosides from Scoparia Dulcis	National Research Institute of Chinese Medicine	Taipei	Chia-Chuan CHANG
337	New Cytotoxic Prostanoids from Taiwanese Soft Coral Clavularia Viridis	National Taiwan University	Taipei	Ya-Ching SHEN
338	Nortriterpene Lactones from the Fruits of Schisandra Arisanensis	National Taiwan University	Taipei	Ya-Ching SHEN
339	Anticancer and Anti-AIDS Clinical Trials Candidates from Traditional Chinese Medicine (TCM)	University of North Carolina at Chapel Hill	USA	Kuo-Hsiung LEE
340	Hepatoprotective and Antioxidant Effects of the Methanolic Extract from Halenia Elliptica	Wuhan University	Wuhan	You-Wei WANG
341	Extracts of Halenia Elliptica Exhibit Antioxidant Properties In Vitro and In Vivo	Wuhan University	Wuhan	You-Wei WANG
342	Chemical Constituents from Kadsura Species and their Bioactivities	Kunming Institute of Botany, Chinese Academy of Sciences	Yunnan	Han-Dong SUN
343	Identification of Tylophorine Compounds as Novel Potent Anti-Coronaviral Agents for Porcine Enteropathogenic Coronavirus Transmissible Gastroenteritis Virus and Human Severe Acute Respiratory Syndrome Coronavirus	National Health Research Institutes	Zhunan	Shiow-Ju LEE
344	Isolation and Evaluation of Biological Activities In Vitro and In Vivo of Phenanthroindolizidine and Septicine Alkaloids from Formosa Tylophora Ovata	National Health Research Institutes	Zhunan	Shiow-Ju LEE

Industry and Academic Collaborations

No.	Title	Institute	Region	Corresponding Author
345	A Case Study of the Key Factors of Globalization of TCM Enterprises	University of Macau	Macau	Hao HU
346	Location-quotient Based Analysis of Industry Structure of Traditional Chinese Medicine in China	University of Macau	Macau	Yi-Tao WANG
347	The Potential Use of Traditional Chinese Medicines in Finding Telomerase Activators	Sierra Sciences, LLC	USA	William ANDREWS

International Collaborations

No.	Title	Institute	Region	Corresponding Author
348	Interaction of Traditional Chinese Medicine Components with Phospholipid Bilayers	Fuzhou University	Fujian	Pingfan RAO
349	The new HanseMerkur Centre for TCM at the University Medical Centre (UKE) in Hamburg	HanseMerkur Centre for Traditional Chinese Medicine at the University Medical Centre, Hamburg Eppendorf (UKE)	Germany	Roland SALCHOW
350	An Investigation of Contemporary Medicinal Plants Based on International Collaborations	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
351	Heritage, Medicinal Material Resources and Our Efforts	Hong Kong Baptist University	Hong Kong	Zhong-Zhen ZHAO
352	Cochrane Reviews for Clinical Trials of Traditional Chinese Medicine	The Chinese University of Hong Kong	Hong Kong	Chi-Chiu WANG
353	Establishment of Sasang Constitutional Medicine Clinical Research Collaboration in Korea	Korea Institute of Oriental Medicine	Korea	Si-Woo LEE
354	Global Development and Influential Countries in Acupuncture Research: A Statistical Analysis	University of Macau	Macau	Yi-Tao WANG
355	Open Access Journals and Globalization of Chinese Medicine	University of Macau	Macau	Hin-Wing YEUNG
356	Qualitative Research Methods as Useful Tools to Explore Chinese Medicine in Beijing and London	Thames Valley University	UK	Nicola ROBINSON

Objective and Standard Assessments of Diagnosis in TCM

No.	Title	Institute	Region	Corresponding Author
357	Objectification of TCM Four Diagnostic Methods in Sub-Health State Research	Beijing University of Chinese Medicine	Beijing	Jia-Xu CHEN
358	A New Platform for Information Extraction and Analysis of Pulse-diagnosis in TCM and it's Applications in Clinic	China Academy of Chinese Medical Science	Beijing	Nan-Yue WANG
359	Canonical Correlation Analysis of TCM Syndrome and Related Laboratory Parameters in 350 Patients with Diabetic Kidney Disease	China-Japan Friendship Hospital	Beijing	Ping LI
360	A Study on the Characteristic and Regularity of Distribution of TCM Syndromes in Patients with Ischemic Stroke	Guangdong Provincial Hospital of Traditional Chinese Medicine	Guangdong	Yan HUANG
361	Patient-Reported Outcome Scales may be Developed for Assessment of TCM Syndromes	The University of Hong Kong	Hong Kong	Run-Qiu CHEN
362	Parametrizing the TCM Diagnosis by Decoding the Physiology of Yin, Yang and the Phases	University of Porto	Portugal	Henry Johannes GRETEN
363	Pulse Waveform Recognition Using Fisher Linear Discriminant in Traditional Chinese Medicine Based on Hemodynamics Principle	Shanghai University of Traditional Chinese Medicine	Shanghai	Yi-Qin WANG
364	Research on TCM Syndromes of CHD Inquiry Based on Latent Structure Model	Shanghai University of Traditional Chinese Medicine	Shanghai	Yi-Qin WANG
365	Development of Body Constitution Questionnaire (BCQ) in Traditional Chinese Medicine	China Medical University	Taichung	Yi-Chang SU
366	Image Processing for Tongue Diagnosis in TCM	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
367	The Nailfold Capillary Microscopic Patterns of Raynaud's Phenomenon in Patients with Systemic Lupus Erythematosus and Progressive Systemic Sclerosis --- An Integrative Medicine View	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
368	Voice Analysis on Patients with Obstructive Sleep Apnea Syndrome	Chang Gung Memorial Hospital	Taipei	Hen-Hong CHANG
369	Quantitative Evaluation of Pathological and Pharmacological Effects on Meridians with Harmonic Pulse apparatus	Taipei Medical University	Taipei	Yu-Cheng KUO

Quality Control (Methodology)

No.	Title	Institute	Region	Corresponding Author
370	Analysis of Regional and Seasonal Variation of Triterpene and Flavonoid Contents in Centella asiatica by High Performance Liquid Chromatography and Chemometric Analysis	The University of Sydney	Australia	George LI
371	Simultaneous Determination of Lithospermic Acid, Rosmaric Acid, Salvianolic Acid B and Salvianolic Acid A in Dog Plasma by HPLC-MS/MS	China Academy of Chinese Medical Sciences	Beijing	Li LIN
372	Simultaneous Determination of Berberine, Dehydrocorydaline, Palmatine and Tetrahydropalmatinein in Dog Plasma by HPLC-MS/MS	China Academy of Chinese Medical Sciences	Beijing	Jian-Xun LIU
373	On the Clinic-combined Standardization of Chinese Medicines	PLA Institute of Chinese Materia Medica	Beijing	Xiao-He XIAO
374	Investigation on HPLC Fingerprint of TCM Prescription "Xiaoyanlidan Tablet" (XYLD) on Market	Institute of Traditional Chinese Medicine and Natural Products, Jinan University	Guangdong	Xin-Sheng YAO
375	Development And Validation of a LC-MS/MS Method for Simultaneous Determination of Six Schisandrins in Wuzhi Tablet	Sun Yat-sen University	Guangdong	Min HUANG
376	Determination on the Contents of Tannins of Sanguisorba Officinalis L.	Sun Yat-sen University	Guangdong	Dong-Mei WANG
377	Separation and Quantification of Monosaccharide Compositions of Astragalus Polysaccharide by Precolumn Derivation HPLC	Hong Kong Baptist University	Hong Kong	Hu-Biao CHEN
378	Chemical Authentication of Sweet and Bitter Gynostemma Pentaphyllum (Thunb.) Makino	Hong Kong Baptist University	Hong Kong	Zhi-Hong JIANG
379	Unveiling the Significance of the Constituents Towards Bioactivity in Natural Products	The Hong Kong Polytechnic University	Hong Kong	Foo-Tim CHAU
380	Gold-Nanoparticles Assisted Laser Desorption/Ionization Imaging Mass Spectrometric Analysis of American Ginseng and Cordyceps	The University of Hong Kong	Hong Kong	Kwan-Ming NG
381	Quality Assessment of RCTs on Danshen Dripping Pills (DSP) in Treating Angina Pectoris	University of Macau	Macau	Yong-Liang JIA

382	Free Radical Scavenging Activity and their Contents of Seven Flavonoids in Eagle Tea	University of Macau	Macau	Shao-Ping LI
383	Study on Qualitative Analysis of Polysaccharides from Chinese Medicines	University of Macau	Macau	Shao-Ping LI
384	Quality Control of the Commonly Used Traditional Chinese Medicine in Taiwan	China Medical University	Taichung	Shu-Jen CHANG
385	Multivariate Data Analysis Using High Performance Liquid Chromatographic, Nuclear Magnetic Resonance Spectroscopic and Infrared Spectroscopic Methods on the Quality Control of Danshen Products	King's College London	UK	Hui-Ying ZHAO
386	Determination of Tanshinone Iia, Salvianolic Acid B and Sodium Danshensu in Salvia Miltiorrhiza Bunge with Different Preparation Methods	King's College London	UK	Jue ZHOU

Regulatory Affairs

No.	Title	Institute	Region	Corresponding Author
387	Is there a Possibility to Register Chinese TCM in Europe?	Sino-European Therapeuticals R&D	France	Li-Ya LU

Acupuncture Session

001

Teleacupuncture bridges science and practice

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Teleacupuncture includes the assisted transmission of biological data over a distance. In 2009, the first teleacupuncture between China and Austria was performed.

In this pilot study first 24-hour ECG (electrocardiogram) recordings registered at the China Academy of Chinese Medical Sciences in Beijing are presented. The ECG was recorded with a sampling rate of 4096 Hz using a system partially developed in Austria (medilog AR 12, Huntleigh Healthcare, Cardiff, UK). The raw data were transferred via internet to the TCM Research Center Graz in Austria from the patients' site computer in Beijing to the control site computer in Graz (distance: 7,650 km). Data analysis of different parameters of heart rate (HR) and heart rate variability (HRV) in the time and frequency domain [1] was performed immediately for control of possible therapeutic effects of acupuncture. The acupuncturist and the monitoring expert were informed about the findings immediately and the success of the therapy could be demonstrated objectively [2,3].

For the spectral analysis of heart rate variability a new method, the so-called 'Fire of Life' illustration, was applied. The state of health of a 31-year-old patient before, during and after acupuncture treatment sessions was documented. Despite several limitations, transcontinental teleacupuncture opens up new possibilities in public health. This could probably be useful under special circumstances (cooperation between experts from different continents) as demonstrated in our Sino-Austrian collaboration.

The investigations are part of the project "Bioengineering and clinical assessment of high-tech acupuncture – a Sino-Austrian research pilot study", supported by the Austrian Federal Ministries of Science and Research and of Health and the Eurasia Pacific Uninet, and of project no. 13463 supported by the Jubilaeumsfonds of the Oesterreichische Nationalbank.

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2. Valentini J (2010) Transcontinental teleacupuncture between Beijing and Graz: A contribution to needle and laser acupuncture research. Diploma thesis, Medical University of Graz.
3. Litscher G (2010) Translational research in acupuncture – teleacupuncture bridges science and practice. Health 2(1):16-19.

002

Clinical Observation on 40 Cases of Eczema Treating by Integrated Herbal Medicine and Acupuncture

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Objective: To evaluate the clinical effect of an integrated therapy of Herbal Medicine and Acupuncture for treating Eczema. **Methods:** 40 cases were randomly assigned to two groups: 20 cases in herb-acupuncture group (therapeutic group) and 20 in simple herb group (control group). Clinical data before and after and treatment were carefully observed, and were assessed by the statistical model of average ± Standard deviation. χ^2 test was employed to analyze the non-graded data, analysis of variance and t test were employed to analyzed the graded data. **Results:** The total effective rate of therapeutic group was 95%. Statistical difference was detected in comparison of symptomatic effect of rash morphology from the two groups (x^2=4.80, P = 0. 0.028). The observation indicated that after half-year treatment, the average clinical pathology scores of eczema reduced in therapeutic group, which was significantly different from that of the control group. **Conclusion:** The integrated therapy of herbal medicine and Acupuncture had better effect than the simple herb group for improving the rash morphology of Eczema.

Keywords: Eczema; Combination of Herbal Medicine and Acupuncture; clinical observation.

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003

Comparing the Efficacy of Traditional Fire-cupping and Vacuum-cupping

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The goal of this study is to investigate and compare the effects of *fire-cupping* and *vacuum-cupping,* by evaluating increase in local blood perfusion.

Methods: 10 females and 3 males (average age 35 years) were enrolled in the experiment. Using the especially developed jars with manometer, each of the volunteers was given traditional fire-cupping on the left side of the back first, and the pressure in the jars was measured. Then vacuum-cupping was applied on the other side of the back and the pressure was adjusted to that of the fire-cupping jars. Both jars were the same size and stayed on the back for 5 minutes. Changes of local capillary perfusion of the body surface were observed with Laser Doppler Perfusion Imaging (LDPI) before applying the jars, having just removed the jars, and furthermore 5 minutes and 20 minutes after removal of the jars.

Results: Elevation of local blood perfusion with vacuum-cupping was of longer duration and more pronounced than that of traditional fire-cupping, but for both methods, the instant efficacy was the same.

Conclusion: Although Chinese patients generally still prefer the traditional method of fire-cupping, the new vacuum-cupping method can enable a more standardized and faster procedure in future.

Keywords: fire-cupping, vacuum-cupping, LDPI

The investigations are part of the project "Bioengineering and clinical assessment of high-tech acupuncture – a Sino-Austrian research pilot study" and supported by the Eurasia Pacific Uninet.

004

Experimental Study of Effect of Electro-Bian Stone on the Local Blood Perfusion of the Back of the Crus

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Objective To observe the effect of electro-bian stone on the blood perfusion of the back of the crus and to investigate the mechanism of contralateral meridian needling therapy at the thermal stimulus condition. **Methods** Stimulation the area of the back of the right crus (take the midpoint of popliteal space to the achilles's tendon as the center) by the 45℃ Bian stone, and then observe the change of blood perfusion in the area of the correspondent area of the left crus and periumbilicus with laser doppler blood perfusion imaging system. We use local skin blood perfusion on the left relevant position under rest state as control. **Results** The blood perfusion of the back of the left crus not increased remarkably under rest state ($P>0.05$). After the thermal stimulus on the right side, the blood perfusion of the back of the left crus increased remarkably in the seventh minute, there was statistically significant difference (compard with the control group, $P<0.05$), and within 4-30 minutes after thermal stimulus, the blood perdusion not be remarkably attenuated(compard with post 1min, $P<0.05$). **Conclusions** Electro-Bian stone thermal stimulus therapy can increase the opposite side skin blood perfusion of the back of the crus.

Keywords: Local skin blood perfusion ; Electro-bian stone ; contralateral meridian needling ; Laser doppler perfusion imaginge.

005

Research Advancement on Epilepsy Treatment by Acupuncture

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It is concluded that one of the main causes for the failure to treat epilepsy is the tolerance to Antiepileptic Drugs (AEDS) in the research to stubborn epilepsy in recent years.The pathology base is the overexpression of multidrug resistance gene 1 (MDR1). Like the other kind of operations, vagal nerve stimulation (VNS) is a kind of exact therapy for some kind of patients.However, it is prevented from popular use because of high price and high risk. Based on the research result of Auriculo-vagi-visceral Reflex,we concluded that the stimulation of Electro-acupuncture to the branch of vagus in ears would activate the neuron of nucleustractussolitarii (NTS) to discharge and then the epilepsy could be controlled by the desynchronization of electroencephalogram since there exists widely connection between NTS and the other part of brain.We believe that the auricular acupuncture therapy is a kind of effective method to stubborn epilepsy since the mechanism of action is similar to that of VNS. So we carried on the further clinical research aiming at the patients of partial epilepsy who have taken anticonvulsants regularly 1 year or more,aging between 12 and 65 years old, and tumor,progressive encephalopathy,progressively neurodegenerative disorder etc. are excluded. Anticonvulsants continue during the period of research.We can observe that the frequency of epilepsy seizures is less now than before in a part of patients until now.Compared with NVS, the Electro-acupuncture to the branch of vagus is cheap,safe and could be operated conveniently.

006

Revealing acupuncture meridian-like system by reactive oxygen species visualization

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To investigate the reactive oxygen species (ROS) distribution in living animal tissues, two ROS indicators, dichlorofluorescin diacetate (DCFH-DA) and MitoSOXTM Red were applied to visualize ROS on the frontal interior abdominal wall of living SD-rats by tail vein injection and local smearing respectively. Revealed was an unexpected ROS distribution pattern. ROS were demonstrated in a few vertical fluorescent lines, which related to neither veins nor nerves but could be almost perfectly superimposable on a standard human acupuncture meridian network. The phenomenon that cells with high ROS content should be aligned in a regular manner is interesting as well as its resemblance to meridian system.

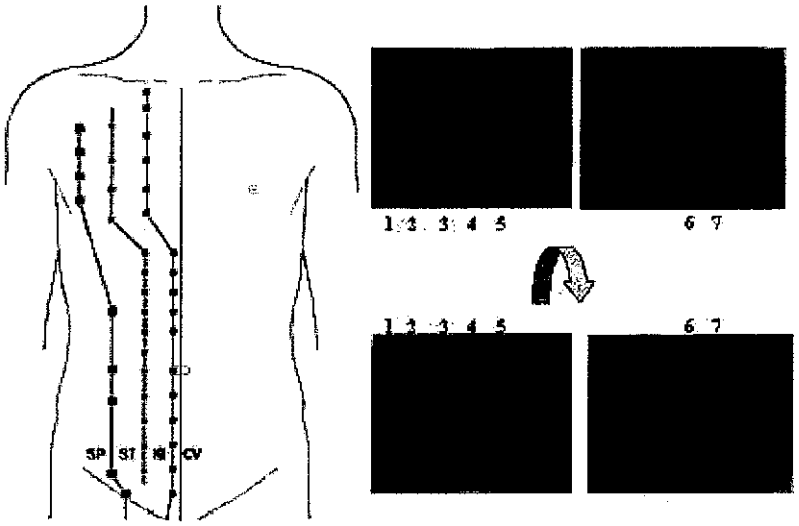

Figure 1 Illustrations for location of human acupuncture meridian and the superimposition with ROS distribution patterns. SP, spleen meridian; ST, stomach meridian; KI, kidney meridian; CV, conception vessel.

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007

Cellular Mechanisms in Acupuncture Points and Effected Sites

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The objective of our work is the elucidation of mechanisms underlying initiation, transmission and the final effects of acupuncture and moxibustion. Here we shall focus mainly on possible cellular events in tissue affected by Chinese medicine treatments using basically electrophysiological techniques combined with molecular biological and radioactive tracer techniques.

In a first part we will review work of our laboratory suggesting that acupuncture-induced pain suppression involves interaction of the δ-opioid receptor (DOR) with the neurotransmitter transporters for glutamate (EAAC1), γ-amino buteric acid (GAT1) and the sodium pump (Na^+,K^+-ATPase). Reduced activity of the transporters resulted from intermolecular interaction with DOR. In addition, EAAC1 became stimulated in response to DOR activation, while GAT1 became inhibited. The Na^+,K^+-ATPase was not affected by DOR activation, but higher sensitivity to DOR agonist was found in response to sodium pump stimulation. These effects may contribute to acupuncture-induced pain suppression.

In a second part we will review work on effects of drugs on membrane transporters. In treatment of asthmatic rats by acupuncture, cyclophylin A becomes over-expressed that can be detected in the serum. Release of airway smooth muscle contraction by cyclophilin-induced inhibition of Na^+/Ca^{2+} exchanger may be the underlying mechanism. As an example for effects of Chinese herb extracts on the transporters described in section one, we review the effect of *Acorus* extract on EAAC1 function showing that α-asarone effectively inhibits EAAC1-mediated current but stimulates glutamate transport. These effects may contribute to reduced excitatory activity.

The generally accepted effect of acupuncture is pain relief. We suggest that modulation of central nervous synaptic activity may be involved through indirect modulation of neurotransmitter transporter activity by endorphins. These transporters may also be the target for drugs of Chinese herbs. Membrane transporters may also be the target for endogenous drugs induced by acupuncture.

008

Electroacupuncture attenuates epileptic seizures

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Epilepsy manifests by recurrent seizures induced by abnormal electrical discharges in the brain. Currently, strategies against epileptic seizures are very limited in spite of its devastating effects on the patients and their families. No drug is effective for relief from epilepsy in more than one third of patients. Therefore, finding a new therapy for epilepsy is of utmost importance. Since there are clinical clues suggesting the beneficial role of electroacupuncture (EA) in the treatment of epilepsy, we proposed this work to verify the effect of EA on experimental epileptic seizures and elucidate the optimal conditions in terms of acupoints and stimulation parameters. In the rat model of experimental epilepsy induced by kainic acid injected into the lateral cerebral ventricle, we observed that EA at head (e.g., DU-14, DU-26), back (e.g., DU-8, EXB-9) or leg (ST-40, KI-1) acupoints attenuated epileptic activity. The efficacy was dependent on EA conditions. For example, high-frequency EA induced a better effect than low-frequency EA in all tested acupoints. Since sodium channels play a key role in neuronal excitability and its up-regulation may lead to epileptic hyper-excitability, we asked if the EA effect is related to the regulation of sodium channels. We therefore studied the role of the delta-opioid receptor (DOR) in the regulation of sodium channels because EA increases DOR expression in the brain. We found that in the oocytes co-expressed sodium channels and DOR, DOR expression/activation reduced sodium currents. Taken together, it is likely that EA induces DOR up-regulation and thus inhibits sodium channel activity as well hyper-excitability. This may, at least partially, account for the mechanism of the EA-induced inhibition of epileptic seizures.

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009

Internal Validity vs External Validity: Paradox in Acupuncture Clinical Trial Studies

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Acupuncture is an inseparable part of tradition Chinese medicine (TCM), as its practice is based upon the philosophy and theory of TCM. In recent years, with the advent of evidence based medicine (EBM), the efficacy of acupuncture treatment has been scrutinized by randomized, controlled clinical trials (RCT). The results of most, if not all, well designed RCTs showed negative results or minimal efficacy for acupuncture, which contradicted with previous empirical findings. Before the resutls of a RCT can be generalized, it is important to examine carefully the experimental protocols of the RCT for external validity. To determine if the results of recent high quality RCTs evaluating the efficacy of acupuncture treatment for musculoskeletal pain could be generalized, we examined the experimental protocols of these studies. We found that while these studies have high internal validity, they were commonly conducted in experimental settings and the procedures of acupuncture were more or less standardized. As patients' belief and perception about acupuncture, as well as patient-practitioner relationship, are known to have an influence on the outcomes, the artificial nature of the experimental settings would reduce the external validity of the study. Moreover, because individualized treatment is the essence of TCM, the standardized procedures of acupuncture would also greatly impair their external validity. Results of our analysis suggest that negative results of a RCT must be interpreted with cautions, bearing in mind their low degrees of external validity. Furthermore, pragmatic acupuncture trials, which have higher degrees of external validity, should be encouraged as they are consistent with the philosophy and practice of TCM.

010

Acupuncture in the Treatment of Knee Osteoarthritis: A Meta-analysis

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Introduction: Osteoarthritis of the knee (OAK) is named "*Bi* syndrome" in traditional Chinese medicine. Acupuncture therapy has been widely applied to treat arthritis including OAK clinically. This study aimed to assess the efficacy and safety of acupuncture therapy in randomized clinical trials (RCTs) for OAK.

Method: RCTs to examine the efficacy and/or safety of acupuncture therapy in OAK treatments were valid. Jadad's scale was used to assess the quality of eligible trials. Published data were estimated by odd ratio (OR) or standardized mean difference (SMD) with 95% confidence interval in meta-analyses.

Result: (1) Total 251 clinical trials were retrieved, and 86 RCTs met the inclusive criteria were identified. (2) 37 RCTs out of 86 included RCTs were assessed as high-quality trials. (3) In the short-term study of acupuncture vs. sham acupuncture group, acupuncture was more effective to reduce pain (P=0.005) and stiffness (P=0.001), improve joint function (P=0.001) and quality of life (QoL) in physical function (P=0.0008). (4) In the long-term study of acupuncture vs. sham acupuncture group, acupuncture was more effective to reduce pain (P=0.007) and stiffness (P=0.01), improve joint function (P=0.0008) and QoL in physical or mental function (P=0.02). (5) In the short-term study of acupuncture vs. waiting list or general care group, acupuncture was more effective to reduce pain (P<0.00001) and stiffness (P<0.00001), improve joint function (P<0.00001) and QoL in physical (P<0.00001) or mental function (P=0.003). (6) In the long-term study of acupuncture vs. general care group, acupuncture was more effective to decrease pain (P<0.00001) and improve joint function (P<0.00001). (7) In the study of acupuncture vs. medication group, acupuncture treatment showed a higher number of improved patients (P<0.00001). (8) No adverse events occurred during the acupuncture treatments.

Conclusion: The results of this meta-analysis suggest that acupuncture should be an effective and safe therapy in the treatment of OAK, albeit further high-quality clinical trials should be performed to verify the evidence in this study.

This project was supported by the grant (HA105/48 PT2) from The Hospital Authority of Hong Kong

Keywords: Acupuncture, knee osteoarthritis, meta-analysis

011

Acupuncture in the Treatment of Low Back Pain: A Meta-analysis

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Introduction: Low back pain (LBP) is one of the main causes of disability, and results in a significant healthcare and socioeconomic burden. Acupuncture therapy has been widely applied to treat LBP worldwide. This study aimed to assess the efficacy and safety of acupuncture therapy and identify acupoints, meridians and manipulations used commonly in clinical trials.

Method: Electronic databases and hand-search materials were used for screening eligible randomized clinical trials (RCTs). Data analysis: Jadad's scale was used to assess included RCTs. Clinical data were estimated by odd ratio (OR), standardized mean difference (SMD) or weight mean difference (WMD) with 95% confidence interval in meta-analyses.

Result: (1) 82 RCTs met the inclusive criteria were identified and 25 RCTs (30.49%) were assessed as high-quality trials. (2) In the acupuncture vs. sham acupuncture study, acupuncture was more effective to reduce pain (P=0.0006), improve the function (P<0.00001), and the number of improved patients (NIP, P=0.02). Meanwhile, acupuncture also showed a higher effect to reduce pain in sub-group meta-analyses on chronic LBP (P=0.01), but a similar effect to reduce pain in acute LBP (P=0.32) and a similar NIP in chronic LBP (P=0.07). (3) In the acupuncture vs. medication study, acupuncture was more effective to improve NIP in patients (P<0.00001) and in patients with lumbar disc herniation (P=0.001) or in patients with acute lumbar muscle sprain (P<0.00001). In addition, acupuncture alone had similar contributions as medications to reduce pain (P=0.87), while acupuncture plus medication was more effective than medication alone to reduce pain (P<0.0001). (4) No adverse events occurred during the acupuncture treatment. (5) Top 10 frequently used acupoints clinically such as BL40 (Weizhong) and EX-B2 (Jiaji), and commonly chosen meridians such as BL (Bladder) and GB (Gallbladder) were identified. (6) Filiform needle, electroacupuncture and warm needle were commonly chosen manipulations used in LBP treatments.

Conclusion: The results of this meta-analysis suggest that acupuncture should be an effective and safe therapy in the treatment of LBP.

This project was supported by the grant (HA105/48 PT2) from The Hospital Authority of Hong Kong)

Keywords: Acupuncture, low back pain, meta-analysis

012

Clinical Observations on Laser Acupuncture in Simple Obesity Therapy

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A previous study has shown that laser acupuncture is a useful healing method for the treatment of visceral postmenopausal obesity in combination with a low-calorie diet. We observe and evaluate the therapeutic effect of laser acupuncture in subjects of simple obesity with a non-restrictive diet protocol. Subjects included 73 women and 22 men with simple obesity and body mass indices ≥ 27 kg/m^2. Daily energy intake recommendations for obese females and males were 1620.0 and 1894.2 kcal in average, respectively. The gallium aluminum arsenide Handylaser Trion was used to apply 0.25 J of energy to each of the following acupuncture points three times per week for four consecutive weeks: Stomach, Hunger, ST25, ST28, ST40, SP15, and CV9. The subjects' body weights and body mass indices were recorded before treatment, and again at four weeks after treatment, and the percent reduction in each parameter was calculated. Statistically significant reductions in body weight and body mass index were detected after four weeks of treatment. The mean reduction and mean percent reduction in body weight were 3.17 kg and 3.80% ($p < 0.0001$), respectively. The corresponding values for the body mass index were 1.22 kg/m^2 and 3.78% ($p < 0.0001$), respectively. We concluded that laser acupuncture was found to exert a therapeutic effect on simple obesity by reducing both body weight and body mass index. Moreover, subjects showed good compliance with this comfortable and non-restrictive diet protocol.

013

Technology Innovation of Acupuncture in the World: An Empirical Study Based on Patents

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Objective: This article aims to characterize acupuncture knowledge flow and technology development among inventors' countries by statistics and citations of patents to evaluate the national strengths and global communications that facilitate subsequent innovation and collaborations on acupuncture frontiers.

Methods: The USPTO patent full-text database was searched and all patents titled with "acupuncture" were retrieved. Statistical analysis was performed using SPSS. Patent citation network analysis was processed by Ucinet and NetDraw. Case studies were conducted on the most cited patents.

Results: The invention pool consisted of 101 patents with inventors from 16 countries. Significant correlations existed between: (1) the amounts of patent claims and amounts of forward citations ($r=0.246$, $P<0.05$); (2) patent amounts categorized by nations and their entry time of first acupuncture patent ($rho= -0.526$, $P<0.05$).

US Patent No. 4479496 filed by the USA and No. 4408617 filed by France were basic patents for two related major citation subgroups. Furthermore, the visualized network showed a quadrangle cluster among the USA, Canada, France and Japan (total degree centrality = 115, share centrality = 0.625). The USA, Canada and Taiwan formed a triangle cluster with the highest total tie strength of 46. China and Israel were in the upper chain of knowledge flow with only output citations.

Conclusions: A highly cited acupuncture patent tends to be valuable and pioneering. Patents' first-mover executions consolidate national cumulative strengths and advantages of technology on acupuncture. The USA, Canada, France and Japan lead central positions in the international technology delivery system. While the USA, Canada and Taiwan exchange acupuncture knowledge with one another most frequently. China and Israel only play output roles in acupuncture skill and device innovation.

014

Introducing Double-Blinding in Acupuncture Research

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Background: It is an old saying that scientific studies are as good as their controls. As effectless placebos do not exist, adequate controls are difficult to obtain in acupuncture research. As a result, the credibility of the studies is often doubted by Western scientists and results are often contradictory.

The gold standard of clinical sciences, double-blinding, was so far not available. Therefore, although scientific proof of a principal and specific effect of acupuncture was achieved in animal and human experiments, prospective, randomized trials such as the GerAc- and ART studies have so far not been able to prove specific effects on a controlled basis. Also, a meta-analysis of 33 studies showed no difference between the use of acupuncture points and random skin areas. In some of the studies, even single blinding was not achieved as verum and placebo points could be found out via an internet site of patients. These negative data are one of the reasons why academic institutions hesitate to recognize acupuncture in the West, and thereby diminish the reputation of TCM on the whole.

Intention: Academic recognition of Acupuncture is necessary to add impact on the process of integration of TCM as a scientific system. We developed a double-blinding and triple-blinding assay to measure the acute effect of acupuncture in humans (Heidelberg blinding assay) and to enhance the quality of clinical acupuncture research.

Result: We have tried out the use of this assay and found positive results for a couple of clinical conditions such as peripheral arterial occlusive disease, gonarthrosis, pain after tonsillectomy, nasal congestion as measured by rhinomanometry, pain and lung function after sternotomy and even heart failure.

015

Low Power Laser Irradiation on Cytochrome c Release and the Opening of TRPV Channel in RBL-2H3 Cells

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Background: Laser irradiation can promote wound healing, but the mechanism is unclear. Mast cells are found to extensively exist in skin tissue and accumulate at the site of the wound, we suspect that the mast cell might be the key factor involved in the mechanism of laser irradiation. It's proved that after laser irradiation, the elevation of intracellular calcium ($[Ca^{2+}]_i$) appeared immediately and followed by histamine release, however the detailed procedure is unclear, this study aimed to establish the role of cytochrome c release caused by low power laser and the relationship with the opening of TRPV.

Materials and Methods: Histamine release from RBL-2H3 cells was measured by the method of fluorescence staining with the highly selective reagent *o*-phthalaldehyde (OPA). Fluorescence measurements of matters in RBL-2H3 Cells after being irradiated were measured by confocal fluorescence microscopy, and the effects of laser irradiation after the cells were added with Bcl-2 which blocks cytochrome c release from mitochondrial to cytoplasm was also carried out.

Results: The cytochrome C fluorescence intensity increased significantly after cells irradiated, however, when cells were first incubated with Bcl-2, the increase was not evident. The pH fluorescence intensity of the irradiated cells increased significantly after irradiation and then slowly decreased for photobleaching effect, while the block ones increased little. The intracellular $[Ca^{2+}]_i$ fluorescence intensity of the normal ones increased significantly. Although the laser irradiated on the block ones, no significant increment of Ca^{2+} fluorescent intensity was found.

Conclusions: Results show irradiation of 406nm laser would lead to cytochrome c release, and then the intracellular pH will increase (alkalization), which could be a trigger to open the TRPV channel and at last lead to increased intracellular Ca^{2+} which was the result of the Ca^{2+} influx of the extracellular buffer.

016

An Engineering Cybernetics Approach to Acupuncture and TCM - Yin-Yang Wuxin Dynamics and Ear Acupoint Electronics Device

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We have developed an "engineering cybernetics" approach (invented by Qian Xuesen and Tsien Hsue-shen) to acupuncture and traditional Chinese medicine (TCM). It is the dynamics for the ancient Chinese Yin-Yang Wuxin principle. The inputs to the engineering cybernetics system is provided by the ear acupoint electrical impedence device developed by Professor Yang Huayuan of the Shanghai TCM University in Shanghai, China. This device can measure the bipolar excess/deficiency, yang/yin, hot/cold syndromes of TCM. By connecting these bipolar measurements with the state variables representing the anatomical components (e.g., organs), we generate a map of the observables to the internal state variables. Thus the Ying-Yang Wuxin dynamics can be operated in real-time. The system has control variables that represent drug and therapeutic treatments. Finally the current status of the patients is represented by the next-time state variables.

The above theory provides a scientific principle for TCM which has been mysterious and often difficult to understand for western scientists. We expect the principle will establish a solid foundation for the research and practice of integrative medicine, Chinese herbal drug design, acupuncture and nutritional products. This cybernetics approach offers a quantitative methodology for TCM that rigorous clinical trials can be established. Currently, we are building bioinformatics and database tools for this novel approach as well as experimentation with some common diseases.

017

Effect of Acupuncture on CD4+CD25+ Regulatory T Cells in Tumor-bearing Mice

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Objectives : To investigate the molecular mechanism of acupuncture in modulating tumor immunosupression by observing $CD4^+CD25^+$ regulatory T cells and the JAK-STAT5 signal transduction in the tumor-bearing mice.

Methods : Balb/c mice were randomizedly divided into the control group, tumor-control group, moxibustion treatment group (1.5mg, 2 cones per day, 6 times) and electro-acupuncture treatment group(2Hz 15mA per day, 6 times). The tumor growth and survival rate were observed, the number of $CD4^+CD25^+$ regulatory T cells was counted and the mRNA and protein expression of JAKI, JAK 3, STAT5a, STAT 5b were detected by RT-PCR and western blotting analysis.

Results : There was a significant decrease of tumor growth and increase of survival rate in the moxibustion treatment group and electro-acupuncture treatment group comparing to the tumor-control group. The number of $CD4^+CD25^+$ regulatory T cells decreased in electro-acupuncture treatment group while increased in moxibustion treatment group comparing to the tumor-control group. A higher expression of the JAK3 mRNA was observed in electro-acupuncture treatment group comparing to control group. Decreased STAT5a mRNA expression was observed in in the moxibustion treatment and electro-acupuncture treatment group comparing to the tumor-control group. Significant decreased protein expressions of JAK1, JAK3, STAT5a and STAT5b were observed in the moxibustion treatment group and electro-acupuncture treatment group comparing to the tumor-control group.

Conclusion : Acupuncture treatment can suppress the tumor growth and increase of survival rate of H_{22} tumor-bearing mice. Such effects may have a close relation with the change of the number of $CD4^+CD25^+$ regulatory T cells and the rate of $CD4^+CD25^+$ regulatory T cells and $CD4^+$ T cells. The effects of acupuncture on $CD4^+CD25^+$ regulatory T cells may relate with the down regulation of the mRNA and protein expression of JAK1, STAT5a and STAT5b.

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018

Study on the Characteristics of Infrared Spectrums of Moxibustion

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Objective: To explore the characteristics of infrared spectrums of moxibustion.

Methods: An infrared radiation spectrum detecting system with features of high sensitivity and a wide range of wavelength was applied to detect spectrums of traditional moxibustion and acupoint.

Result: It was found that the spectrums of three traditional indirect moxibustion, namely the moxibustion with monkshood cake insulation, moxibustion with garlic insulation and moxibustion with ginger insulation, were quite similar to that of the acupoint. They all had the peak of radiation around 10μm, which could produce syntonic radiation, and further produce therapeutic effects of acupoint. Based on this study, an infrared laser treating instrument with 10.6μm specific wavelength had been developed. In the animal experiments, it was found that the 10.6μm infrared laser irradiation was evidently effective to increase the heartbeat of the rabbits that had bradycaridia caused by injection of pituitrin. In a randomized, sham-controlled clinical trial, it was found that the 10.6μm infrared laser irradiation was evidently effective to reduce the pain of the patients suffering osteoarthritis of knee.

Conclusion: The results indicate that the syntonic radiation between the indirect moxibustion and acupoint is the scientific basis of the bioeffect of indirect moxibustion.

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019

Influence of Acupuncture on Heroin Addicts' Bias of Attention

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Objective: To survey heroin addicts'bias of attention, induced to refrain from heroin by heroin-related clue, and the improving effect of acupuncture based on ERP · **Method:** Design program of positive, negative and heroin-related pictures ,record heroin addicts' EPR (event-related potentials) when they watching three kind of pictures before and after acupuncture. Compare and analyze the difference of the amplitude, the latent period and EEG interfered by acupuncture. **Result:** 1) The heroin addicts' bias of attention to dissimilar category of picture has an obvious difference, F (2,4)=1799.909 , sig=0.001<0.05 ; 2) Acupuncture and the category of pictures have obvious interaction, F=626.706, sig=0.002<0.05. **Conclusion:** Interveneing action of acupuncture can effectively correct the heroin addicts' bias of attention. It suggests acupuncture can be a therapeutic method to improve heroin addicts' cognitive function and has potentiality to prevent from re-abusing.

Keywords: Heroin addiction ; Acupuncture ; Bias of Attention ; ERP

020

Laser Acupuncture in Patients with Idiopathic Carpal Tunnel Syndrome - a Pilot Study

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Objectives: The aim of this pilot study was to investigate the efficacy of laser acupuncture treatment compared with sham laser acupuncture treatment in patients with mild to moderate idiopathic carpal tunnel syndrome (CTS) as measured by subjective symptoms assessment in a randomized controlled study.

Methods and Results: 20 patients with idiopathic mild to moderate CTS were randomly divided into two treatment groups : (1) administered laser acupuncture in PC -7 , PC-6 on the affected side with 1 minute duration for each acu-point in their 10 sessions over 2 weeks.(n= 10) (2) For sham treatment, the same machine with red beans was pasted on the acupoints in the same way with same protocol as for true laser stimulation, but the laser apparatus was not switched on(n= 10). Baseline assessments including a standard questionnaire termed global symptom score (GSS). Patients completed standard questionnaires at baseline and after four weeks identically. The changes in GSS were analyzed to evaluate the statistical difference.

Results: Laser acupuncture group had significant reduction from baseline GSS at week 2 (from 24.67±14.02 to 9.5±10.0, P=0.005) while sham laser acupuncture group showed no significant change from baseline GSS (from 23.8±5.67 to 20.8±5.36, P=0.63). Patients with Laser acupuncture treatment had a significant decrease in GSS compared to sham laser acupuncture group at week 2 (P=0.004). Laser acupuncture was well tolerated with minimal adverse effects.

Conclusion: Laser acupuncture treatment is better than sham laser acupuncture treatment in patients with mild to moderate idiopathic CTS as measured by subjective symptoms assessment. However, further investigation with a larger sample size is recommended.

021

The Evaluation of Risk Factor in Needle Sickness

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Introduction: Despite the public impression of "safe and harmless" about acupuncture, needle sickness during acupuncture does happen from time to time. As no studies in Taiwan so far focused on this topic, we have decided to conduct a research concerning this issue by using epidemiological studies to evaluate risk factors for needle sickness and to elucidate potential risk factors with literature review.

Materials and Methods: 1. Retrospectively investigate and compare in experiment (needle fainting cases in out-patient clinic in Keelung Division, Chang Gung Medical Foundation) and control group various factors as well as their correlation with needle sickness. Factors studies include demography, present illness, past history, diet preference and previous adverse reactions during acupuncture. 2. Individuals with needle sickness are interviewed to elucidate unnoticed risk factors.

Result: Among the 9626 person-time treatments, 40 individuals developed 43 needle sickness (3 of which has two consecutive needle fainting), a 0.4% incidence rate. Male comprises 55.8% while female comprises 44.2% of all cases. Mean age: 55.2 (from 20 to 84 years old) with two peaks at age 50-60 and age 70-80. When the 1st and 2nd frequent factors (first time acupuncture, acupuncture before meal) excluded, a 3rd most important factor emerged: individual's underlying medical problem, plus the drug they take. Among which benzodiazepines were found with statistical significance.

Conclusion: Benzodiazepines in hypertensive patients is a risk factor for needle sickness. More aggressive and detailed screening should be taken to avoid needle sickness.

022

A Neurovascular Transmission Model of Nitric Oxide for Acupuncture

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Several studies employing the human and animal models have shown that acupuncture enhances the generation of nitric oxide (NO) and increases local circulation. Specifically, electroacupuncture (EA) seems to prevent the reduction in NO production from endothelial NO synthetase (eNOS) and neuronal NO synthase (nNOS) that is associated with hypertension; this process involves a stomach-meridian organ but not a non-stomach-meridian organ such as the liver. How can we explain the phenomena of EA and meridian effect? Here, we proposed a neurovascular transmission model for acupuncture effect.

1. Acupuncture induced mechanotransduction, and Mechanical force is able to change NO production.
2. The NO production Changes the local blood vessels microcirculation and skin sympathetic nerve activation.
3. The mechanical force of the needle coupled with cyclic strain of blood vessels changes the hemodynamic balance of the artery tree. This has an effect on the various meridian organs' blood distribution and microcirculation.

Briefly, the acupuncture stimulus is able to induce a burst of NO production through mechanotransduction at the local acupuncture point and this NO diffuses and changes the blood flow either at the local and/or organ microcirculation level. The result of acupuncture is differential production of NO in various meridian organs, which are connected via tissue/cells coupled to the cyclically strained blood vessel; this is able to change the frequency of resonance. This has an effect on the artery tree changing the various meridian organs' blood distribution and microcirculation.

023

Auricular Acupuncture in Obese Women: A Randomized Controlled Trial

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Introduction: Acupuncture has been utilized to treat obesity. A well-controlled study of auricular acupuncture is lacking.

Aims: The aims of this randomized study are to examine the effect of auricular acupuncture on obese women and to explore the relationship between the effect of auricular acupuncture and obesity-related hormone peptides.

Methods: Forty-five of 60 obese women aged between 16 and 65 years with body mass index (BMI) > 27 kg/m^2 and who had not received any other weight control maneuvers within the last 3 months completed this study. The subjects were randomly divided into Groups A and B. Group A (n = 23) received auricular acupuncture while Group B (n = 22) received sham auricular acupuncture using placebo needles, twice each week for 6 weeks. The subjects' body weight (BW), BMI, waist circumflex (WC) and obesity-related hormone peptides were measured at the beginning of the study and after 6 weeks of treatment.

Results: This study found no statistical difference in % reduction in BW, BMI and WC between the group receiving 6 weeks of auricular acupuncture treatment and the control group. After treatment, Group A revealed significant increase in ghrelin level and decrease in leptin level. On the other hand, Group B who received sham auricular acupuncture showed no significant difference in ghrelin and leptin levels.

Conclusion: This study found no statistical difference in % reduction in BW, BMI and WC between the two groups. The auricular acupuncture is considered safe and may have potential benefit on obesity-related hormone peptides.

024

Evaluation of Effect of Auricular Stimulation on Obese Women: A Randomized, Controlled Clinical Trial

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Background: In previous study, we had found that auricular acupuncture may have potential benefit for obese treatment among obese women. Since the side effects of auricular acupuncture like dizziness and infection had been reported previously. We'd like to find out whether the stimulation of metal beads on auricular acupoints would do similar therapeutic effect as well as auricular acupuncture.

Aims: The aim of this randomized study is to investigate the therapeutic effect of different auricular stimulations in obese women.

Methods: Seventy one of 90 obese women, who fit in with our inclusion criteria: age between 16 and 65 years, body mass index (BMI) > 27 kg/m^2 and hadn't taken any weight-control treatments with the last 2 months, completed this study. The participants were randomized divided into three groups: Control Group (n=23) who received sham auricular acupuncture, Metal Bead Group (n=24), and Auricular Acupuncture Group (n=24). The subjects received their treatment three times a week for 4 weeks, and their body weight (BW), waist circumference, hip circumference; biochemical characteristics and obesity related hormone were measured at first treatment and 4 weeks after.

Results: We found significance differences between weight, BMI, waist circumference within Metal Bead and Auricular Acupuncture group after 4 weeks of treatment. In Auricular Acupuncture group, triglyceride level in blood was reduced with statistical significance after treatment while there's no significance change in other groups. There was one found dizziness in Auricular Acupuncture group, and no other side effects were reported.

Conclusion: This study shows that metal bead stimulation on auricular acupoints may do similar therapeutic effect of weight, BMI and waist circumference among obese women, while different effects of biochemical characteristics between these two groups. Metal beads may be a potential material of auricular stimulation for obese treatment as well as auricular acupuncture with less adverse effect.

025

Scalp Acupuncture Based on Dynamic Qi Detection Instead of Using Standard Location Might Help Improving Parasthesia

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Acupuncture had been considered as a mechanical stimulation with subsequently neural and humoral complex reaction, which had been applied to treat various neuromuscular diseases, such as myositis, fibromyalgia, migraine, stroke, and spinal cord injury. In classic acupuncture theories, the needling process is aimed to activate patient's qi to reach therapeutic effects. The dynamic change of qi could be detected by qigong practitioners. Vis versa, the acupuncturist could combine qi detecting technique with acupuncture to needle the point with most therapeutic benefits. Based on clinical experience, we found that different area of four limbs present qi-referring points on the scalp. Therefore, needling certain referring areas on scalp could improve some patients' sensory loss and muscle power impairment immediately.

In a 57-year-old male patient with spinal cord injury at C3-7 s/p laminectomy for 1 month with central cord syndrome, acupuncture on the qi-referring points on the scalp significantly improve the parasthesia of four limbs which was his major problem during admission. Notably, the improvement of sensory loss could be seen immediately during acupuncture.

There are still some limitations of this new scalp acupuncture skill, especially about the variable ability of acupuncturists to qi detection which consequently affecting the consistency and reproducibility of this qi-detection-dependent scalp needling method. Although the limitations exist, the reasons that (1) the preliminary results showed good potential of this new scalp acupuncture in treating neural diseases and (2) the qi practicing part of this acupuncture skill could be substituted by other methods, made it worth to introduce this new method.

Keywords : Scalp Acupuncture, Parasthesia

026

What Do Acupuncturists Do – Fertility Related Practice in the UK?

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Randomized controlled trials ask specific questions for specific conditions, often with standardized interventions and outcomes. Traditional acupuncturists believe evidence based research should reflect clinical practice. If clinical treatment is tailored to individual patients, it is difficult for researchers to capture 'what acupuncturists do'. Conversely, in areas of specialist practice, standard treatment protocols are popular. The question is whether this reflects the advocated, traditional and individual approach and how this protocol use is viewed by the profession.

Increasingly patients with fertility issues access acupuncture to improve their prospects of conceiving. The British Acupuncture Council (BAcC) supported a study to investigate this area of specialist practice amongst its traditionally trained members, who tend to have a generalist and holistic approach. All UK BAcC practitioners (n=2580) were asked to complete a questionnaire. Quantitative data were analyzed using SPSS. Qualitative data were grouped into themes and content analyzed using Atlas.ti software.

From 861 responses (33% of members), 73% were female, average of 11 years in practice. For 80% of practitioners most fertility work was related to assisted conception, with 70% using a fixed protocol of points. Over 60% had completed specialist gynaecology and obstetrics training for acupuncturists, but few liaised regularly with conventional medicine. Content analysis of qualitative data identified perceived benefits were; stress reduction/relaxation, a holistic approach, the effectiveness of acupuncture for regulating the menstrual cycle, emotional support, patient empowerment and ability to work alongside conventional medicine.

This research with UK traditional acupuncturists provided detailed quantitative and qualitative data about fertility-related practice. Using acupuncture protocols to support assisted conception may not sit easily with the perceived holistic, individualized approach to acupuncture treatment but is prevalent.

The importance of understanding the breadth of acupuncture practice, its outcomes, and the use of mixed method approaches as critical components for assessing acupuncture research will be discussed.

027

The Integration of Traditional Chinese Medicine into the Health Care System of the Republic of The Philippines

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University of Oxford, UK

The Philippine Institute of Traditional and Alternative Healthcare (or PITAHC),was formed as a corporation under the Department of Health of the Philippines in 1997, for facilitating integration of traditional medicine into the formal health care system of the Philippines. Thus far, PITAHC has primarily integrated acupuncture, acupressure, and tui-na into the formal health care system. This research assesses the process and outcomes of this integration by comparing top-down and bottom-up TCM integration in two different municipalities in the Philippines with two municipalities that did not integrate TCM.

A mixed methods approach of collecting both qualitative data (of semi-structured interviews, free lists and pile sorts) and quantitative data (from Department of Health morbidity and mortality reports for communities in the four municipalities) informed the collection of further qualitative data.

Using a modified grounded theory approach, non-random convenience and snowball samples of N=100 per communities of four socio-economically and environmentally comparable municipalities in the Philippines were analysed. Key policy stakeholders at international, state and local levels were also interviewed in order to contextualise this policy.

Communities were compared in terms of increased health care access, increased use of TCM, increased referral between biomedical and TCM practitioners, the effects of TCM integration on population health, and changes to local health care pluralism as a result of integration.

Qualitative data was analysed using *NVivo, SPSS* and *Ethnograph.* Quantitative data was analysed with *SPSS.*

Acknowledgments: Professor Gerard Bodeker, Dr. Dawn Chatty, and Dr. Jessica De Leon.

028

To Unveil the Effect of Acupuncture as a Treatment for Chronic Low Back Pain - a Pilot fMRI Study

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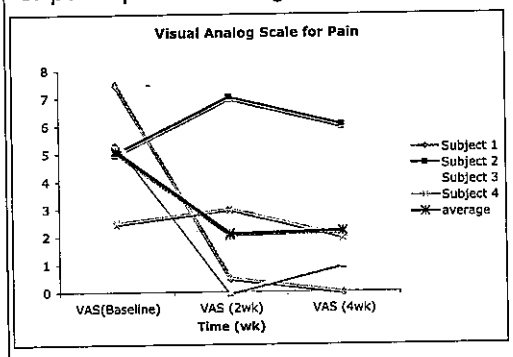
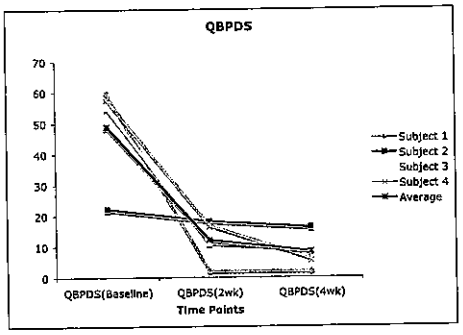
Introduction: Chronic pain patients exhibit the deficits in cognitive control. We hypothesize that acupuncture treatment can improve the cognitive control in these patients. We therefore designed the following f-MRI study to determine the differences between pre- and post 4-week continuous auricular acupuncture in a group of patients suffering from nonspecific low back pain (CLBP).

Methods: Following the approval of IRB, adults 18- 60 years old with non-specific CLBP were enrolled into this study. All patients underwent a comprehensive review of medical history and medical examination. We allowed at least 7 days after enrollment to establish the average level of pain. The intake assessments include varies pain and disability at time of enrollment, 2 week and 4 week post-acupuncture interventions. Then they received auricular acupuncture treatment at the locations of shenman, lower back and analgesic points with retaining needles for four weeks. The participants were asked to return to study center for replacement of auricular needles every 2 weeks. All participants underwent the stop signal task under MR imaging at time of enrollment and after 4 weeks acupuncture treatment. The primary outcomes including the level of pain, disability and the error processing.

Results: This study is still ongoing. A total of 4 patients aged 30-55 year-old participated in this study. Majority of participants had significant reduction of pain and disability (Figures shown) after 4wk of treatment. There is an increase effect size at the thalamus during error processing which is a component of cognitive control.





Conclusions: Base on our preliminary study, we suspect that acupuncture treatment might have an effect on the improvement of cognitive control. The drawback of this study is lack of treatment control. Additional study should be conducted to evaluate whether the changes in activities at thalamus during error processing is not caused by repetitive testing.

029

Novel Two-stage Analytic Approach in Extraction of Strong Herb-herb Interactions in TCM Clinical Treatment of Insomnia

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In our work, we aim to investigate strong herb-herb interactions in TCM for effective treatment of insomnia. Given that extraction of herb interactions is quite similar to gene epistasis study due to non-linear interactions among their study factors, we propose to apply Multifactor Dimensionality Reduction (MDR) that has shown useful in discovering hidden interaction patterns in biomedical domains. However, MDR suffers from high computational overhead incurred in its exhaustive enumeration of factors combinations in its processing. To address this drawback, we introduce a two-stage analytical approach which first uses hierarchical core sub-network analysis to pre-select the subset of herbs that have high probability in participating in herb-herb interactions, which is followed by applying MDR to detect strong attribute interactions in the pre-selected subset. Experimental evaluation confirms that this approach is able to detect effective high order herb-herb interaction models in high dimensional TCM insomnia dataset that also has high predictive accuracies.

030

Development Prospect of Chinese Medicine Digitization Projects

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The increasing popularization and internalization of Chinese medicine, accompanied with the advancement of information technology, presents a broad applied prospect for integrating computer technology with vast and complicated information of Chinese medicine. Based on accumulated experience on the development of the Medicinal Plant Images Database (http://www.hkbu.edu.hk/lib/electronic/libdbs/mpd/index.html), authors put forward the following ideas to stimulate thinking for the standardizations and development directions on the future Chinese medicine digitization projects. 1). Database technology: establish and promote a database interoperability standards, strengthen database searching capabilities such as keyword, federated, category, and fussy search; develop multiple databases cross searching functionality. 2). Multimedia technology: combine the research and studies of the Chinese medicine with advanced multimedia technology, including text, sound, images, videos, and computer animation, to make this traditional science full of vigor and life. 3). Three-dimensional image technology: use computer 3-D graphics and animation to assist the learning of complicated and complex concepts of Chinese medicine theory, such as Zang Fu organs, meridians, acupuncture points and etc.; employ 3-D virtual technology to illustrate the microscopical structure of Chinese Materia Medica. 4). Barcode recognizing technology: in order to achieve rapid and simple identification purposes, establish standard barcode format and label information for tongue inspection and pulse manifestation in Chinese Medicine, as well as authentication of Chinese Materia Medica in the areas of morphology, DNA, microscopical study. 5). Teamwork approach: fully utilize the knowledge and expertise from multidiscipline such as Chinese medicine, computer science, database management, and multimedia technology, to achieve common goal by joint effort. 6). Resource sharing: advocate the advantages of open access to digitized Chinese medicine information on the web, including timely, efficient, and cost-effective research collaboration through international network and popularization of Chinese medicine.

031

Establishment of A Dynamic Ethnomedicinal Database Based on Encyclopedia of Medicinal Plants

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The 4-volume *Encyclopedia of Medicinal Plants* (simplified Chinese version) has been named one of the 22 most outstanding imported science books (2007) in China. Its English version has also been well recognized at the 5th annual meeting of the American Society of Pharmacognosy and the 8th meeting of the Consortium for Globalization of Chinese Medicine. The entire book is consisted of the Eastern Chapter (volumes 1-2, commonly used medicinal plants of traditional Oriental medical systems, such as those from China, Japan, the Korean Peninsula, and India), the Western Chapter (volume 3, commonly used American and European medicinal plants, such as those from Europe, Russia, and the United States) and the Lingnan Chapter (volume 4, medicinal plants commonly used and produced in the Lingnan area, including those commercially circulated via this area). A total of 500 commonly used ethnobotanicals (involving over 800 species of medicinal plants) are recorded with the latest botanical, phytochemical, pharmacological and clinical data. 1358 high resolution digital pictures of the original plants, medicinal materials and their plantation sites are included. The characteristics and perspectives of each individual ethnobotanical are reviewed. Using multimedia techniques, the contents of *Encyclopedia of Medicinal Plants* are available on-line as an ethnomedicinal database, continuously updated and providing comprehensive information on contemporary medicinal plants. The related voucher specimens are deposited at Bank of China (Hong Kong) Chinese Medicines Center.

This ethnobotanical database is serving as a bridge that facilitates academic and cultural communication regarding ethnomedicinal plants.

032

"Poisonous Drugs" and "Sweet Drugs" - Analysis of the Culture of Drug Classification in the "Yellow Emperor's Internal Classic"

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"Poisonous drugs" and "Sweet drugs" are the concepts of drug classification proposed in the "Yellow Emperor's Internal Classic", reflecting the early stage of drug application. The herbs which have thick nature of property and flavor, rapid efficacy, eliminate the pathogenic factor and cure disease, and may cause discomfort or side effects are known as "poisonous drugs"; and those with smooth property and sweet flavor, mild efficacy, aim to restore *qi* or reinforce vital energy, and no unpleasant or side effects are known as "sweet drugs". This cognitive style of drug properties is undoubtedly related to the prevalence of the Taoist in Qin and Han dynasties, which is taking *dan* (sublimated pellet) to achieve the immortality of life. The classification of "poisonous drugs" and "sweet drugs" in the "Yellow Emperor's Internal Classic" had been further developed into "Three Grades of Medicines" in the book called "Shen Nong's Herbal Classic", written in the Eastern Han Dynasty, with a clear expression of academic characteristics that there was the mutual interaction between the early Chinese Medicine theory and Taoist theory.

033

The Pathophysiology of "Heat"/Calor

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I. The integration of Chinese Medicine in western health care systems depends on a logical access to its theory on the basis of pathophysiology, as the target parameters for proof of efficacy and quality control can be defined by using physiological data to enhance study designs and direct data acquisition to the inherent effects of TCM more precisely.

II. The guiding criteria (ba gang) are considered the backbone of Chinese Medicine. They have previously been described as functional features (symptoms) leading to the overall assessment of human functions on the basis of a regulatory (cybernetic) model referring to the mathematical basis of the I Ging as revealed by Leibniz in the 17th century (Heidelberg Model of TCM). Leibniz (1646 - 1716) revealed the yin yang code of binary numbers as a mathematical basis to describe circular functions. These functions roughly describe the periodicity of homoeostasis as a cybernetic process. Accordingly, the regulatory meaning of yin, yang and the phases (wu xing) could be decoded and the language of Chinese Medicine translated into the language of physiology.

III. The Heidelberg Model can furthermore explain the symptoms allocated to the technical term "heat"/calor on a rational physiological level. The basis of "heat" is considered to consist of 1) an increase of microcirculation and 2) an increase of sympathetic CNS responsiveness. This produces a) local pathophysiological changes such as red tongue, red skin, burning sensation (mast cell S-P reflex), the sensation of warmth and a pre-inflammatory state and b) systemic changes such as lack of volume in the central vessels leading to an increase in heart rate and pulse, sympathetic overdrive and CNS excitability and water-saving mechanisms. The resulting key symptoms include dry tongue, mouth, stool, sparse concentrated yellowish urine. The pathophysiological understanding of "heat" and "cold" patterns may be regarded as a crucial step in parametrizing complex patterns of TCM in the future.

034

SAPHRON TCM Database: Bioinformatic Approaches and its Application for Drug Discovery

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University of Eastern Finland, Finland[2]
University of British Columbia, Canada[3]

SAPHRON is a database of Traditional Chinese Medicine that has been developed by Shanghai Innovative Research Centre of Traditional Chinese Medicine (SIRC-TCM) since 2001. The database contains comprehensive information including TCM prescriptions, herbs, compounds and related pharmacological activities. The present study characterized chemical property of those compounds from TCM herbs in SAPHRON and compared the compounds contained in SAPHRON with other commonly used databases of synthetic small molecules. To further explore the potential application of SAPHRON for drug discovery, we have taken a basic bioinformatic approach to analyse SAPHARON data at levels of prescription, herb and compound. Our preliminary attempt showed that this approach is extremely useful in extracting valuable information from SAPHRON database. Our results suggest that the statistically processed information extracted from SAPHRON database may provide important leads for further development of novel drugs from TCM herbs.

035

Bioinformatics Services Derived from Chinese Herbal Databases - Linking Eastern Medicine with Western Medicine

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Shanghai Center for Bioinformation Technology, School of Life Sciences and Technology, Tongji University, Shanghai

To a same disease state, the patients can be treated in a Western style or Eastern style (herbal medicine) which is quite different in drug prescription. The western medicines are usually compounds designed to specific therapeutic targets with obvious efficacy and clear mechanism approved by FDA. On the other hand, the Eastern treatment is often involving herbal formulas with multiple herbs and even hundreds of compounds mixed together while the targeted proteins and mechanism are vague and difficult to be illustrated. Despite of that, the low side effects and widely accepted efficacy have won a rising use of herbal medicine in patients especially for those with chronic diseases.

A series of questions have been perplexing the researchers of drug discovery in respect of herbal medicine. What ingredients are active compounds? Will they be metabolized into more active ones in vivo? What are their potential targets and targeted pathways? Do herbal compounds have overlapping therapeutic targets with western drugs? How can we integrate the evidences from clinical and –omics data into herbal study? And so on. In order to solve above, our group has spent years collecting the herbal information from TCM recipe, chemical composition of the herb, molecular structure of active ingredients, therapeutic and clinical indication, all the way to the metabolites of the compound, molecular targets of active ingredient, pharmacological action and related literatures. Various bioinformatics services with solid statistics have been developed based on that, such as knowledge mining, molecular modeling and systems biology technologies. Alzheimer's disease and Cardio Vascular Disease are under analysis. The services are expected to be helpful to herbal mechanistic study and potential new drug discovery.

036

Analysing Complex Interactions in TCM Data

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Herbal Medicine in Traditional Chinese Medicine relies on the effects of interactions among complex combinations of ingredients. Combinations of ingredients chosen for particular cases are selected from a wide range to promote desirable interactions. Interpreting these interactions to select the desirable effect has traditionally been understood using systems such as the Seven Emotions system (Chan, 2000). This includes several classifications such as 'Mutual Reinforcement' and 'Mutual Antagonism' that represent a strengthening or lessening of effects. However, these existing frameworks for understanding interactions do not have an adequate quantitative basis for evaluation.

The complexity of analysing TCM treatments is due to the high dimensionality of the data that needs to be examined. Effective analysis of TCM data requires the ability to handle large numbers of possible combinations and a way to detect and interpret interactions between components. Appropriate tools to analyse interactions in data are not sufficiently developed.

Literature in the field of epidemiology has provided quantitative methods to analyse simple interactions between factors (e.g. Rothman, 1976). However, the interactions in TCM formulae are often far too complex for existing epidemiological methods.

Our research aims to develop a framework that will integrate computational models with the statistical approaches from epidemiology to quantitatively analyse TCM data. This framework will allow us to efficiently detect different classes of interactions and their implications. The contribution we aim to make for the practitioner is the establishment of a sound basis for quantitative description of the effects of particular formulae. The contribution for researchers is a way to discover and evaluate complex interactions for further intensive investigation.

Chan, K. 2000. *"Interactions Between Chinese Herbal Medicinal Products and Orthodox Drugs",* Harwood Academic Publishers, Amsterdam, The Netherlands

Rothman, K.J. "The Estimation of Synergy or Antagonism," *Am. J. Epidemiol.* (103:5), May 1, 1976 1976, pp 506-511.

037

Functional Networks for Salvia Miltiorrhiza and Panax Notoginseng in Combination Explored with Text Mining and Bioinformatical Approach

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China Academy of Chinese Medical Sciences, Beijing

Salvia miltiorrhiza (SM) and Panax notoginseng (PN) in combination (SMPN) have been widely used primarily in Traditional Chinese Medicine for the treatment of coronary heart disease, and its pharmacological activity should be complicated because of its multiple components. Here, we combine text mining with bioinformatics to predict functional networks for the combination. 53 genes related with SMPN were found with text mining. Protein-protein interaction information for these genes from databases and Literature data was searched. Eihgt highly-connected regions were detected by IPCA algorithm to infer significant complexes or pathways in this network. The most relevant functions and pathways extracted from these subnetworks by Biological Network Gene Ontology tool were related to small GTPase mediated signal transduction, mRNA process, transcription, apoptosis, regulation of immune effector process, phosphorylation about enzyme linked recptor protein signaling pathway, positive regulation of ubiquitin-protein ligase activity, positive regulation of biological process. The results suggested that the therapeutic mechanisms of SMPN were likely to associate with proliferation and apoptosis of endothelial cell, apoptosis of arterial smooth muscle cell, apoptosis and regulation of immune system process within macrophages during foam cell formation, cardiocyte apoptosis. Analysis of the subnetwork composition indicated that there were some nodes came from intersection between SM network and PN network in each subnetworks, and in the most subnetworks were dominant, the nodes came from SM network more than from PN network.

Analysis of Ginkgo Biloba L. Leaf Ttranscriptome Using a "Next Generation" Sequencing Technology Based on 454 GS FLX Titanium Platform

Xiao-han Lin, Hong-Mei Luo, Ying Li, Chao Sun, Shi-Lin Chen

Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences (CAMS) & Peking Union Medical College (PUMC), Beijing

In this study, we used massive parallel pyrosequencing on the Roche 454 GS FLX Titanium platform to generate a substantial EST dataset for analysis of gene expression profile and discovery of novel candidate genes related to *G. biloba* secondary metabolism. A total of 64057 ESTs with an average read length of 412bp were generated. These 454 ESTs were combined with the 21590 *G. biloba* ESTs in GenBank. The combined ESTs were assembled into 22304 unigenes in which 13922 novel unigenes were identified by 454 sequencing. The unigenes were assigned to putative functions with Gene Ontology (GO) terms using BLAST searches. Unigenes with homology to known key enzymes were found in these ESTs, including 26 unigenes encoding 14 enzymes and 78 unigenes encoding 10 enzymes involved in ginkgolide/bilobalide and flavonoid biosynthesis pathways, respectively. Additionally, a total of 89 unigenes encoding cytochrome P450 enzymes and 20 unigenes encoding transcription factors might be related to flavonoid biosynthesis. This 454-EST study in *G. biloba* contributes significantly to our understanding of functional genomics and discovery of novel candidate genes in non-model medicinal plants. These candidate genes will increase the opportunities for ginkgolide/bilobalide and flavonoid biosynthesis pathway-based studies. EST-SSRs generated by 454 sequencing will be a powerful resource for further studies such as taxonomy, genomics, and secondary metabolism in *G. biloba* species.

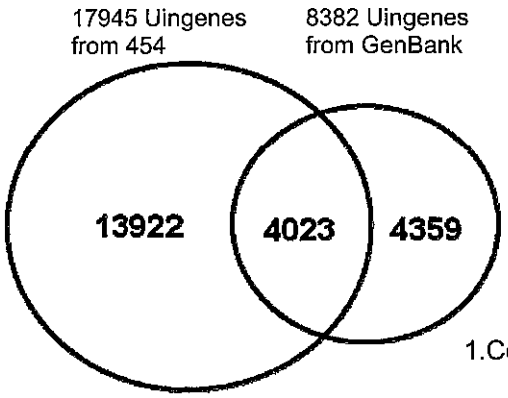


Figure 1.Comparison of *G. biloba* unigenes from 454 EST and GenBank EST

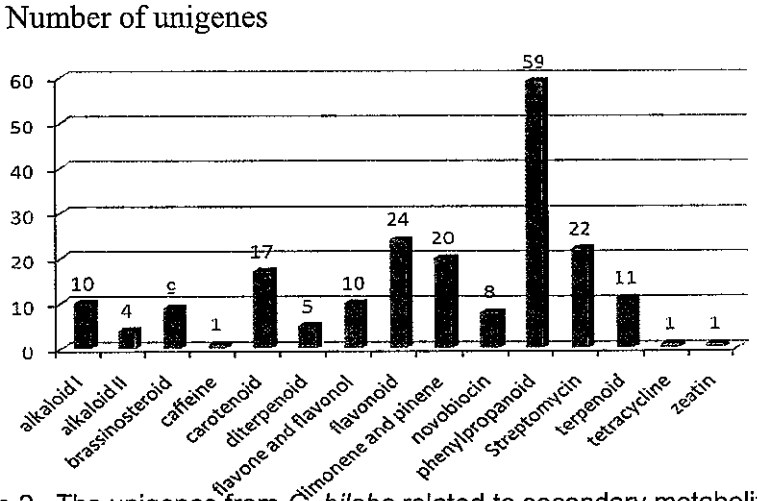


Figure 2. The unigenes from *G. biloba* related to secondary metabolites

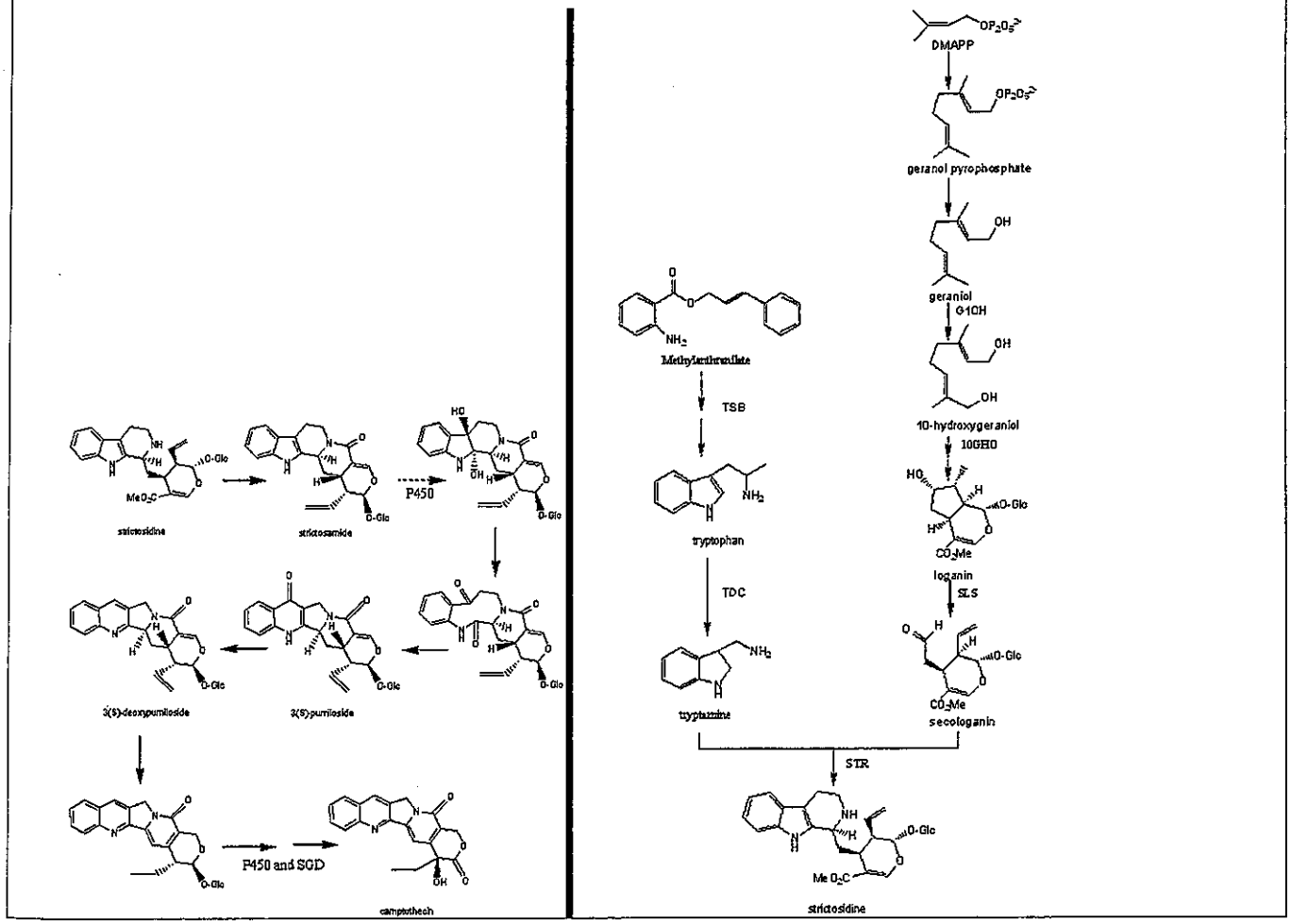
039

Transcriptome Analysis for Camptotheca Acuminata Young Leaves for Discovering Putative Genes Relative to Secondary Metabolism

Yong-zhen Sun, Hong-Mei Luo, Ying Li, Chao Sun, Shi-Lin Chen

Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences (CAMS) & Peking Union Medical College (PUMC), Beijing

Camptotheca acuminata is a Nyssaceae plant named happy tree that is indigenous in southern China. A total of 30357 transcriptom unique sequences of *C. acuminata* young leaves were obtained using 1/8 run Rhche/454 GS FLX titanium sequencing platform of next-generation sequencing. After annotation against the five public databases, 21213 unique sequences had been annotated at least one time against the databases. Functional categorization of the sequences was carried out through Gene Ontology classification from matches to the Arabidopsis. All genes involved in the camptothecin biosynthesis pathway were found before strictosidine synthesis in the ESTs pool except 2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase. This includes geraniol-10-hydroxylase and strictosidine synthase which were two key enzymes in the upstream biosynthesis of camptothecin. We also presumed the possible chemical reaction step following strictosamide formation. Based on the proposed step, cytochrome P450s (CYP450s) were possible candidate genes for the hydroxylation reaction in camptithecin synthesis. 98 CYP450s were found in our data pool distributed to 28 subfamilies, including geraniol-10-hydroxylase and secologanin synthase of the upstream reaction. Putative camptothecin transport genes were also searched and 27 putative MDR transporter genes belonging to the ATP-binding cassette (ABC) transporters super family were discovered in our database according to reports of other alkaloids producing plants. These data provide useful information for further study of camptothecin synthesis and transport of *C. acuminata*. Therefore, high-throughput sequencing is an efficient and cost-effective method for obtaining secondary metabolite biosynthesis and transportation genes of medicinal plant.



040

Proteomic Profile of Primary Isolated Rat Mesangial Cells in High Glucose Culture Condition and the Decreased Expression of PSMA6 in Renal Cortex of Diabetic Rats

Zhiguo Li, Haojun Zhang, Xi Dong, Frank J. Burczynski, Patrick Choy, Fang Yang, Hui Liu, Ping Li, Yuewen Gong

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Introduction: Diabetic nephropathy (DN) is one of the most important complications of diabetic patients. The current study is to employ proteomic technique to investigate protein profile of rat mesangial cells under high glucose culture condition to simulate its protein dynamic change in the development of diabetic nephropathy. **Methods:** Primary isolated rat glomerular mesangial cells were cultured under 5.4 mM for normal control and 30 mM for high glucose for 0, 8, 16, 72 hours and 25 days respectively. Cellular total proteins were isolated by two-dimensional gel electrophoresis and identified by MALDI-TOF-MS. Some of these proteins were documented in rat models of diabetes by Western blot. **Results:** 2-DE analyses revealed 28 differentially expressed protein spots between normal and high glucose groups. And all were successfully identified with the PMF method. Representatively, SOD1, PCBP1 and PSMA6 were validated by Western blot analysis with protein extractions from normal and high glucose groups. The abundance of these proteins was consistent with that found in 2-DE. Moreover, the expression of SOD1, PCBP1 and PSMA6 in renal cortex was further examined in two rat models of diabetes - streptozotocin-induced and spontaneous OLETF models. The abundance of SOD1 and PCBP1 proteins did not show significant difference between normal control and diabetic rats. However, the abundance of PSMA6 protein was significantly reduced in the renal cortex of both STZ-induced and spontaneous OLETF diabetic rats. **Conclusion:** Proteomic analysis identified 28 differentially expressed proteins in primary isolated rat mesangial cells between normal and high glucose treatments. The expression of one identified protein was found to be consistent with the expression in renal cortex of two rat diabetic models. Therefore, identification of protein expression patterns in mesangial cells can be employed to develop a therapeutic target for treatment of diabetic nephropathy.

041

Reversal of Hypoxia Response by Danshen-Gegen Decoction in Rat Myocardium Cells H9C2

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City University of Hong Kong, Hong Kong

In China, both Radix Salviae miltiorrhizae (Danshen) and Radix Puerariae (Gegen) have long been used for the treatment of coronary heart diseases, particularly for myocardial infarction and angina pectoris. Their anti-oxidant, anti-proliferation, cardioprotection, vasolidation, anti-hypertension and anti-atherosclerosis effects have been demonstrated by a number of *in vitro*, *ex vivo* and *in vivo* biological assays. However, the molecular mechanisms behind such effects remain poorly understood. In this study, the effect of Danshen-Gegen decoction (DG) on hypoxic responses insulting in heart-derived H9c2 cells was investigated. It was found that DG could significantly reverse the expression of hypoxia-inducible factor 1 (HIF-1α). Changes in cell viability, cell cycle distribution and nitric oxide production under hypoxia or co-treatment of DG and hypoxia were also examined. A functional-specific rat cDNA microarrary, which consists of 100 genes related to apoptosis, cell cycle and proliferation, antioxidant, cytokine and inflammatory as well as cardiovascular disease biomarkers was constructed to study the gene expression profiles of H9C2 cells under hypoxia or co-treatment of DG and hypoxia. Moreover, expression of multiple signaling molecules, e.g. Akt, c-Jun. Erk2, IkappaB, JNK and p38 MAPKS were studied simultaneously using Luminex technology. According to these results, molecular pathways were proposed to elucidate the role of Danshen-Gegen decoction in myocardium cells for the prevention of hypoxic injury.

042

Proteomic Profiling of Spinal Cord and Dorsal Root Ganglia: Altered Protein Regulation Following Inflammatory Bowel Diseases Induced by Trinitrobenzene Sulfonic Acid

Xiao-jun Zhang[1], Hua Wang[2], Chi Chung Lee[1], Hsiang-fu Kung[2], Wendy W. L. Hsiao[1], Shun Tan[1], Hong-xi Xu[3], Zhao-xiang Bian[1]*

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Previous study has shown that TNBS-induced colitis had a profound impact on the gene expression profile of colon and spinal cord. The affected genes are related to a number of biological functions: inflammation, immunity, transport, metabolism, signal transduction, tissue remodeling and angiogenesis. In the present study, we used a two-dimensional electrophoresis (2-DE)-based proteomic technique to determine the global protein expression changes in spinal cord and dorsal root ganglia (DRG). The proteins derived from lumbosacral enlargement spinal cord and DRG were resolved by 2-DE. We discovered 39 proteins that displayed different expression levels in TNBS-induced colitis rat model, including proteins involved in cell signaling, cellular metabolism, redox regulation and stress response. These data indicated that TNBS-induced colitis lead to the regulation of protein expression in the primary afferent nervous system, which may be related to the structural and functional changes caused by colitis.

043

Plasma Proteome Analysis of Anti-cancer and Anti-hyperlipidemia Effects of Triterpenoids from Gynostemma Pentaphyllum in the *APC*$^{min/+}$ Mouse Model

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APC$^{min/+}$ mice, a commonly used mouse model for colorectal cancer, manifest both high number of intestinal polyps and hyperlipidemia, which make the *min/+* mouse an ideal animal model for drug intervention studies for both hyperlipidemia and colorectal cancer Triterpenoids, produced in many plants, are widely used in Asian medicine. *Gynostemma pentaphyllum (Gp),* also called jiaogulan, is a rich source of dammarane-type triterpenoids and is used as a traditional Chinese herbal medicine for the treatment of various diseases including cancer and hyperlipidemia. However, the proven efficacy and the underlying mechanism have not been investigated systematically. Using the *Apc*$^{min/+}$ mouse as the animal model, treatment with Gp total triterpenoids saponins (GpS) markedly reduce the numbers and sizes of polyps. In conjunction with 5-fluorouracil (5-FU), the size and numbers of polyps of the treated animals were further reduced. Besides the anti-cancer effect of GpMix, we have also shown that the GpMix can effectively suppress the plasma triglycerides and cholesterol levels in *Apc*$^{min/+}$ mice. To delineate the precise mechanisms of the anti-cancer and anti-hyperlipidemia effects of GpS, we performed plasma proteomic analysis of the plasma obtained from animals treated with and without GpS.

Plasma protein profiling resulted revealed that 23 proteins shows differential expression, of which 18 of them are directly related to cancer, cell structure, inflammation, oxidation and cell proliferation, including serum amyloid A1 and A2, serum amyloid P-component, major urinary proteins, glutathione peroxidase 3, complement C3, ceruloplasmin, hemopexin, retinol-binding protein 4, alpha-antitrypsin, haptoglobin, suppressor of cytokine signaling, gelsolin, vitamin D-binding protein, kininogen 1, alpha-2-marcoglobulin, beta-2-glycoprotein and serotransferrin. In the same treated animals, 5 lipogenesis proteins including apolipoprotein A-I, apolipoprotein A-II, apolipoprotein A-IV, apolipoprotein C-III and apoplipoprotein E by which the activity of lipoprotein lipase is tightly regulated also shown differential expression. These plasma protein profiling data shown above provide underlying mechanisms of anti-cancer and anti-hyperlipidemia effects of GpS in *APC*$^{min/+}$ mice.

This study was financially supported by Research Grants Council of Hong Kong under HKBU2/07C, HKBU 26307 and FRG08-09/II-61 Grants to WLW HSIAO.

044

Identification of Biomarkers Responsible for Anti-arthritic Effect of Qingfu Guanjieshu Capsule

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Background: Qingfu Guanjieshu (QFGJS) capsule is a candidate botanical drug product derived from a Chinese medicinal formula for treatment of rheumatoid arthritis. Previous pharmacological studies revealed that QFGJS significantly inhibited experimental arthritides and acute inflammation, accompanied by reduction of pro-inflammatory cytokines and mediators, and elevation of anti-inflammatory cytokines. The current study aims to investigate the underlying mechanisms of QFGJS in treating collagen II induced arthritis (CIA) in rats by using 2-D gel and MALDI-TOF-MS/MS analysis.

Methods: Arthritis was induced in Wistar rats by intradermal injection of collagen II emulsion at day 0 and day 7, QFGJS (2.8g/kg) were orally given to rats at day 12 when the establishment of experimental arthritis was confirmed in rats until day 30 when the rats were sacrificed for collection of ankle synovium. During the experiment, both hind paws volume were measured with a plethysmometer every two days and the arthritic scores were assessed against a standard scoring system. At the end of experiment, the rats were sacrificed by overdose of anesthetics and the synovium of both hind extremities of each rats were collected for protein extraction, 2-D gel electrophoresis with standard protocols. Differentially expressed protein spots on 2-D gel were collected and trypsined for characterization of protein with MALDI-TOF-MS/MS analysis.

Results and conclusions: The results demonstrated that QFGJS at 2.8g/kg given for 19 days significantly ameliorated the arthritis induced by collagen II. From 18 ankle joint synovium samples, i.e. 6 biological replicates from normal rats (normal) , CIA rats treated vehicle (CIA) and CIA rats treated with QFGJS (QFGJS), 2-D gel analysis revealed 91 proteins differentially expressed among three groups from over 1000 proteins. Of the 91 proteins, 65 proteins were identified by MALDI-TOF-MS/MS analysis. With the identified differentially expressed proteins, a network among these proteins was established, and biomarkers responsible for the anti-arthritic effects of QFGJS were initially identified.

045

HuaLiuFang and its Separated Prescription Drugs Serum Impact on Differentially Expressed the Gene of Uterine Leiomyoma Cells Fibroids

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Objective: Hua Liu Fang and its separated prescription drugs blood serum acted on, the change of differentially expressed genes of uterine leiomyoma cells cultured in vitro was investigated to screen the target gene of the drugs.

Methods: Using BiostarH140s chip(contain 14000 cDNA), we screened different expression genes of ten pair of uterine leiomyoma and its adjacent uterine smooth muscle tissue and looking for uterine leiomyoma morbility-associated genes by cluster analysis.

Result: Hua Liu Fang and its separated prescription drugs blood serum can change the gene expression of uterine leiomyoma cells. There are 17 genes down-regulated and 20 genes up-regulated in nourishing qi group, 26 genes down-regulated and 41 genes up-regulated in resolving mass group, 40 genes down-regulated and 46 genes up-regulated in dissipating retention group, and 15 genes down-regulated and 44 genes up-regulated in Hua Liu Fang group. These different expression genes are mainly associated with cell signal transduction, transcription, cell cycle, transport protein and encoding protein with kinase activity.

Conclusion: Hua Liu Fang and its separated prescription drugs blood serum can change gene expression level of uterine leiomyoma cells and the different expression genes are the genes mainly associated with cell signal transduction, transcription, cell cycle and encoding protein with kinase activity.

Between the incidence of uterine leiomyoma and uterine leiomyoma gene expression with the obvious correlation .In recent years,some research found that Chinese herbs can impact on the gene expression in uterine leiomyoma ,This may be of Chinese Medicine treatment of uterine fibroids one of the mechanisms

In this study,BiostarH140s microarray-based tumor on serum Recipe and its role in 72h, uterine leiomyoma cell in primary culture to screen differential gene expression Screening Qi, Endometriosis Chinese
Medicine of the target gene. Chinese Medicine treatment of uterine fibroids for the practice to provide the retical and experimental basis

046

Proteomic Analysis of Anti-cancer Effects by Tanshinone IIA in Cervical Cancer Cells

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Tanshinone IIA, the diterpene derivative, is a potent anticancer drug that has been found to be effective against several tumor types . However, the exact information underlying the antitumor effects of tanshinone IIA in cervical cancer is poorly understood. We thus tried to show the anti-cancer effect of tanshinone IIA, isolated from Salvia miltiorrhiza, on Hela cell line by using a proteomic analysis and to investigate the mechanism of actions.

Our study showed that Tanshinone IIA would exhibit strong growth inhibition against human cervical cancer cells in dose- and time-dependent manners. Flow cytometric analysis of cell cycle progression revealed that G2/M arrest was initiated after a 24-h exposure to the drug. It also resulted in DNA fragmentation and degradation of poly (ADP- ribose) polymerase. Furthermore, we performed a comprehensive proteomic analysis to survey global protein changes induced by tanshinone IIA treatment on HeLa cells. Significant changes in the levels of cytoskeleton proteins as well as stress-associated proteins were observed. Western blot analysis and immunofluorescence staining were used to confirm the levels of protein expression. The cytotoxic effect of tanshinone IIA was associated with regulated expression of 12 proteins. Computational docking methods indicated that tanshinone IIA could stably bind to the β-subunit of the microtubule protein. An interaction network analysis of these 12 proteins using MetaCore software suggested that tanshinone IIA treatment regulated the expressions of proteins involved in apoptotic processes, spindle assembly, and p53 activation, including α- and β-tubulin, Maspin, and GRP75. Taken together, our results suggest that tanshinone IIA strongly inhibited the growth of cervical cancer cells through interfering in the process of microtubule assembly leading to G2/M phase arrest and sequent apoptosis.

Keywords: Tanshinone IIA, Proteomics, Cancer, Apoptosis

047

Discovery of Potential Biomarkers Associated with Induced Stress in Rats Using Artificial Intelligence Technologies

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Purpose: Investigation of the application of artificial intelligence technologies to discover potential biomarkers representing main biological responses to the effects of the development of disease.

Methods: A group of 10 rats were given electrically induced stimuli continually for 5 days as a mean of generating stress to rats. 144 experimental data were collated, recording the variation of the composition of 4000 chemical substances in biological samples as a result of the application of electrically induced stimulation over the study period.

Artificial neural networks (ANNs) and neurofuzzy logic were applied for data mining activities to identify potential biomarkers in the database. In the modelling process, data were randomly divided into training set for generating ANNs and neurofuzzy logic models and validation set for evaluate the predictability of trained models.

Results: A neurofuzzy logic model was successfully generated which enabled the discovery of 14 potential biomarkers representing major cause-effect relationships between the composition of biochemical substance and the development of disease. A further investigation was conducted to validate the robustness of the discovered knowledge by comparing the quality of models based upon original database and the database containing only identified biomarkers as independent variables. Results show that the predictability of both ANN models is similar with the validation R^2 above 0.97, indicating that the 14 biomarkers explain 97% of variability of the causal relationship between biochemical substance and the development of disease. Thus these are considered to be the likely bio-markers associated with induced stress in this study.

Conclusion: This study showed that AI is useful technology discovering hidden knowledge of potential biomarkers associated with the development of disease. The methodology developed in this study can be potentially applied to assist the establishment of mechanistic understanding of TCM based therapy by linking biomarkers, disease development and multicomponent existing in TCM.

048

MRMPath: A Web-Based Tool that Identifies Peptide Transitions for LC-MRM-MS Analysis and its Application to Biological Pathways

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Multiple reaction ion monitoring-mass spectrometry (MRM-MS) of peptides derived from the proteolysis of proteins enables the quantitative analysis of large numbers of targeted proteins. MRMPath is a web-based tool (http://www.uab.edu/MRMPath) that can be used to identify and process peptide fragments from tandem mass spectrometry data by processing MASCOT-derived result files or by identifying suitable peptides following extraction of protein sequences from on-line resources dedicated to disseminating information related to biochemical (metabolic or signaling) pathways. MRMPath leverages the vast resources developed in the KEGG pathway (http://www.genome.jp/kegg/) and other web sites. When the user chooses a pathway and a species, MRMPath dynamically extracts the pathway from KEGG and presents the pathway with the proteins involved in the pathway highlighted. When a user clicks on the protein of choice, MRMPath's peptide fragment creating and processing algorithm deploys. Each protein is subjected to an *in silico* tryptic digest to obtain peptide fragments for further bioinformatic processing. Those peptides that are between 8 and 25 amino acids long are selected, but those containing methionine, cysteine or tryptophan residues are deleted. Each peptide fragment is then subjected to a dynamic BLAST analysis. The top 10 results are presented to the user in a webpage. Each result contains a link to the source of the BLAST matched gene and protein in Genbank. Peptides are also fragmented *in silico* to produce suitable *b*-ions and *y*-ions for MRM-MS analysis. Finally, results can be output into an Excel spreadsheet for direct uploading into the mass spectrometer. Summary: The web-based interface ensures that investigators can access MRMPath remotely, dynamically and only need the use of a browser. it is not necessary to download software and using the tool does not require a specific computer operating system.

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049

Immunologic Complexity of Tumor, Spleen and Liver Transcriptional Program in Mice Treated with Chemotherapy and Traditional Chinese Medicine (PHY-906)

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Although TCM has been applied predominantly to control symptoms in cancer patients, it has been observed that some herbal products may have direct or indirect anticancer properties. However, a mechanistic explanation is lacking. To obtain and overview of the effects of a well-characterized herbal combination on cancer tissues, we applied system biology approach and scanned the alterations in the transcriptional program induced by PHY-906 following its administration as a single agent and in combination with Irinotecan. We selected a well-characterized pre-clinical model in which PHY-906 and Irinotecan were administered orally to female BDF-1 mice bearing subcutaneous Colon 38 tumor implants, These effects were compared with those observable in non cancer-bearing tissues such as the liver and the spleen of the same animals. The results demonstrated that 1) PHY-906 and Irinotecan alone induce significant alterations in all tissues evaluated (tumor, liver and spleen); 2) PHY-906 and Irinotecan alone generally induce repression of transcription in the tumors; 3) the effects of PHY-906 are reverted in the presence of a chemotherapeutic agent such as Irinotecan, with a high prevalence of transcripts being up-regulated; 4) PHY-906 alone bears a general immune-suppressive effect in tumors when given alone while, when given in combination enhances pro-inflammatory effects. Most important of all, PHY-906 together with Irinotecan triggers unique changes which are not triggered by each one alone. These preliminary findings encourage further assessment of the mechanisms of action of the drug in experimental animal models and testing in the clinics.

050

Pathway and Gene Expression Changes in Tumor, Spleen and Liver Tissues in Mouse Treated with PHY906, CPT-11 and their Combination

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Background PHY906 is a traditional Chinese herbal medicine which has been used for the treatment of diarrhea and nausea/vomiting in the Orient. Preliminary results from a phase I/II randomized clinical study of PHY906 as a modulator of chemotherapy in patients with advanced colorectal cancer showed that PHY906 reduced host toxicity from anti-cancer agent CPT-11. The pathway analysis results based on the gene expression from three tissues including tumor (colorectal cancer), spleen and liver from mice treated with PBS, PHY906, CPT and CPT combined with PHY-906 were reported here.

Results The complete experimental data set including 111 samples. A two-color spotted array was used for gene expression profiling and Lowess normalization was applied to the data. PCA result revealed that in natural conditions (PBS) the gene expression was very different in tumor, normal spleen and liver tissues. The genes differentially expressed (6136 annotated genes, $p<0.05$) by tumor compared to other two tissues significantly($p< 3.075e-9$) related to the tumor and digestive system biomarkers, such as glandular and epithelial neoplasms, digestive system neoplasms, digestive system diseases, colorectal neoplasms, etc. in the MateCore database. In the pathway analysis, we focused on the non-immune response canonical apoptosis pathways. Comparing pathways affected by PHY906 or CTP alone and their combination, it demonstrated that the combination therapy enhanced both in the number of differentially expressed genes and the magnitude of the expression of the genes associated with cell death, cellular development, growth and proliferation, and DNA replication, recombination, and repair functions that related to apoptosis pathways, including cancer related PTEN signaling, and others such as apoptosis signaling, Myc mediated apoptosis signaling, Retinoic acid mediated apoptosis signaling, JAK/Stat Signaling, etc. Differentially expressed genes in each treatment that were common in all three tissues were also discovered, such as alpha and beta hemoglobin, which have been confirmed by RT-PCR.

Conclusions (1) The impact of treatment in different tissues being different is tissue specific. (2) The impact of combination treatment is not as the simply additive effect of CPT-11 or PHY906 alone (3) The enhancement of all death related gene expression triggered by PHY906 and CPT-11 in tumor tissue (4) The approach is a system biology approach.

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051

Inhibitory Effect of Sheng Qi Formula (SQF) Combined with Chemotherapy Drugs on Myeloid-derived Suppressor Cells in the 4T1 Murine Mammary Cancer Model

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Myeloid-derived suppressor cells (MDSCs), which are characterized by the expression of CD11b, Gr-1 (Ly6G/C) and IL-4Rα in mice, have recently been recognized as critical mediators of tumor progression in numerous solid tumors due to their inhibition of antigen-specific immune responses. Sheng Qi Formula (SQF), a traditional Chinese herbal medicine, is commonly used to decrease the side effects of chemotherapy and as a stand-alone anti-cancer therapy. Mice bearing 4T1 tumors had markedly elevated percentages and numbers of Gr-1 and CD11b double positive myeloid suppressor cells (up to 60 percent of all cells versus 5 percent in normal mice) in the spleen resulting in splenomegaly. Our previous study has shown oral administration of SQF alone significantly delayed tumor 4T1 development in vivo and reduced the percentage and number of Gr-1 and CD11b double positive in both splenic and peripheral compartments. In this study, we present the novel finding that combining gemcitabine or cyclophosphamide with SQF markedly enhanced anti-tumor efficacy compared with the chemotherapeutic drugs alone. Importantly, the combination of gemcitabine with SQF therapy markedly decreased tumor incidence and tumor volume. Flow cytometry revealed that treatment with SQF reduced the percentage and number of IL-4Rα, Ly6G and CD11b positive cells in both splenic and peripheral compartments. Interleukin1 beta, which is known to elevate levels of splenic Gr-1 and CD11b double positive myeloid suppressor cells, was down regulated by in vivo SQF treatment. Preliminary data shows hydrogen peroxide production by MDSC cells can be inhibited by SQF in vitro. These data demonstrate that these Herbal medicines have potent effects on tumor-induced alterations in host immunity and may provide a new means of reducing myeloid immunosuppressor cells.

052

Oxymatrine Diminishes Cancer Stem-like Cells of Breast Cancer MCF-7 Cell Line

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Accumalating evidence has indicated that breast cancer stem-like cells (CSCs) are the roots of cancer initiation, relapse and metastasis. The plant alkaloid oxymatrine has many biological activities including the ability to induce cell cycle arrest and apoptosis, which makes it a potentially useful agent targeting on cancer cells. So in order to confirm whether it can eradicate CSCs, we analyzed the effects of Oxymatrine on MCF-7 breast cancer cells as well as the Wnt/β-catenin signalling transduction pathway. Cancer stem-like cells (side population, SP) identification and sorting were performed. Inhibitory effects of oxymatrine on the sorted SP and non-SP cells were evaluated. SP cells were identified with 3-5% in MCF-7 cells. Oxymatrine caused a dose-dependent reduction in the proliferation of MCF-7 cells and a decrease in SP cells (reduction rate reached 90%. The inhibitory effect of Oxymatrine on SP cells was higher as compared to non-SP cells. Oxymatrine treatment suppressed the activity of Wnt/β-catenin signaling pathway via decreasing total β-catenin, increasing phosphorylated β-catenin cytoplasm, and downregulating the expression of c-myc and cyclinD1. These results indicate that the growth inhibitory effects of oxymatrine treatment on MCF-7 cells may be partly related to SP and Wnt/β-catenin signaling pathway. Oxymatrine may be a novel therapeutic drug targeting on breast CSCs. Further work needs to be confirmed.

053

Rational Design, Synthesis of Isatin Compounds for their Anti-lung Cancer Activity

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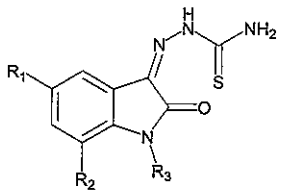
The mortality rate of cancer is currently very high in developed countries, accounting for more than 20% of all deaths. Lung cancer is one of the most commonly diagnosed cancers and can be treated using chemotherapy. While chemotherapy is the foundation of cancer therapy, the use of chemotherapeutics is often limited due to undesirable side effects and a limited choice of available anticancer drugs. This clearly underscores the need for development of novel chemotherapeutic agents for more effective cancer treatment. Mcl-1 is protein found in lung cancer cells and is a member of the Bcl-2 anti-apoptotic protein family. Noxa is specifically bind to the BH3 binding groove of Bcl-2 family proteins. Most other potent inhibitors of anti-apoptotic proteins fail to bind to Mcl-1. This is evidence that Mcl-1 has critical structural differences compared with other anti-apoptotic proteins and strongly suggests that specific targeting of Mcl-1 should be possible.

Isatin (1H-Indole-2,3-dione) is one of the most promising new classes of heterocyclic molecules having many interesting activity profiles and low toxicity in human subjects. A hybrid pharmacophore approach was used to design and synthesize isatin–benzothiazole analogs to examine their anti-lung cancer activity and possible targets. The activity of all 19 compounds were determined using 10 different human lung tumor cell lines A549, H157, H1299, H460, H1944, H358, H1792, 686LN, 292G and Calu-1. We also tested the inhibitory activity of these compounds on the interaction between Mcl-1 and Noxa by homogeneous time-resolved fluorescence resonance energy transfer (TR-FRET) assay.

Compound 8 emerged as the most active compound against H157, H1792, H358, Calu-1 and 292G cell lines with IC_{50} values of 2.6μM, 0.7μM, 11.2μM, 10.8μM and 8.7μM respectively. Compounds 4 and 10 showed no cytotoxicity against any cell lines, but did show selective disruption of the interaction between Mcl-1 and Noxa. Compound 2-5 and 9 showed no cyctotoxicity against 10 cell lines. None of the 19 isatin analogs were effective against A549, H1299, H460, H1944 cancer cell lines. The selective cytotoxic effect of this series of compounds suggests that some may be effective for the control of lung cancer with low side effects.



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2 R_1=Cl R_2=H R_3=H
3 R_1= Br R_2=Br R_3=H
4 R_1= Br R_2=Br R_3=CH_3
5 R_1=F R_2=Br R_3=H
6 R_1=Br R_2=Br R_3= o-fluorobenzyl
7 R_1=Br R_2=Br R_3= m-fluorobenzyl
8 R_1=Br R_2=Br R_3= p-fluorobenzyl
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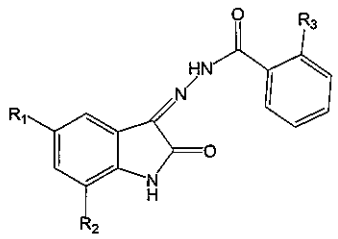

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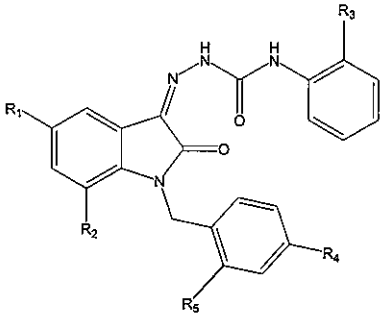

15 R_1= Br R_2=Br R_3=OH R_4=F R_5=H
16 R_1= Br R_2=Br R_3=H R_4=F R_5=H
17 R_1=Br R_2=H R_3=F R_4=F R_5=H
18 R_1=Br R_2=H R_3=OH R_4=H R_5=Cl
19 R_1=Br R_2=Br R_3=F R_4=F R_5=H

054

Enhancement of Cancer Chemotherapy by Phytochemicals – an Approach for the Integration of Traditional Chinese Medicine into Western Medicine

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Tumors develop drug resistance leading to treatment failure and fatal outcome. Novel strategies would be of great benefit to improve cancer chemotherapy. The multi-factorial nature of drug resistance implies that the analysis of gene and protein expression profiles may better predict drug resistance than single gene or protein expression studies.

We have analyzed clinical biopsies of different tumor types by microarray-based mRNA and immunohistochemistry-based protein analyses, hierarchical cluster analyses and cluster image mapping. The expression profiles predicted not only response to chemotherapy, but also survival times of patients. This may have implications for individualized therapy options in the future. One strategy of personalized cancer therapy is to use phytochemicals modulating drug resistance of tumors.

By bioactivity-guided isolation, we isolated a panel of phytochemicals from medicinal plants used in traditional Chinese medicine with activity towards cancer cells. As an example, the anti-malarial artemisinin from *Artemisia annua* L. and its semi-synthetic derivatives inhibit the energy-dependent drug efflux of ATP-binding cassette (ABC) transporters P-glycoprotein/MDR1 and MRP1, which contribute to the multidrug resistance phenotype in tumors and to the blood brain barrier. Artesunate exerts synergistic activity in combination with Erlotinib, a small molecule tyrosine kinase inhibitor of the epidermal growth factor receptor (EGFR) in transfected human glioblastoma multiforme cells. The inhibition of specific kinases in the downstream signaling pathways of EGFR is responsible for this synergism. Furthermore, artesunate synergistically interacts with Rituximab, a monoclonal antibody against CD20 to treat Non-Hodgkin lymphoma. Rituximab affects the transcription factors NF-kappa B, Sp1, and YY1, which leads to altered expression profiles of anti-oxidant stress response or apoptosis-regulating genes, thereby increasing the activity of artesunate towards Non-Hodgkin lymphoma cells.

In conclusion, the exploitation of synergistic interactions between phytochemicals and established anticancer drugs represents an attractive concept for the integration of phytochemical and phytotherapeutical approaches into cancer chemotherapy regimens.

055

Inhibition of P-glycoprotein at the Blood Brain Barrier by Phytochemicals Derived from Traditional Chinese Medicine

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The blood brain barrier (BBB) controls the transport of xenobiotic compounds from blood into brain and maintains the brain's integrity towards harmful insults. A major functional constituent of BBB represents the efflux transporter, P-glycoprotein (P-gp) I capillary endothelium. P-gp is highly expressed at the luminal membrane of brain capillary endothelium cells. Hence, P-gp still represents a major obstacle to the effective treatment of common central nervous system diseases. One attractive concept in experimental neurology to overcome failure of drug treatment is to selectively modulate BBB function by P-gp inhibitors to facilitate drug penetration into the brain.

To identify novel P-gp inhibitors, we applied the calcein assay in flow cytometry, spectrofluorometry, and confocal microscropy. The assays were done with P-gp-expressing CEM/ADR5000 and P-gp-negative parental CCRF-CEM cells. In parallel, brain capillaries were isolated from pigs and porcine brain capillary endothelial cells were cultured. Protein and mRNA expression profiles were determined by microarry analyses, real-time RT-PCR, and Western blot. We analyzed 70 phytochemicals, twelve of which strongly interacted with P-gp. Intracellular calcein fluorescence increased to >500% of controls (fluorescence in absence of P-gp inhibitors), suggesting high affinity of these compounds to P-gp.

In conclusion, identification of novel P-gp inhibitors from phytochemicals derived from TCM may have high impact on the development of strategies to modulate BBB function for therapy of brain diseases.

056

Chemical Components with Inhibitory Activities Against Prostate Cancer Cells from Dysosma Versipellis

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Four podophyllotoxins and four flavonoids were isolated from the roots of *Dysosma versipellis*. Their structures were elucidated by spectroscopic methods. Aryltetralin lignans 1-4 showed potent inhibitory activity against the growth of androgen-sensitive LNCaP and androgen-independent PC-3 human prostate cancer cell lines with the IC_{50} values in the ranges of 0.030–0.056 μM and 0.032–0.082 μM, respectively. While the flavonoids 5–8 only exhibit a weak activity with their IC_{50} values about 100 times larger than those of compounds 1–4. In order to investigate the possible role of flavonoids, compounds 1 and 5-8 were docked into the active pocket of tubulin. We found that the affinities of these small molecules to tubulin were as follow: podophyllotoxin (7.93)> quercetin-3-*O*-beta-D-glucoside (7.03) > kaemoferol-3-*O*-beta-D-glucoside (5.64) > quercetin (3.75) > kaemoferol (3.55). It can be seen that flavonoids showed affinities to tubulin and the glycosides were more tightly bound to tubulin than glycone. So flavonoids might be used to attenuate the toxicity of podophyllotoxins on tubulin.

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057

20(S)-Protopanaxadiol, a Metabolite of Ginsenosides, Induces HepG2 Cell Apoptosis and Endoplasmic Reticulum Stress

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For the past decades, an increased understanding of molecular mechanism of ER stress-induced apoptosis led to the development of a new concept recently that the endoplasmic reticulum (ER) is a potential target for new anticancer drugs. 20(S)-Protopanaxadiol (PPD), a major metabolite of ginseng, has demonstrated its anticancer effects on several cancer cell lines. However, the molecular mechanism of anticancer effect of PPD is not yet well established. In the present study, we showed that PPD inhibited cell growth and induced apoptosis in human hepatocarcinoma HepG2 cells. PPD stimulated massive cytoplasmic vacuolization and a dramatic change of Endoplasmic reticulum (ER) morphology. PPD also triggered ER stress, which supported by the observations that PPD treatment upregulated ER stress-associated genes, including *Bip*, *GRP94*, *CHOP*, *ATF4*, and *p58^{IPK}*, and proteins such as Bip and CHOP. Moreover, PPD induced the phosphorylation of PERK and eIF2α, the splicing of XBP1 mRNA, and the cleavage of AFT6, suggesting that PPD activates three arms of the unfolded protein response (UPR). Knockdown of CHOP by CHOP siRNA significantly reduced the PPD-mediated apoptosis in HepG2 cells. These observations suggest that PPD-induced apoptosis is mediated by an ER stress response and PPD may be further studied as a potential liver cancer chemotherapeutic agent.

058

Furanodienone Induces Apoptosis and Inhibits Cell Invasion via Downregulation of Akt Phosphorylation and NF-κB Activation in Human Prostate Cancer Cells

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Furanodienone is a compound isolated from Rhizoma Curcumae (EZhu in Chinese) which is commonly used in cancer treatment in China. The aims of this study are to investigate the anticancer effects of furanodienone on the androgen independent prostate cancer cells and to identify the underlying mechanisms. After 48 h of incubation, furanodienone inhibited the growth of PC-3 cells with the IC_{50} value of 80 μM. Furanodienone (80 μM) treatment induced apoptosis evidenced by the flow cytometric detection of sub-G1 DNA content and the appearance of apoptotic nuclei after DAPI staining. We also found that furanodienone inhibited the invasion of PC-3 cells through matrigel. These effects of furanodienone were accompanied by the increased cleaved forms of caspase-9 and PARP, reduced activated nuclear factor kappa B, decreased expression levels of Bcl-xl, p-Akt (Ser^{473}), MMP-9 and COX-2. Findings of this study suggest that the anti-cancer effects of furanodienone in PC-3 cells are mediated, at least in part, by its ability to inhibit PI3K/Akt and NF-κB pathways.

059

Isolation of Active Ingredients with Anti-cancer Activity of Total Triterpenoids Saponins of Gynostemma Pentaphyllum by Cell-based Co-culture Activity-guided Fractionation Assay

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Triterpenoids, produced in many plants, are widely used in Asian medicine. *Gynostemma pentaphyllum (Gp)*, also called jiaogulan, is a rich source of dammarane-type triterpenoids (GpS) and is used as a traditional Chinese herbal medicine for the treatment of various diseases including cancer and hyperlipidemia. In our laboratory, we have been investigating the anticancer activities of GpS using *in vitro* and *in vivo* models. In the animal study, GpS treatment markedly reduced the numbers and sizes of polyps in $Apc^{min/+}$ mice, a commonly used mouse model for colorectal cancer, manifest both high number of intestinal polyps and hyperlipidemia. In conjunction with 5-fluorouracil (5-FU), the size and numbers of polyps of the treated animals were further reduced. We have developed a Rat 6 (R6) cell system by which the inhibitory effects of non-cytotoxic chemicals can be assessed by focus formation assay upon transfection of ras oncogene to the host cells in our laboratory. In our co-culture assay, we have demonstrated that R6/GFP-Ras transformed cells grew into large foci in the absence of GpS. However, in the presence of GpS, R6/GFP-Ras transformed cells grew only into small foci. Intriguingly, the anti-cancer inhibitory activities of GpS require the presence of co-cultivated normal R6 cells. Based on this unique inhibitory effect of GpS, we used this co-culture activity-guided fractionation assay to isolate the potential non-toxic active ingredients from GpS. Among the nine isolated fractions, we have found one of the isolated fractions (YS54) has almost completely inhibited the growth of R6/GFR-Ras transformed cells at 500-1000μg/ml. Then, we further isolated 10 major constituents from YS54 fraction; we have found three of these active constituents have shown strong inhibitory effect at 250μg/ml which has shown no observable toxicity to the normal cells. In conclusion, using this cell-based co-culture activity-guided fractionation assay, we have isolated the potential non-toxic active ingredients from GpS with anti-cancer activities.

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Pharmacokinetics Study of Triterpenoids Saponinsn with Anti-cancer Activities after Oral Administration of Total Saponins of Gynostemma Pentaphyllum in Mouse Plasma

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Gynostemma pentaphyllum (Gp), also called jiaogulan, contains rich source of dammarane-type triterpenoids saponins (GpS) and is used as a traditional Chinese herbal medicine for the treatment of various diseases including cancer and hyperlipidemia. Previous study has proven that bioactive components of Gp are generally attributed to triterpenoids saponins, known as gypenosides. In our laboratory, we have been investigating the anticancer and anti-hyperlipidemic activities of GpS using *in vitro* and *in vivo* models. In the animal study, GpS treatment markedly reduced the numbers and sizes of polyps in $Apc^{min/+}$ mice, a commonly used mouse model for colorectal cancer, manifest both high number of intestinal polyps and hyperlipidemia. Beside the anti-cancer effect of GpS, we also found that the GpS can effectively suppress the plasma triglycerides and cholesterol levels in $Apc^{min/+}$ mice. To our best knowledge, there is no pharmacokinetics study of total gypenosides of Gp has been performed.

The aim of this study is to evaluate pharmacokinetics of mouse exposure of several key gypenosides with anti-cancer activities after oral administration of GpS. In our study, parallel blood sampling and UPLC-ESI-MS method has been used for pharmacokinetics evaluation of GpS in mouse plasma. After oral administration of 6g/kg of GpS, gypenoside-III, gypenoside-IV, gypenoside VIII, gypenoside G, 20(S)-gensenoside Rg3 and 20(R)-gensenoside Rg3 were simultaneous determined in mouse plasma in different time points (0 hr – 24hrs) by UPLC-ESI-MS method. The pharmacokinetic parameters of all six gypenosides were different from each other. $T_{1/2}$ range from 5.5 hr to 13.6 hr, C_{max}: range from 0.41 to 46.08μg/ml, T_{max}: range from 3hr to 9hr, $AUC_{0-\infty}$: range from 2.42 to 1040μg · mL/h, respectively. In conclusion, a UPLC-ESI-MS method has been developed to determine these six gypenosides in mouse plasma after oral administration of GpS. This systematic investigation of the pharmacokinetics information of gypenosides from GpS can provide an important for linking and understanding GpS administration to its therapeutic effects.

This study was financially supported by Research Grants Council of Hong Kong under HKBU2/07C and HKBU 26307 Grants to WLW HSIAO.

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The Triterpenoids Saponins of Gynostemma Pentaphyllum, alone or in Combination with 5-fluorouracil, Exert Anti-cancer Effects in the ApcMin/+ mice and the Colorectal Cancer Cell Lines

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Triterpenoids, produced in many plants, are widely used in Asian medicine. *Gynostemma pentaphyllum,* also called jiaogulan, is a rich source of dammarane-type triterpenoids with potential anti-carcinogenic activity. In the present study, we investigate the potential anti-cancer effect of total saponins of *Gynostemma pentaphyllum* (GpS) and 5-Fluorouracil (5-FU), individually or in combination in $Apc^{Min/+}$ mice, a mouse model for human familial adenomatous polyposis (FAP). We demonstrate that GpS significantly reduced the intestinal polyps in $Apc^{Min/+}$ mice compared with the control group. The combined treatment of GpS and 5-FU further reduced the intestinal polyps in all regions of the gut. Strikingly, GpS and 5-FU combined treatment almost completely suppressed the small intestinal polyps. Such efficacy can not be achieved with 5-FU alone in the non-toxic dose range. The synergistic effect of GpS and 5-FU was also observed in a drug resistant, p53 mutant HT-29 cell line, but not in the HT-29 cell line carrying wild-type p53, indicating that GpS may reverse the drug resistant property of HT-29 cell line and other similar cell types. Collectively, we demonstrated that the triterpenoids from Gp exerts strong inhibitory effect against polyp formation. In addition, combination of GpS and 5-FU treatment can significantly increase the anti-cancer efficacy in the animal and cellular models. The most important is that GpS is well-tolerated and no systemic GpS-associated side-effects and toxicity were observed throughout the entire experiments in mouse and normal cell line. Our data potentially open the door for using the combination of 5-FU and the botanical triterpenoid compounds as adjuvant chemotherapy for the treatment of colorectal cancer in clinical trials.

This study was financially supported by Research Grants Council of Hong Kong under HKBU2/07C and HKBU 26307 Grants to WLW HSIAO.

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Compound A, a Novel Ginsenoside Derivative, Induced Apoptosis and S-phase Arrest of Lewis Lung Carcinoma Cells through Activation of MAP Kinases and Suppression of NF-κB Activation

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Backgrounds: As many cytotoxic agents are frequently used for traditional chemotherapy of cancers, it is still in great demanding to search for more specific agents targeting carcinoma tissues but not on normal tissues of the body. Compound A, which is a synthetic novel derivative of ginsenoside Rh2, exhibited specific cytotoxic effect to several cancer cells but no marked impairment to normal cell line of fibroblasts. We thus aimed to further evaluate its value as well as the action characteristics and underlying molecular mechanisms as a potential anti-cancer agent.

Methods: The nuclear fragmentation in LLC-1 cell lines was monitored by DAPI staining. The distribution of cell cycle was analyzed using flow cytometry analysis. To further investigate how compound A arrest cell cycle and induce apoptosis, the protein markers related to cell cycle and apoptosis were examined by Western blotting.

Results: In response to compound A treatment, the cell shape of LLC-1 became round up and the apoptotic morphological changes including cellular shrinking and chromatin condensation were clearly seen. Compound A could significantly induce cell cycle arrest in S phase in association with concomitant down-regulation of cyclin A, cyclin D1, c-myc and pRb expressions and up-regulation of p21 and p27 which are the two key factors for S phase arrest. Compound A induced apoptosis was accompanied with up-regulation of p53 activity and down-regulation of Bcl-2. In addition, Compound A could activate all MAP kinases and inhibit NF-κB activation.

Conclusions: Taken together, the current study demonstrated that down-regulation of cyclin A, cyclin D1, c-myc and pRb, suppression of NF-κB activation and Bcl-2 level, up-regulation of p21 and p27 and activation of all MAP kinases and p53 may contribute to compound A-induced S phase arrest and apoptosis of LLC-1 cells

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Ginseng Extract Inhibits in Vitro and in Vivo Growth of Mouse Lewis Lung Carcinoma via Modulation of ERK-p53 and NF-κB Signaling

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Asian ginseng (AG) is the most commonly-used medicinal herb in Asian countries. It is often prescribed for cancer patients as a complementary remedy. However, whether AG in fact benefits cancer patients remains unknown because some studies reported that AG facilitates tumor growth which contradicts its usage as a dietary remedy to cancer patients. In addition, most of works done on ginseng for anti-cancer were to use chemical components rather than whole root extracts used in clinics. Thus, intensive studies using the type of ginseng as its clinical form are necessary to validate its benefits to cancer patients. In this study, anti-tumor potency and underlying molecular mechanisms of the ethanol extract of AG (EAG) were examined in mice with Lewis lung carcinoma (LLC-1). We showed that EAG significantly suppressed tumor growth in LLC-1 bearing mice with concomitant down-regulation of PCNA proliferative marker, and it exhibited specific cytotoxicity to cancer cells. EAG also induced MAPK and p53 signaling in LLC-1 cells, which suppressed cyclin B-cdc2 complex and in turn induced G2-M arrest and apoptosis. Although EAG could activate NF-κB signaling, the proteasome inhibitor of MG-132 could effectively prevent NF-κB targeted gene expression induced by EAG and then sensitize LLC-1 cells to induce EAG-mediated apoptosis. Collectively, EAG in a relatively high dose significantly suppressed tumor growth in LLC-1 bearing mice, indicating that AG may benefit lung cancer patients as a dietary supplement. This is the first report demonstrating possible combination of EAG with proteasome inhibitors could be a novel strategy in anti-cancer treatment.

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Induction of Cell Anergy in Human Jurkat T cells by Matrine through Regulation of MAPK and NFAT Signaling Pathways

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In the current study, ionomycin, the effect of well-known T cell anergy inducer, was used to optimize the conditions of a validated human Jurkat cell anergy model; and then used this model to evaluate matrine, derived from the root of *Sophora flavescens* Ait., for inducing T cell anergy. The cytotoxicity of matrine was determined by MTT method. IL-2 mRNA expression, an indicator of T cell anergy, and anergy-associated genes, including CD98 and Jumonji, were determined by an RT-PCR method. The cell signaling pathways, including NFAT and MAPKs, were examined by western blotting. The results showed that 7-11 passage of the cells, 1.0 μM ionomycin and stimulation for 16 h are optimum for T cell anergy induction. Matrine was effective in inducing T cell anergy in human Jurkat cells. The cells exposed to matrine and ionomycin showed markedly decreased mRNA expression of IL-2, when the cells were stimulated by antigens, anti-OKT3 plus anti-CD28. Mechanistic study showed that ionomycin and matrine could up-regulate the anergy-associated gene expressions of CD98 and Jumonji and activate NFAT nuclear translocation in absence of cooperation of AP-1 in anergic Jurkat cells. Pre-incubation with matrine or ionomycin could also shorten ERK and suppress JNK expression on the anergic Jurkat cells when the cells were re-stimulated with anti-OKT-3 plus anti-CD28 antibodies. Thus, matrine might be a strong candidate for further investigation as a T cell anergy inducer.

065

Saikosaponin-d (Ssd) Suppresses the Cancer Cells Growth through Down-regulation of NF-κB Signaling and its Targeted Genes Expression, with Concomitant Induction of Apoptosis in HepG2 Cells

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Saikosaponin-d (Ssd) is a triterpene saponin derived from the medicinal plant, Bupleurum falcatum L. (Umbelliferae). Previous findings showed that Ssd exhibits a variety of pharmacological and immunomodulatory activities including anti-inflammatory, anti-bacterial, anti-viral and anti-cancer effects. In our study, we have demonstrated that Ssd inhibited TNF-α induced NF-κB activation through suppression of IκBα degradation, NF-κB p65 phosphorylation and its nuclear translocation in human liver cancer (HepG2) and human cervical cancer (HeLa) cells. We further revealed that Ssd suppressed the TNF-α induced NF-κB dependent gene expression involved in anti-apoptosis (Bcl-2, Bcl-xL, XIAP, FIIP, Survivin, c-IAP1/2), metastasis (ICAM-1, MMP-9 and VEGF) and cell proliferation (c-myc, cyclin D1 and COX-2) in various cancer cell lines (HepG2, HeLa and MCF-7). In addition, Ssd on one hand enhanced the inhibitory effect of TNF-α on HepG2 and HeLa cells when combined treatment was applied. On the other hand, Ssd per se spontaneously induced apoptosis and caspase activation in these two cancer cells. These findings shed a light on the potential of Ssd in treating inflammatory diseases as well as cancers.

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Screening for Compounds with Anti-cancer Effects from Ginsenosides and their Derivatives

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Backgrounds: *Panax ginseng* C.A. Meyer is one of the most popularly-used medicinal plants over the world. As a complementary remedy, it is often to be used for treatment of cancer in China and other Asian countries. Therefore, it is meaningful to screen bioactive compounds from ginsenosides or their derivatives having potent inhibitory effect on the growth of several tumor cells.

Methods: Cytotoxicities of the tested substances, i.e., extract of *Panax ginseng* (RSE), hydrolysate of RSE, protopanaxadiol type ginsenosides (PPDs), protopanaxatriol type ginsenosides (PPTs), ginsenosides and novel derivatives of ginsenosides, were determined against several cancer and normal cell lines, including Lewis lung carcinoma (LLC-1), non-small cell lung cancer (H1299), lung adenocarcinorma (A549), breast adenocarcinoma (MCF7), hepatocellular carcinoma (HepG2), cervix adenocarcinoma (Hela) and normal lung fibroblasts (CCD19Lu), by using MTT assay.

Results: Significant and dose/time-dependent cytotoxicities were revealed when cells were treated with RSE and the hydrolysate of RSE for 24, 48 and 72 hr treatment, respectively. The PPDs and PPTs were able to potently reduce cell survival rates with dramatically increased cytotoxicity after acid hydrolysis; however they also induced potent cytotoxicity to the normal lung fibroblast cells. All the synthetic novel derivatives of the PPD-type ginsenoside Rh2 exhibited different potencies of cytotoxicity in a dose-dependent manner, although this effect varied among various cell types. Interestingly, a derivative of Rh2 and a derivative of PPD displayed no significant cytotoxic effect up to 100 μM, which indicates that they have specific cytotoxic effect to cancer cells.

Conclusions: The derivatives from Rh2 and PPD show a significant potency to induce cytotoxicity in LLC-1 and other cancerous cell lines, but no marked impairment to normal cell line of fibroblasts. Studies on elucidating the underlying molecular mechanisms of the effects of these two derivatives of ginsenosides on suppressing cancer cells are highly expected.

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Suppression of T Lymphocyte Activation by Pseudolaric Acid B through Inhibition of NF-κB Signaling Pathway and p38 Phosphorylation

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The roots of *Pseudolarix kaempferi* has been using by traditional Chinese practitioners to treat various inflammatory and microbial skin diseases for centuries. Pseudolaric acid B (PAB) is a major bioactive component of the medicinal plant. In the current study, the in vitro immunosuppressive effect of PAB on T cell activation and the underlying mechanisms were investigated. Human T lymphocytes isolated from human buffy coat by Ficoll-Hypaque method were employed in the experiments. The cytotoxicity of PAB was determined by MTT method. T cell growth factor, IL-2, was determined by the ELISA method. The T cell activation markers, including CD69 and CD25, were determined by flow cytometery. Proliferation of human T lymphocytes induced by ionomycin plus PMA or by anti-OKT-3 plus anti-CD-28 was measured by BrdU method. NF-κB and MAPK, which are mainly involved in the T cell activation, were examined by western blotting. Results showed that PAB dose-dependently suppressed human T cell activation, showing inhibition of CD25 and CD69 expression, IL-2 production and human T lymphocyte proliferation induced by PMA plus ionomycin or by anti-OKT-3 plus anti-CD-28. Mechanistic study demonstrated that PAB inhibited nucleus translocation of NF-κB p65, phosphorylation and degradation of IκB-α, as well as phosphorylation of p38 in MAPKs pathway. Thus, it could be concluded that PAB suppressed T lymphocyte activation through inhibition of NF-κB and p38 signaling pathways; this would make PAB as a strong candidate for further study as an anti-inflammatory agent.

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Anticancer Effects and Mechanisms of Sesquiterpene Compounds Isolated from Atractylodes Macrocephala in B16 Melanoma Cells

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The dried rhizome of *Atractylodes macrocephala* Koidz. (Baizhu in Chinese), is a traditional Chinese medicinal herb which can invigorate the function of the *spleen* and replenish *qi*. In combination with other Chinese herbs Baizhu has been prescribed for the management of cancers. In this study we isolated sesquiterpene compounds from Baizhu, and investigated their anticancer effects and mechanisms in B16 cells. Eight sesquiterpenes from Baizhu were identified and all of them showed growth inhibitory effects in B16 cells. Atractylenolide I (AT-I), atractylenolide II (AT-II), and atractylenolactam (ATR) were the most potent compounds with the IC_{50} of 76.46, 84.02 and 54.88 μM, respectively. Flow cytometric analyses demonstrated that treatment with any of the three compounds for 48 h caused a dose-dependent delay of cell cycle progression from G1 phase to S phase. AT-II exerted the most potent G1-arresting activity and was further investigated for its action mechanisms. Treatment with 75 μM AT-II for 48 h induced apoptosis determined by nuclear morphologic changes of DAPI-stained cells and flow cytometric analysis of Annexin V-FITC/PI-stained cells. Immunoblot analysis for the regulators of cell cycle progression and apoptosis process demonstrated that AT-II (50-100 μM) dose-dependently decreased Cdk2 and Bcl-2 expression, increased the expression of phospho-p53, p21, c-myc, p27, and activated caspases-8, -9 and -3. Moreover, it was demonstrated that a chemical inhibitor of p53, pifithrin α, significantly decreased AT-II-induced growth inhibition and apoptosis, which was accompanied by the decrease of AT-II-mediated cleavage of caspase-3. Taken together, we demonstrated the anticancer effects of sesquiterpene compounds isolated from Baizhu and revealed the underlying molecular mechanisms in B16 cells. These findings provide the basis for further investigations to develop sesquiterpene compounds from Baizhu or their derivatives as therapeutic agents against malignant melanoma.

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Photodynamic Therapy of Pheophorbide a inhibits the Proliferation of Human Breast Cancer cells via Caspase - Dependent and - Independent Apoptotic Pathways in vitro

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Being one of the common causes of death for women, breast cancer is conventionally treated by surgery and radiotherapy, and supported by adjuvant chemo- or hormonotherapies. However, adverse side effects and drug resistance may be resulted. In our previous study, a photosensitizer Pheophorbide a (Pa) was purified from a traditional Chinese herb, *Scutelleria* barbata (半枝蓮). In this study, the anti-proliferative effect and the underlying mechanisms of photodynamic therapy with Pa (Pa-PDT) on breast tumor were investigated.

The results of MTT assay showed that IC_{50} values of Pa on human breast tumor MCF-7 cells were 0.5 μM and 60 μM at 24 hours of incubation, with and without photo-activation. When examining the primary culture of human mammary epithelial cells, the IC_{50} values of Pa-PDT in the four patients' samples were slightly higher than that on MCF-7 cells. Mechanistic studies showed that Pa was localized to the mitochondria and reactive oxygen species were found to be released from MCF-7 cells after Pa-PDT. As evidenced by the results of cell death detection ELISA and chromatin condensation detected by Hoechst staining, apoptosis was found to be a major mechanism for Pa-PDT-induced tumor cell death, although G_2/M phase cell cycle arrest was also detected on MCF-7 cells after Pa-PDT. By Western blot analysis, increased expression of tumor suppressor protein p53, cleavage of caspase-9, caspase-7 and PARP indicated the involvement of caspase-dependent pathway. On the other hand, mitochondrial membrane depolarization and mitochondrial cytochrome *c* release were also observed. Apoptosis inducing factor (AIF) release demonstrated the caspase-independent mechanism of Pa-PDT. The non-competitive binding property of Pa with estrogen receptor α implied a possible usage of Pa in treating estrogen receptor-negative breast tumor which is commonly observed in late stage of the disease. Angiogenesis and the development of tumor metastasis are intrinsically connected. The anti-angiogenic potential of Pa-PDT is being investigated.

Investigations on the in vitro Anti-tumor Activities of Rubinoboletus Ballouii

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Many compounds isolated from macrofungi are reported to possess antitumor activities. *Rubinoboletus ballouii* (RB), (family *Boletaceae*), is commonly found in Asia. Up till now, very little is known about the chemistry and bioactivities of this mushroom and no scientific reports are found on this species. Therefore, the objective of the present study is to investigate the *in vitro* anti-tumor activities of RB.

Four different extracts were produced: a) water extract; b) 95% ethanolic extract of the residue after water extraction; c) 95% ethanolic extract; d) water extract of the residues after ethanolic extraction. The *in vitro* anti-tumor activities of these extracts were investigated against a panel of different human cancer cell lines using MTT assay.

Our results showed that the 95% ethanolic extract of RB possessed the most selective direct cytotoxic activities against human breast cancer cells MCF-7 and MDA-MB-231, with IC_{50} of 615 and 592μg/ml, respectively. Other three extracts possessed direct cytotoxic activities against breast cancer cells, though the effects were not selective (i.e. also exhibited high toxicity against human normal liver cells WRL-68, with IC_{50} < 800 μg/ml).

With the promising results of the 95% ethanolic extract, fractions A-L were produced using high speed counter-current chromatography (HSCCC). Based on the MTT assays screening against MCF-7 cells, fraction L (which exhibited the highest cytotoxic effect) was further fractionated into eight sub-fractions (L1-L8) using preparative thin layer chromatography (PTLC). Among these sub-fractions, L4, L6 and L7 showed higher toxicity than fraction L against MCF-7 cells, when the concentrations were lower than 200μg/ml.

In conclusion, this is the first study reporting the potential anti-tumor effect of *Rubinoboletus ballouii*.

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Induction of Apoptosis and G_0/G_1 Cell Cycle Arrest by Guttiferone K, Isolated from Garcinia Cowa, on Human Colon Cancer Cells

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Plants of the *Garcinia* genus have been traditionally used for their anti-inflammatory, anti-oxidant and gastro-protective properties. The isolated bioactive compounds have been recently studied for their anti-tumor effects in a wide range of cancer types. The present study aims to examine the mechanisms underlying the cytotoxic effects of guttiferone K, a polyisoprenylated benzophenone isolated from the twigs of *Garcinia cowa*, on colorectal cancer.

Cytotoxic effects of guttiferone K were studied using MTT and lactate dehydrogenase assays. Flow cytometry, DAPI staining, Western blot and caspase-3 activity assay were used to investigate effects on cell cycle and apoptosis.

Guttiferone K reduced the viability of Colon-26 and HT-29 cells in a concentration- and time-dependent manner with IC_{50} values of 4.9 ± 0.6 and 5.4 ± 0.2 μM after 24h incubation. Flow cytometry results showed that guttiferone K arrested HT-29 cells in G_0/G_1 phase and induced a concentration-dependent accumulation of cells in sub-G_1 apoptotic phase. This was accompanied with a decreased protein expression of cyclins and cyclin-dependent kinases specific to G_1/S phase transition and an increased expression of cip/kip family (p21 and p27) of tumor suppressors after 12h and 24h incubation. Guttiferone K induced chromatin condensation and nuclear fragmentation. Procaspase-3, -8 and -9 and PARP were also cleaved after guttiferone K treatment, suggesting the involvement of intrinsic and extrinsic apoptotic pathways. The induction of caspase-3 activity by guttiferone K was reduced by caspase-3 inhibitor (Ac-DEVD-CHO), indicating that the cytotoxic effects were mediated by the apoptosis cascade.

This study demonstrated for the first time, the *in vitro* anti-cancer effect of guttiferone K through apoptosis and cell cycle arrest on colorectal cancer. However, its effects on an *in vivo* cancer model must be investigated to confirm its anti-tumor potential.

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Reversal of Pgp-mediated Multidrug Resistance by Novel Tenacigenin B Derivatives

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Background: P-glycoprotein (Pgp, ABCB1) is an important member of ATP-binding cassette (ABC) transporter which plays a vital role in multidrug resistance (MDR). Novel tenacigenin B derivatives, extracted from *Marsdenia tenacissima*, were found to sensitize Pgp-overexpressing drug resistant cancer cell lines to a Pgp substrate anticancer drug doxorubicin. The possible interaction of five selected novel tenacigenin B derivatives with Pgp was evaluated in the present study.

Methodology and Principal Findings: Pgp-overexpressing SW620 Ad300 cells and sensitive parental SW620 cells were used. Cytotoxicity assay using sulforhodamine B staining showed that all compounds tested increased drug sensitivity of SW620 Ad300 cells but not the sensitivity of SW620 cells. Flow cytometric analysis showed that all compounds tested significantly decreased the efflux of rhodamine 123, a Pgp substrate. However, reverse transcription-PCR and Western blot analyses showed that all compounds tested did not alter Pgp expression at both mRNA and protein levels. Furthermore, the results from Pgp ATPase assay suggested that all compounds tested did not inhibit Pgp-ATPase activity.

Conclusions: Novel tenacigenin B derivatives overcome Pgp-mediated drug resistance by interacting with the substrate binding site(s) on Pgp and thus hindering the transporter activity, independent of the regulation of Pgp expression and inhibition of Pgp-ATPase activity. These findings may be useful for cancer combinational therapy with novel tenacigenin B derivatives to restore sensitivity to chemotherapy for cancer patients.

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Mechanistic study of Bioactive Ingredients of Phellodendron chinense on Human Ovarian Cell Line

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According to the American Cancer Society statistical report in 2009, ovarian cancer accounts for approximate 3% of all cancer among women and causes more death per year than any other cancer of the female reproductive system. The currently used chemotherapy cannot sustain long-term survival and there estimated 130,000 deaths per year occur for ovarian cancer worldwide. Therefore, there is a need to search for more effective and safe drugs especially the herbal medicine. In recent years, phytochemicals has shown promises as potential agents against cancers.

Here, we investigated the effect and mechanism of two bioactive ingredients, berberine and palmatine, of Ph*ellodendron chinense* on a human ovarian cancer cell line, OVCA429. Berberine and palmatine exhibited a dose- and time-dependent anti-proliferative effects. Berberine was much more potent than palmatine for the ovarian OVCA429 cells. LD50 of berberine was 80uM and of palmatine was 350uM for 48 hours. By detecting the cell size change at pre and post treatment with the fowcytomer, the two bioactive ingredients were able to trigger cells shrinkage, which is one of the apoptotic feature. Interestingly, LD50 of berberine and of palmatine could induce apoptotic cell death as quantitated by Annexin V assay. Cell cycle analysis revealed that berberine and palmatine arrested the cell cycle at G0/G1 phase. Sub-G1 fraction of apopotic cell death for berberine was 23.00 ± 4.36%; while for palmatine was 22.60 ± 1.46% when treatment time was extended to 72 hours. Finally, activation of caspase-3 was detected at 48hours (for berberine, 37.03 ± 3.78%; for palmatine, 37.93 ± 2.82%). Taken together, the results clearly suggested that berberine and palmatine could induce cell death for this late stage ovarian cancer cell line.

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Type1 and Type 2 Cell Deaths on Anti-tumor Effect of Berberine in Liver Cancer Cells

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The anti-tumor action of berberine has been under extensive study. The aim of this study is to draw a comprehensive picture of berberine's action on tumor cell death. The human hepatocellular carcinoma cells were used to monitor both autophagic celld death and mitochondrial apoptosis induced by berberine in cells. Immnunostaining and immunobloting analysis elucidated the involvement of related signal transduction in the activation of autophagy and apoptosis. We found that berberine could induce autophagy and apoptosis in human hepatocellular carcinoma cells. Berberine induces destabilization of mitochondrial membrane potential and increases the membrane permeability and releases pro-apoptotic Cytochrome C. Overexpression of beclin-1 and inhibition of Akt signaling consistently involve in berberine-induced autophagy in hepatocellular carcinoma cells and the suppression of Bcl-2 and activation of Bax induce cleaved activation of caspase-9 and subsequent caspase-3 and thereby result in apoptosis of hepatocellular carcinoma cells. Inhibition of autophagy by genetic operation attenuates the cancer cell death induced by berberine. These results revealed the potential of berberine as a therapeutic agent targeting on both cell death for hepatocellular carcinoma therapy. This study was supported by The University Grant Committee (UGC) of Hong Kong SAR of China (Project Code: 764708M).

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Synergistic Effects of Tian-Xian Liquid (TXL) on Anti-tumorigenicity in vivo

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Introduction: According to the Hong Kong Cancer Registry, colorectal cancer ranks second among other cancer incidence, and the incidence rate increase yearly. While conventional approach of treatment still brings about adverse effects. Chinese medicine is considered as an attractive alternative. Tian-xian Liquid (TXL) as a commercially available Chinese medicine decoction has been proved to possess anti-proliferative effects on human colorectal cancer through G1 phase arrest in cell cycle.

Aim: In our study, the synergistic effects of TXL was studied by comparing anti-tumorigenic effects of TXL and its bioactive fractions [butanol fraction (BU), ethyl-acetate fraction (EA) and aqueous fraction (WA)] on human colorectal cancer *in vivo* (HT29 xenografted in five-week-old nude mice model).

Results and Discussion: Our results showed that TXL and its fractions possess inhibitory effect of the growth of xenograft size *in vivo* after two-week treatment.

Immunoblotting assay revealed that protein level of p21 increased significantly in TXL but not its bioactive fractions, indicating the cell cycle arrest at G1 phase was the most effective in TXL group. Effect of all treatment groups on protein level of PCNA was not significant. The protein level of MMP-1 in TXL group plunged very significantly, and a significant decrease in MMP1 in BU group was observed too, but not in EA and WA group. This suggests synergistic effects exist in effect of TXL on anti-metastasis. All treatments significantly suppressed protein level of MDR-1, suggesting the reversion of multi-drug resistance *in vivo* by the TXL and its fractions. Such effect was the most significant in TXL group, thus supporting the synergistic effect of TXL on reversion of multi-drug resistance in our model.

Summary: In our study, TXL was proved possess anti-tumorigenicty as indicated by the elevation in protein level of p21, and the suppression of MMP-1 and MDR-1.The effects were most significant in TXL but not single bioactive fractions, thus supporting the synergistic effects of TXL on treating human colorectal cancer.

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076

Anti-metastatic Evaluation of Tian-Xian Liquid (TXL) and its Bioactive Fractions in Human Colorectal Cancer Cells and Xenograft Models

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Colorectal carcinoma is the second most prevalent cancer and will rank top in the cancer list by 2010 (Hong Kong Cancer Registry). Traditional Chinese medicine acts as an attractive and complementary alternative for tumour therapy with minimal side-effects and traumatic injuries. Tian-Xian Liquid (TXL), one of the well-known natural medicinal herbal formulations, has been commercially used as an anticancer dietary supplement for more than 10 years without known adverse effects.

This study aimed to comparatively elucidate the anti-metastatic property of TXL and its bioactive fractions [butanol fraction (BU), ethyl-acetate fraction (EA) and aqueous fraction (WA)] on human HT-29 colorectal cancer cells and nude mice xenografts.

For the cancer cell model, TXL and its bioactive fractions have similar anti-proliferative effects as demonstrated by MTT assay. At 4 hour-incubation, IC_{50} values were obtained at 1% (V/V) TXL, 1.25% (V/V) BU, 5% (V/V) EA and 0.3125% (V/V) WA. At IC_{50}, TXL and all four bioactive fractions significantly reduced the MMP2 mRNA expression by real-time PCR. TXL and EA significantly down-regulated both the active form of MMP2 protein and VEGF protein from 24 to 48 hours. Further, only TXL, EA and WA effectively inhibited HT-29 cell migration at 48 hours incubation by wound-healing assay.

For the colorectal cancer xenografts, the VEGF protein was down-regulated in TXL- and WA-treated xenografts, but not in VEGF mRNA expression. And MMP2 mRNA expression was reduced by TXL-, BU- and EA-treated xenografts. Further, TXL, BU and WA effectively inhibited the tumor growth without altering the body weight of the xenografts.

To conclude, TXL demonstrated the most effective anti-metastatic ability on human colorectal cancer *in vitro* and *in vivo* through the reduction of both MMP2 and VEGF expressions than its bioactive fractions indicating TXL is more effective than its single fractions on human colorectal cancer.

Acknowledgement: The research study was supported in part by a grant from Seed Funding Programme for Applied Research (no.: 200807160015) and the contract research funding from China-Japan Feida Union Company Limited.

077

Ellagic Acid as an Zinc-Chelating Agent to Inhibit Cell Invasion and Angiogenesis

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Ellagic acid is a dietary polyphenolic compound that presents antioxidative, anti-inflammatory, anti-angiogenetic and anti-carcinogenic activity both in vivo and in vitro study. The aim of this study is to investigate ellagic acid as a zinc chelating agent on MMP-2 inhibition to serve as a target to inhibit tumor cell invasion and tumor-induced angiogenesis. In this report, we found that the neovascularization of embryo chorioallantoic membrane (CAM) was inhibited by ellagic acid, which implicated the potential anti-angiogenic effect of ellagic acid. Further study using an in vitro matrix-induced tube formation of HUVECs again confirmed the anti-angiogenic activity by ellagic acid exerted no inhibitory effect on the growth of HUVECs. The migration of HUVECs as analyzed by transwell assay was suppressed markedly by ellagic acid dose-dependently as well. Matrix metalloproteinases (MMPs) play the key role in cell invasion and angiogenesis. Our results demonstrated that ellagic acid inhibited MMP-2 activity and suppressed its secretion from HUVECs. The suppression of secretion correlated well with the up-regulated mRNA and protein levels of RECK. All of the above processes treated with ellagic acid can be overcome by the addition of zinc. It is concluded that ellagic acid exhibit anti-angiogenic and anti-migration activity which is mediated by suppression of MMP-2 activity and secretion associated with up-regulation of RECK due to zinc chelation activity.

078

Relationship of Cytokine Level with Cancer Cachexia and Therapeutic Effects of Chinese Herbs on Cancer Cachexia Mice

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Aim: To investigate the relationship between cytokine levels (IL-6 , IL-10 , TNF and IFN-γ))and cancer cachexia on murine model , and to observe the effects of 5-FU+Chinese herbs(low or high dose) on cancer cachexia and survival of mice.

Method: C57BL/6 mice bearing Lewis lung carcinoma were used to establish murine cancer cachexia model. The serum cytokine levels (IL-6 , IL-10 , TNF and IFN-γ) and the changes of physiological conditions (body weight, food and water intake) of the mice were measured at different time points before and after treatment with daily force-feeding with Chinese herbs (compound formula) (low dose: 1.5 mg/g ; high dose: 3mg/g) or saline.

Results: The mice in cancer cachexia group had significantly higher serum levels of IL-6 , IL-10 and TNF and lower serum levels of IFN-γ and lower body weight than those in healthy control group. Compared to saline treatment, Chinese herbs intervention apparently down-regulated the levels of IL-6, IL-10 and TNF ($P < 0.001$) , and up-regulated the levels of IFN-γ($P < 0.001$) remarkably prolonged the survival of mice.

Conclusion: The results suggest that serum IL-1, IL-6 , TNF and IFN-γ are possibly associated with cancer cachexia . Chinese herbs (compound formula) may potentially improve cancer cachexia through up-regulating and down-regulating levels of cytokines.

Keywords: Cancer cachexia, cytokine, IL-6 , TNF,Chinese herbs

079

Glycyrol induces apoptosis in human Jurkat T cell lymphocytes via the Fas-FasL/caspase-8 pathway

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Glycyrrhiza uralensis (Leguminosae) has long been used to treat inflammatory ailments, such as gastric ulcers, arthritis, and rheumatism. From this traditional herbal plant, glycyrol, a coumestan with anti-bacterial and anti-inflammatory activities, was first isolated and synthesized to test its apoptosis-inducing properties in human Jurkat cells. Flow cytometry analysis indicated that glycyrol can arrest the cell cycle in S phase and subsequently induce apoptosis in both time- and dose-dependent manners. Glycyrol was revealed to activate the Fas/FasL-FADD-caspase-8 pathway in human Jurkat cells, bypassing the p53 and mitochondrial-mediated cascade (IC_{50} 19.1 μM). Our previous research on glycyrol showed a glucocorticoid-like mode of action, suppressing NF-κB-regulated gene transcription regardless of NF-κB DNA binding, which suggests the inhibitory activity of glycyrol on the pro-survival response of NF-κB in cancer cell lines. The summary of these findings indicate that glycyrol can be a potential anti-tumor compound that can induce cell cycle arrest and subsequent apoptosis.

080

Induction of Nucleolin Translocation by Acharan Sulfate in A549 Human Lung Adenocarcinomas

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Acharan sulfate (AS), isolated from the giant African snail *Achatina fulica*, is a novel glycosaminoglycan, consisting primarily of the repeating disaccharide structure α-D-*N*-acetylglucosaminyl (1→4) 2-sulfoiduronic acid. AS shows anti-tumor activity *in vitro* and *in vivo*. Despite this activity, AS is only weakly cytotoxic towards cancer cells. We examine the interactions between AS and cell surface proteins in an effort to explain this anti-tumor activity. Using flow cytometry anaysis and affinity column chromatography, we confirm that AS has strong affinity to specific cell surface proteins including nucleolin in A549 human lung adenocarcinomas. Surprisingly, we found the translocation of nucleolin from nucleus to cytoplasm under the stimulation of AS (100 μg/ml) *in vitro*. Also, as nucleolin exits the nucleus, the amounts of growth factors such as bFGF, and signaling cascade proteins, such as p38, p53 and pERK, are altered. These results suggest that the communication between AS and nucleolin plays a critical role on signal transduction in tumor inhibition.

081

Platycodin D, a triterpenoid saponin from Platycodon grandiflorum induces cell cycle arrest and caspase-mediated apoptosis in human cancer cell lines

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Natural products have played major roles in drug discovery including development of anti-cancer agents. Especially, saponins have been reported to have important anti-cancer properties. Platycodin D (PD) is a triterpenoid saponin isolated from the root of *Platycodon grandiflorum* (Campanulaceae). We investigated its anti-proliferative activities in human non-small cell lung carcinoma (NSCLC) A549 and human gastric adenocarcinoma AGS cell lines. To identify anti-cancer mechanism of PD, a series of assays including cell proliferation assay, cell cycle analysis, and immunobloting analysis were conducted in terms of apoptosis related protein regulation. PD exhibited the growth inhibition activities with IC_{50} values of 21.5 μM in A549 and 25.6 μM in AGS cell lines, respectively. The cytotoxic effects of PD were accompanied by a G (2)-M phase cell cycle arrest of the cell cycle both in dose and time dependent manners and the characteristics of apoptosis were further determined by DAPI staining, DNA fragmentation assay, annexin V and propidium iodide (PI) double staining induced exposure ratio of phosphatidylserine (PS) to the cell surface and increased sub-G(1) ratio. Apoptosis induced by PD was also confirmed by increased cleaved PARP-1, decreased procaspase -3, -8, and -9. The apoptotic effect of PD is known to associate with the inhibition of pro-survival protein such as Akt and Erk. The present results indicate that PD induces cellular apoptosis in A549 and AGS cell lines by the activation of caspase cascade and can be a potent anticancer agent against human lung and gastric cancers, in which it has a potential to be compatible with the conventional chemotherapy.

082

The in vitro anti-breast cancer activity of furanodiene, a natural product isolated from Ezhu

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Aim: This study was designed to evaluate the anti-breast cancer activities of furanodiene (*fur*), a natural product isolated from *Ezhu*, *in vitro*. **Method**: Two breast cancer cell lines MCF-7, MDA-MB-231 were used and treated with different doses of *fur*. The anti-proliferative effect of *fur* was measured by MTT and the LDH release in the cultural medium was measured with a LDH commercial kit. The mitochondrial function changes after *fur* treatment were investigated using JC-1 fluorescent dye. Effect of *fur* on cell cycle was performed with PI staining and analyzed by flow cytometry. The three-dimensional cell invasion model was used to evaluate its anti-invasion activity. Related proteins expression was detected by western blot. **Results**: Fur could significantly inhibit the proliferation of MCF-7 and MDA-MB-231 cells in a time- and dose-dependent manner. The LDH release was also dramatically increased in both cell lines after *fur* treatment. JC-1 fluorescence ratio (Red/Green) was dramatically decreased suggesting the loss of mitochondrial membrane potential. Flow cytometry showed that *fur* induced cell cycle arrest at the G0/G1 phase. MDA-MB-231 cell metastasis was siginificantly inhibited by *fur*. The protein expression of p-cyclin D1, total cyclin D1, p-CDK2, Rb, p-FAK, Integrin αV, p-P85 and β-catenin was significantly inhibited by *fur*. **Conclusion**: These results indicated that *fur* suppresses breast cancer cell growth by inducing cell cycle arrest *via* regulation of mitochondrial-function and p-cyclin D1, total cyclin D1, p-CDK2 expression. Furthermore, *fur* could also significantly inhibit tumor cell metastasis, which might be mediated by regulating integrin pathway. Therefore, the present study demonstrated that *fur* had significant inhibitory effects on breast cancer through cells proliferation and metastasis *in vitro*, suggesting its anti-tumor potential.

Keywords: furanodiene; breast cancer; proliferation; cell cycle; apoptosis; metastasis

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083

Orient Dredging Regimen Exercise(ODRE) Plays a Role in the Prevention and the Recovery of Cancer Diseases

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As a part of complementary and alternative medicine (CAM), exercise therapy such as Orient Dredging Regimen Exercise (ODRE) has been widely used for improving the health situation and preventing cancer diseases. The possible mechanisms have also been investigated in the further studies.

ODRE has a long history of thousands of years. It is an integration of static stretching poses, breathing exercises, meditation, awareness guide and the other related methods unifying physical and mental activities which is specifically different from the common general exercise programs. ODRE includes Tai Chi, Five Animal Frolic, Ba-duan-jin Exercise, Breath Practice based on Traditional Chinese Medicine (TCM) and Yoga as well. Studies have shown that ODRE has very positive benefits for not only improving surgical outcomes, reducing symptom experience, managing side-effects of radiation and chemotherapy, but also improving psychological health of the cancer patients. Most studies have indicated that ODRE has beneficial roles in preventing and rehabilitating breast cancer, colorectal cancer, lung cancer, and prostate cancer.

The mechanisms of ODRE therapy are much complex. Most studies have shown that ODRE has significant modulatory effects on neuro-endocrine-immune network. Firstly, ODRE significantly elevates NK cell activity and enhances immune function of neutrophils, macrophages, T and B lymphocytes. Secondly, ODRE reduces the progression of mammary carcinogenesis induced by the involvement of stress hormones such as catecholamines and prolactin, which are associated with cancer pathogenesis. Thirdly, ODRE primarily activates vagal afferent, affects the production of β-endorphin, and regulates function of hypothalamic–pituitary–adrenal axis. In addition, ODRE plays positive roles in promoting cardiorespiratory fitness and increasing metabolism excretion of metal waste.

It would be much better and important that the patients are instructed by appropriately trained and professionally accredited exercise specialists to practice ODRE. It is also necessary to explore the potential mechanisms through modern cellular and molecular biological techniques.

084

Induction of G2/M Phase Arrest and Apoptosis by Oridonin in Human Laryngeal Carcinoma Cells

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Oridonin, an active component isolated from the plant *Rabdosia rubescens*, has been reported to exhibit antitumor effects. In this study, the mechanism involved in oridonin-induced growth inhibition, including apoptosis and G_2/M phase arrest, in human laryngeal carcinoma HEp-2 cells deficient in functional p53, was investigated for the first time. Compound oridonin triggered the mitochondrial apoptotic pathway, as indicated by increased Bax/Bcl-2 ratios, reduction of mitochondrial membrane potential ($\Delta\psi m$) as well as a substantial increase in apoptosis-inducing factor (AIF) and cytochrome *c*. Inhibition of caspase-9 in HEp-2 cells did not protect the cells from oridonin-induced apoptosis, and cleaved caspase-9 was not detected, indicating that apoptosis occurred via a caspase-9-independent pathway. Cell cycle blockage was associated with down-regulation of cell cycle related cyclin B1, cdc2 and cdc25c levels, as well as up-regulation of p21, phospho-Cdc2 and phospho-Cdc25C levels. The results also suggested that G_2/M phase arrest and apoptosis mediated by oridonin occurred via a p53-independent but in a p21/WAF1-dependent manner in HEp-2 cells. In addition, the generation of reactive oxygen species (ROS) was found to be a critical mediator in growth inhibition induced by oridonin. Blocking ROS generation with N-Acetylcysteine (NAC) or catalase (CAT) significantly prevented G2/M arrest by reversing the changes of G2/M regulatory proteins and completely protected the cells from oridonin-induced apoptosis. Taken together, the results indicate that oridonin is a potentially effective agent for the treatment of laryngeal squamous cell carcinoma.

085

Biologics as a New Class of Active Principles in Herbal Medicine

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Peptide and protein biologics are therapeutics and prophylactics known for their desirability of high specificity and low toxicity. They display a wide range of biological activities such as antimicrobial, immunomodulation, neurotransmission and hormonal functions. Most are derived from animal sources with few representatives from plants. In herbal medicine, these biologics have not received much attention because of the common perception that they are unstable and unavailable as a source of active principles in decoctions. This bias is explained by their heat instability during decoction preparations, poor absorption through the gastrointestinal tract and their susceptibility to enzymatic and acidic hydrolysis under harsh environment inside our stomach.

Here we report that peptides and proteins are a class of active principles in plants hitherto unexplored in herbal and Chinese medicine. They are a large group of disulfide-rich peptides which are categorized into family according to the amino acid sequence homology and spacing between cysteine residues. These peptides have recently gained great interest among the scientific community due to their remarkable stability and many justified biological functions. They possess a well-defined 3D structure with a clustering of hydrophobic side-chains externalized by the knotted sulfide core. Such structural elements constitute the compactness and accounts in part for their stability to heat and chemical denaturation, and also amphipathicity in promoting absorption through gut. These advantages enhance the potential of plant biologics as active principles in medicinal plants.

086

Mechanism Study of Migration Inhibition on Human Lung Non-small Carcinoma Cell by Extract of Pericarpium Citri reticulatae

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Matrix Metalloproteinases (MMPs), a family of endopeptidases with the ability of degrade ECM proteins, play a fundamental role in inflammation, tissue remodelling, tumour invasion and metastatic progression (1). Several soluble MMPs involved in the degradation of collagens, laminins and fibronectin are produced by cancer cells raising the possibility that they might contribute to their invasion across basement membranes and interstitial tissue (2). During apoptosis, MMP members were required for remodelling of the cell matrix and cell-to-cell contact (3).

In this study, the inhibition effect of extracts from non-processed and steam-processed Pericarpium Citri reticulatae (*Citrus reticulate* Blanco., coded as CR) on the migration of human lung non-small carcinoma cell H460 was revealed by the cross wound assay. We found that only the extract from the processed CR (pCR) under concentration of 300 μg/ml was able to inhibit the migration of H460. Then, the Affametrix gene chip was used to examine the relative gene expression on inhibition of H460 cells migration after treatment with extract of pCR. The gene expression of MMPs family members was detected and confirmed by Quantitative Real Time-PCR with endogenous control genes, GAPDH and RPLP0. In the brief conclusion, the gene expression of MMP1 is the key of the mechanism of inhibition migration on H460 cells treated with extract of pCR, and the major component of pCR, hesperetin which hydrolyzed from hesperidin in original Pericarpium Citri reticulatae, could be the active role in this effect of migration inhibition on H460.

087

The Characteristics of eIF3i in Prostate Cancer Treatment with penta-O-galloyl-β-D-glucose (5GG) Via Proteomic And Western Analysis

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Prostate cancer is the second leading cause of cancer-related death among men in the U.S. Bone damage or tumor cells that proliferate in bone tissue induce inflammatory responses. Inflammation in bone tissue is associated with the expression of transforming growth factor-✩, which in turn induces the expression of EGF in osteoblasts and osteoclasts. In our previous study, penta-O-galloyl-✩-D-glucose (5GG) suppresses prostate cancer bone metastasis by transcriptionally repressing EGF-Induced MMP-9 expression. To identify proteins involved in 5GG repression tumor bone metastasis, we utilized a proteomic approach to reveal protein expression changes in prostate cancer cell line PC3 following 5GG treatment. The eIF3i is one of targets via proteomic analysis. Eukaryotic initiation factor 3 (eIF3) is involved in initiation process of protein translation and overexpression of its subunit eukaryotic translation initiation factor I (eIF3i) has been observed in carcinomas. Nevertheless, the potential role of eIF3i in cancer metastasis is poorly understood. We found that treatment of PC3 with 5GG decreased migration activity and the protein expression of eIF3i by in vitro invasion assay and immunoblotting. But, the eIF3i mRNA level was not consistent with protein expression by 5GG treatment in PC3. In addition, stimulation of cell with 5GG reduced AKT and mTOR phosphorylation. We suggest the protein expression of eIF3i was regulated by AKT/mTOR involved protein synthesis pathway. Furthermore, PC3 cells transfected with eIF3i shRNA that significantly reduced the number of invasion cells. Thus, eIF3i plays a critical role in prostate cancer metastasis.

088

Deoxyelephantopin Suppresses Lung Metastasis of B16 Melanoma in Mice

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The objective of this study is to identify novel phytocompounds from medicinal plant as chemopreventive agent for skin melanoma. *Elephantopus scaber* L. (Asteraceae) is a traditional herbal medicine claimed for anti-cancer effects. We evaluated the *in vitro* and *in vivo* efficacy of a major sesquiterpene lactone constituent of *E. scaber*, deoxyelephantopin (DET), for its anti-B16 melanoma cell activity and the underlying molecular mechanism. Our data show that DET could induce cell cycle arrest at G2/M phase at 5 μM, with the decrease of cyclins A, B1, and D1 protein expression. When increased DET concentration to 8 μM, apoptotic hallmarks PARP and caspase 3 were activated in a time-dependent manner. DET also inhibited B16 cell migration accompanied with inhibiting of MMP-9 activity. A non-invasive real-time *in vivo* imaging system to monitor the melanoma cell growth and metastasis in mice is created in this study. The stable B16 melanoma cell clone carrying COX-2 promoter driven-luciferase gene was established and used to comparative study of the efficacy of DET and a chemotherapeutic drug cisplatin in C57BL/6J mice. We observed that Pre-DET10 (10 mg/kg BW), and cisplatin (CP, 2 mg/kg BW) have similar profound effect on inhibiting lung metastasis of B16 melanoma and increase of median survival rate in tested mice (tumor control: 33 days, pre-DET10: 43 days, CP2: 43 days). Notably, Pre-DET10 treatment has little or no side-effects compared to cisplatin treatment in mice. This report presents the novel pharmacological effect of DET which may be worthy for further development into an agent against skin melanoma.

089

Deoxyelephantopin Sensitizes Human Breast Cancer MDA-MB-231 Cells via Activation of Extracellular Signal-Regulated Kinase 1/2 and Inhibition of Signal Transducers and Activators of Transcription Signaling

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Breast cancer is very common for women. It is often highly resistant to chemotherapy, and there is still no effective cure for patients with advanced stages of this disease. In this study, we evaluated the effect of deoxyelephantopin (DET), a phytocompound extracted from *Elephantopus scaber* plant (Asteraceae), as a possible anti-tumor active ingredient against human breast cancer MDA-MB-231 cells. We observed that DET could effectively suppress the growth of test tumor cells *in vitro* in a cell apoptosis assay. In response to DET treatment, a significant decrease in transforming growth factor-beta (TGF-β) level was observed in test cells. DET effectively inhibited the cell growth by inducing a G_2-M phase cell cycle arrest and apoptosis in test tumor cells. This cell cycle arrest is associated with an increase in level of p21, phospho extracellular signal-regulated kinase 1/2 (ERK-1/2) and Bax-2. Interestingly, decreased levels of phospho-NF-κB, NF-κB downstream signaling pathway molecules like survivin, Bcl-2, MMP-9, VEGF, cyclin-D1, -D3, CDC-2, CDK-4 and caspase-3 were observed in DET-treated MDA-MB-231 cells. We also observed a strong inhibitory effect of DET on signal transducers and activators of transcription (STAT) -1, -3 and -5 at the total protein levels, and at the phosophorylation levels of STAT-3 and -5. DET also significantly inhibited the cell adhesion, migration and spreading activities of test tumor cells. Our findings suggest that DET may warrant further systematic investigation for potential translational research applications to breast cancers.

090

Effect of Moscatilin in Esophageal Cancer

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Esophageal cancer is one of the most poor response malignancies to conventional treatment. Several studies have indicated that moscatilin a bibenzyl derivative from the orchid dendrobrium moscatum, and the stem of dendrobrium loddigesii possesses anticancer activity. However, its antitumor effect against esophageal cancer has not been explored.

We investigated the effect of moscatilin on growth of human esophageal carcinoma cells and its possible mechanisms.

Preliminary result: moscatilin inhibited growth of SKGT-4 and 81T/VGH cells in a dose - dependent and time - dependent manner. SKGT-4 cells treated with moscatilin had morphological changes such as chromatin condensation and multinuclei observed by Liu's staining.

091

Aloe-Emodin Reverses Epithelial-to-Mesenchymal Transition in Metastatic Oral Cancer Cells by Targeting Twist

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In Taiwan, the death rate of human oral cancers is the highest within head and neck cancer. The cancer metastasis causes poor clinical outcome and higher death rates of patients. Recently, it has indicated that epithelial-mesenchymal transition, EMT plays an important role in cancer metastasis. Previous researches showed *twist* overexpression was associated in EMT and cancer metastasis. *Twist* is a trsnscriptional factor involved in EMT. *Twist* may reduce the E-cadherin regulated adhesion activity leading to increase the abilities of cell invasion and metastasis. It also could cause poor clinical outcome, and therapeutic resistance of radiation therapy and chemotherapeutic agent. In the present study, the oral cancer cells FADU was stable transfected with *twist*. Our study showed that *twist* may induce EMT and lead to develop some characteristics of cancer stem cell. Interestingly, our data showed that Aloe-Emodin significantly inhibited FADU/*Twist* cell proliferation. We also found that Aloe-Emodin treatment resulted in the up-regulation of E-cadherin and down-regulation of vimentin, which was consistent with morphologic reversal of EMT phenotype leading to be epithelial. Moreover, we found that Aloe-Emodin could down-regulate the expression of the major EMT regulators, Twist transcription factors. Overall these findings demonstrate Aloe-Emodin was able to reverse EMT to suppress the invasive property of metastatic oral cancer cells at the transcriptional level.

092

Evaluation on Bioactive Compounds of Six Golden Camellias and Anti-cancer Effects in Breast Cancer Cell Lines

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Tea is the most popular beverage worldwide. The golden camellia tea be known for "Queen of the tea family ", is traditional used to keep health fit as tea and drinking in China. Golden camellia belongs to golden camellia group, camellia genus, one of the rarest flowers in the world. There have been few research studies that document the value of golden camellia tea. The purpose of this study is to investigate the content of bioactive compounds and the anti-cancer effects in the leaves of *Camellia murauchii, C. impressinervis, C. euphlebia, C. thunhinensis, C. nitidissima var. microcarp, C. nitidissima*. Catechin is the major polyphenol in the tea. To compare total catechin and total polyphenol content by folin-ciocalteu method and HPLC system, our data showed *C. murauchii* was detected significantly higher than other species. Among these extracts, our results showed that total amino acids and antioxidant activity were different between these camellias. *C. euphlebia* had the highest content of amino acids in these species. Interestingly, *C. thunhinensis* had the highest antioxidant activity in all species, but it had lowest total polyphenol contents and total amino acids. In addition, the golden camellia tea was used to test the biological functions including anti-proliferation and apoptotic effects in human breast cancer MCF-7 cells. Our data showed that *C. thunhinensis remained* most active using both flow cytometry and the cleavage analysis of apoptosis-relatied molecules.

093

Osthole Suppresses Fatty Acid Synthase Expression in HER2-Overexpressing Breast Cancer Cells through Modulating Akt/mTOR Pathway

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Fatty acid synthase (FASN, EC 2.3.1.85) is a multifunctional enzyme that performs seven sequential reactions to convert acetyl-CoA and malonyl-CoA to palmitate, plays a central role in the anabolic conversion of dietary calories into storage form of energy in mammals. While FASN has been shown to be expressed in many human solid tumors, FASN has also been identified in preneoplastic lesions. HER2, which has also been identified in preneoplastic breast lesions, has been shown to upregulate FASN expression. Osthole, an active constituent isolated from the fruit of *Cnidium monnieri* (L.) *Cusson*, a traditional Chinese medicine, was found to be effective in suppressing FASN expression in HER2-overexpressing breast cells. Osthole preferentially inhibited proliferation and induced apoptosis in HER2-overexpressing cancer cells. Moreover, osthole inhibited the phosphorylation of Akt and mTOR. The use of Akt-overexpression revealed that the modulation of Akt, mTOR was required for osthole-induced FASN suppression. Finally, we showed that osthole could enhance paclitaxel-induced cytotoxicity in HER2-overexpressing cancer cells. These results suggested that osthole has the potential to advance as chemporeventive or chemotherapeutic agent for cancers that overexpress HER2.

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(-)-Epigallocatechin Gallate Induces Fas/CD95-mediated Apoptosis through Inhibiting Constitutive and IL-6-induced JAK/STAT3 Signaling in Head and Neck Squamous Cell Carcinoma Cells

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In this study, we examined the effects of several plant-derived natural compounds on head and neck squamous cell carcinoma (HNSCC) cells. The results revealed that (-)-Epigallocatechin gallate (EGCG) demonstrated the most efficient cytotoxic effects on HNSCC cells. We then investigated the underlying molecular mechanism for the potent proapoptotic effect of EGCG on HNSCC. Cell apoptosis was observed in the EGCG-treated SAS and Cal-27 cells both in time- and dose-dependent manner. In concert with the caspase-8 activation by EGCG, an enhanced expression in functional Fas/CD95 was identified. Consistent with the increased Fas/CD95 expression, a drastic decrease in the Tyr705 phosphorylation of STAT3, a known negative regulator of Fas/CD95 transcription, was shown within 15 minutes in the EGCG-treated cells, leading to down-regulation of the target gene products of STAT3, such as bcl-2, vascular endothelial growth factor (VEGF), mcl-1, and cyclin D1. An overexpression in STAT3 led to resistance to EGCG, suggesting that STAT3 was a critical target of EGCG. Besides inhibiting constitutive expression, EGCG also abrogated the Interleukin-6 (IL-6)-induced JAK/STAT3 signaling and further inhibited IL-6-induced proliferation on HNSCC cells. In comparison with apigenin, curcumin and AG490, EGCG was the more effective inhibitor of IL-6-induced proliferation on HNSCC cells. Overall, our results strongly suggest that EGCG is a potent inhibitor of constitutive and IL-6-induced STAT3 phosphorylation. This mechanism may be at least partially responsible for EGCG's ability to suppress proliferation of HNSCC cells. Taken together, these findings provide that EGCG may be useful in the chemoprevention and/or treatment of HNSCC.

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NBM-HD-1: A Novel Histone Deacetylase Inhibitor, Semi-Synthesized from a Natural Derivative, with Anticancer Activity Both In Vitro and In Vivo

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Epigenetic changes are key factors in the control of gene expression and are known to be correlated with many diseases. Acetylation is an important histone modification that is primarily regulated by two enzymes: histone acetyltransferase (HAT) and histone deacetylase (HDAC). In recent years, HDAC inhibitors (HDACis) have been developed as promising anticancer agents. Our studies found NBM-HD-1, a compound semi-synthesized from propolin G isolated from Taiwanese green propolis, to be potent suppressor of cell growth in human breast cancer cells (MCF-7 and MDA-MB-231) and rat C6 glioma cells, with IC_{50} ranging from 8.5~10.3 μM. Biochemical studies indicated that NBM-HD-1 is an HDACi. Levels of p21, gelsolin, Ac-histone 3, Ac-histone 4, and Ac-tubulin increased significantly after treatment of cancer cells with NBM-HD-1. p-PTEN and p-AKT levels were markedly decreased after treating cancer cells 1~4 h. We also evaluated NBM-HD-1 on regulating cell-cycle regulators. After treatment with NBM-HD-1, p21 gene expression increased, while cyclin B1 and D1 gene expressions decreased markedly. We also evaluated the effect of NBM-HD-1 on tumor suppressor gene *p53* and *PTEN* expression in rat astrocytes. NBM-HD-1 increased expression of these two genes in a dose-dependent manner. In addition, we found that NBM-HD-1 exhibited potent antitumor activity in xenograft models. In conclusion, Our studies demonstrated that the novel compound NBM-HD-1 is a potent inducer of differentiation in MCF-7, MDA-MB-231, and C6 cancer cells.

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The Inhibitory Activities of Pomegranate on Carbohydrate Digestive Enzymes α-glucosidase and α-amylase

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Pomegranate (*Punica granatum* Linn.) has been traditionally consumed for diabetes mellitus according to Unani and Ayurvedic literatures, and also used in recipes in some parts of China. Recent studies have demonstrated that the flower, peel and seeds of pomegranate exhibited hypoglycaemic activities in several rodent models. In particular, the flowering part of pomegranate showed positive effects against postprandial hyperglycaemia through α-glucosidase inhibition, a rate limiting step for glucose absorption in the gastrointestinal tract. In the present study, the effects of different parts of the pomegranate fruit, including the juice, peels and seeds, on α-amylase and α-glucosidase enzyme activities were evaluated *in vitro*. Various parts of the pomegranate fruit effectively inhibited both rat intestinal α-glucosidase and porcine pancreatic α-amylase enzyme activities in a concentration-dependent manner. The juice, which is the widely available component of the pomegranate fruit, was subjected to bioassay-guided fractionation in order to identify the active fraction against both enzymes. Our results demonstrated that the ethyl acetate fraction of the juice inhibited both α-glucosidase and α-amylase enzyme activities more potently than the other fractions, including the 1-butanol/water fraction and the crude juice. Furthermore, the inhibitory effect of the ethyl acetate fraction against α-glucosidase was found to be directly dependent on sample concentrations and pre-treatment time, but inversely dependent on enzyme and sucrose concentrations. In addition, the activities of several prominent pomegranate phytochemicals which have been previously described were evaluated against α-glucosidase. It was found that gallic acid, quercetin and ellagic acid concentration-dependently inhibited α-glucosidase activities by 83.6%, 54.1% and 44.0%, respectively, at a concentration of 66.7 μg/mL. In summary, the results indicate that the consumption of pomegranate fruit may be beneficial in the management of diabetes mellitus, particularly postprandial hyperglycaemia, by inhibiting dietary carbohydrate digestive enzymes in the gastrointestinal tract.

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Neuroprotective Effect of Wei Nao Kang (WNK) Mediated by Inhibition of NMDA-dependent Ca2+ Influx

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Wei Nao Kang (WNK) is a three-herb formula comprising a mixture of *Gingko biloba*, *Panax ginseng* and *Crocus sativus* extracts designed for the treatment of vascular dementia (VaD). Data from the preclinical studies and a pilot clinical trial indicate the effectiveness of WNK on the improvement of cognitive function impairments associated VaD. This study aims to test a hypothesis that WNK exerts its neuroprotective properties via inhibition of NMDA receptors. Using LDH release and MTT cytotoxicity assays, we showed that NMDA caused delayed death of cortical neurons, preventable by conventional NMDA receptor antagonists MK-801 and APV. Pretreatment with of WNK for 15 min inhibited 200 μM NMDA-induced cell death by maximum of ~50% with IC_{50}=2.3 μg/ml. To determine the mechanism of action underlying the observed effect, we developed a high-throughput intracellular Ca^{2+} assay with Fura-2, using fluorescence microplate reader. It was shown that NMDA induced intracellular Ca^{2+} overload correlated well with the NMDA-induced neurotoxicity. WNK inhibited Ca^{2+} overload, but only partially (~50%), compared to that of the conventional antagonists (MK-801 and APV). Comparative analysis of the contribution of the individual WNK component to the cell protection and Ca^{2+} overload inhibition showed that *Panax ginseng* exerted a greater effect than *Gingko biloba. Crocus sativus* was not active in these assays. Overall, the current study suggests that WNK has demonstrated a neuroprotective property which is at least partially mediated by inhibition of NMDA-dependent Ca^{2+} influx. Further studies are required to investigate molecular mechanisms of WNK upon sub-chronic and chronic administration.

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Study on Mechanism of Delaying Vascular Aging of Senile Mice by Chinese Herbs with Tonifying Qi and Activating Blood

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Objective: explore the functional and structural changes of vascular wall caused by aging in senile mice, as well as the intervention effects of extracts from Panax ginseng, Panax notoginseng (Burk.) and Ligusticum chuanxiong. **Method**: The senile mouse model was established by natural aging, and a total of 84 mice were divided into six groups, aging-model group, young control group, Chinese herbs high-dose group, Chinese herbs medium-dose group, Chinese herbs low-dose group, vitamin E group. Morphological changes of aorta were observed in each group by HE and Masson staining; the concentrations of Ang Ⅱ in plasma and the levels of Anti-superoxide of vascular tissue were analyzed by biochemical testing; advanced glycation end products (AGEs), MMP-2 and TIMP-2 of vascular tissue were examined by ELESA testing. **Result:** In each group treated with Chinese herbs compared with aging-model, pathological analysis showed that exfoliation of endothelial cells was reduced, tunica media was not thickened obviously, and numbers of smooth muscle cells got close to young control group. In Masson staining, Chinese herbs with high dose, medium dose and low dose can decrease the contents of collagen fibers of arotic wall, but did not improve in the smooth muscle. Compared with aging-model group, the levels of Ang Ⅱ in plasma in three Chinese herbs groups were not reduced, but productions of ROS were decreased obviously. Chinese herbs with each dose can reduce AGEs production of vascular tissue, inhibit activities of MMP-2 and regulate balance of MMP-2/TIMP-2 significantly, especially with high dose. **Conclusion:** Chinese herbs with Tonifying Qi and activating blood can ameliorate stiffening and remodeling of vascular wall in senile mice, and ultimately delay vascular aging.

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Amelioration of Diabetic Nephropathy in Otsuka Long-Evans Tokushima Fatty (OLETF) Rats by a Group of Chinese Herbs (Tangshen Formula)

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Objective: Diabetic nephropathy is one of the most important microvascular complications of patients with type II diabetics. The concise mechanism of diabetic nephropathy is unknown and there is no successful treatment option for this condition. The objective of the current research was to investigate the effects of Chinese herbs (Tangshen formula) on diabetic nephropathy in Otsuka Long–Evans Tokushima Fatty (OLETF) rats. Methods: 45 OLETF rats and 20 LETO rats were divided into four groups: LETO control, OLETF diabetic group, OLETF diabetics treated with Tangshen formula group, and OLETF diabetics treated with monopril group. Body weight, blood glucose, and 24 h urinary proteins were measured once every four weeks. Blood samples and kidney tissues were obtained for analyses of total cholesterol, triglyceride, whole blood viscosity, plasma viscosity, and pathohistological examination at 36 and 56 weeks. Results: Compared with control LETO rats, OLETF rats showed significant improvement in all parameters examined in the study. Treatment of OLETF rats with Tangshen formula significantly improved blood glucose, body weight, 24 h urinary protein content, serum total cholesterol, whole blood viscosity and plasma viscosity at certain time points. Moreover, treatment with Tangshen formula did reduce the glomerulosclerotic index and interstial fibrotic index in the kidney of OLETF rats. Conclusion: The Chinese herbs in Tangshen formula could attenuate the development of diabetic nephropathy in an experimental type II OLETF rat diabetic model. The mechanism of Tangshen formula in the attenuation of diabetic nephropathy could be related to its improvement of hyperglycemia, hypercholesteremia, and blood viscosity.

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Proteomic Analysis of Protective Mechanism on Type 2 Diabetic Nephropathy Rats by a Group of Chinese Herbs (Tangshen Formula)

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Objective The study is to explore the mechanism and therapeutic targets of Tangshen Formula on type 2 diabetic nephropathy rats. **Methods:** Spontaneous animal model of type 2 DN——OLETF rats were introduced from Japan. The animals were randomly divided into model group and TSF group, LETO rats were used as control group which were the same genetic background, same week age and sex, but not developing diabetic nephropathy. The rats were sacrificed at 36 and 56 weeks of age, and the renal cortical protein including soluble protein and insoluble protein were respectively prepared. Those Proteins were employed for two-dimensional gel electrophoresis. Then differentially expressed proteins were identified by matrix-assisted laser desorption ionization–time-of-flight mass spectrometry (MALDI-TOF-MS) and some of these proteins would be validated by Western blot analysis. **Results:** 2-DE analyses revealed 19 differentially expressed protein spots between Tangshen Formula and model groups. 5 spots down-regulated (Tsta3 › CRA_a › Lactb2 › BOP1NT › Mixture of A2GP and Zfp90)and 5 up-regulated (Ech1 › Psma1 › Gsto1 › Crystallin › Hmgb1)in soluble protein; 4 spots were down-regulated (Vinculin › Myosin › Uqcrfs1 › Gpx-3)and 5 up-regulated(Timm › Atpase › Ppia › Hypothetical protein › Dmgdh) in insoluble protein. After MALDI-TOF-MS analysis, all 19 protein spots were successfully identified with the PMF method. Representatively, GPx-3 which is differentially expressed in 36 and 56 weeks of age was validated by Western blot analysis. **Conclusion:** Proteomic analysis identified 19 differentially expressed proteins between model and Tangshen Formula groups. The expression of identified proteins was found to be closely related with the reduction of reactive oxygen species › correction of lipid metabolic abnormalities › maintenance of cell structure and function. Tangshen Formula seems to be a potential treatment of diabetic nephropathy by multi-target therapy.

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American Ginseng (Panax Quinquefolius) Prevents Diabetes Induced Retinal Changes

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Diabetic retinopathy (DR) is the most serious ophthalmic complication of diabetes leading to most of the cas of legal blindness in the western world. Furthermore, DR is also the commonest cause of visual impairmen the age group 30 - 65 years.

Oxidative stress contributes to the pathogenesis of several chronic diabetic complications including D Ginseng (Araliaceae), an herb demonstrates widespread biological effects, primarily due to its antioxida properties. The present study was undertaken to investigate the effects of ginseng on DR. As endothelial ce are primary targets in DR, we investigated preventive effects of ginseng on glucose-induced changes in huma umbilical vein endothelial cells (HUVECs). We also examined the preventive effects of ginseng on reti damage in both type 1(STZ-induced) and type 2 models (db/db) of diabetes. HUVECs were incubated with 2 mM glucose for 24 hrs with or without ginseng (ethanolic extract). Diabetic mice were treated for 2 months wi ethanolic extract of ginseng (200 mg/Kg, oral gavage) and were compared with age- and sex-matched control In HUVECs, treatment with ginseng caused significant diminution of glucose-induced fibronectin (FN), EDB FN(its splice variant), endothlin-1(ET-1), vascular endothelial growth factor(VEGF) heme oxygenase-1 (HO-1 mRNA levels. Ginseng further prevented glucose-induced increase in FN, VEGF and ET-1 protein level Glucose-induced oxidative stress detected by intracellular reactive oxygen species accumulation and DN damage in HUVECs were further prevented by ginseng. Both in STZ-mice and db/db mice, treatment wi ginseng significantly reduced blood glucose and glycated hemoglobin levels. Furthermore, ginseng treatme resulted in the reduction of body weight in the db/db mice. In both animal models, ginseng treatment prevente diabetes induced upregulation of retinal FN and $EDB^{+}FN$, VEGF and HO-1 mRNA levels.

These results suggest that ginseng prevents pathogenetic processes leading to retinal damage in diabetes through its antioxidative and antihyperglycemic properties.

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Ginseng Effects on Intestinal Lipid Secretion and Plasma Clearance in Pcyt2-Deficient Mouse Model for Metabolic Syndrome

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We have initially established an elevated intestinal lipid-triglyceride (TG) secretion and a reduced lipid clearance in a new animal model for the human metabolic syndrome-the CTP: ethanolaminephosphate cytidylyltransferase mice (*Pcyt2*$^{+/-}$). In this study, we investigate if ginseng treatments could reduce the elevated TG lipid content in the plasma of the *Pcyt2*$^{+/-}$ mice. The *Pcyt2*$^{+/-}$ 32-week old, obese and hyperlipidemic female mice (n=8) were assigned into two groups of which one group served as control (were orally administered only 0.9% saline) and the other group was treated with ginseng ethanol extract at a daily dose of 200 mg/kg for four weeks. The rate of intestinal lipid secretion at different time points was investigated after a single intragastric fat-load of olive oil containing [^{3}H]-glycerol trioleate (TO). The obtained data demonstrated that the intestinal, postprandial release of [^{3}H]-TO into plasma become significantly reduced in the ginseng treated animals compared to the saline treated littermate controls. To investigate the effect of ginseng on plasma lipid-lipoprotein clearance, at the end of the feeding period the ginseng treated and the saline treated control mice were intravenously injected with [^{3}H]-TO labeled VLDL-like particles. Based on the rate of [^{3}H]-TO disappearance, no difference in plasma lipid clearance between the two groups was found. Ginseng treatments however significantly enhanced the lipoprotein lipase activity in the plasma, liver and heart of *Pcyt2*$^{+/-}$ mice. Our data suggest that ginseng may play multiple roles in reducing plasma TG content, and as such it could represent a valuable application for the treatment of human hyperlipidemia.

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Berberine Ameliorates Renal Injury in Experimental Diabetic C57BL/6 Mice Involved in Suppression of SphK-S1P Signaling Pathway

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Aims/hypothesis: Berberine, a new hypoglycemic agent, is used increasingly in the treatment of diabetes. Recent studies have shown that berberine has beneficial effects on renal injury in Streptozocin (STZ)-induced diabetic rats; however, the mechanisms underlying the effects are not fully understood. Sphingosine kinase – Sphingosine 1-phosphate (SphK-S1P) signaling pathway has been implicated in the pathogenesis of diabetic complications, including diabetic nephropathy. The aim of this study was to investigate the effects of berberine on renal injury in alloxan-induced diabetic C57BL/6 mice, and on the changes of SphK-S1P signaling pathway in diabetic mouse kidney.

Methods: Alloxan-induced diabetic mice were treated orally with berberine (300 $mg \cdot kg^{-1} \cdot day^{-1}$) or vehicle every day for 3 months. To evaluate the effect of berberine treatment, we measured fasting blood glucose, body weight, kidney weight, blood urea nitrogen, serum creatinine and 24 h albuminuria, and examined the following parameters in the kidney: histological changes, the mRNA and protein expression of transforming growth factor β1 (TGF-β1), fibronectin (FN) and collagen IV (Col IV) as well as the changes of Sphingosine kinase activity and sphingosine 1-phosphate production.

Results: Berberine inhibited the increases in fasting blood glucose, blood urea nitrogen, serum creatinine and 24 h albuminuria in diabetic mice. Berberine treated-mice also showed lower kidney/body weight ratio than untreated diabetic mice. Berberine prevented glomerular hypertrophy, TGF-β1 synthesis and extracellular matrix (FN and Col IV) accumulation in diabetic mouse kidney. The SphK activity and S1P production in renal tissues were increased in diabetic mice and reduced by berberine treatment.

Conclusion/interpretation: In conclusion, berberine has suppressing effects on activation of SphK-S1P signaling pathway in alloxan-induced diabetic mouse kidney. This study represents a novel mechanism by which berberine might improve renal function in diabetic nephropathy.

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Effects of Berberine on Matrix Accumulation and NF-kappa B Signal Pathway in Alloxan-induced Diabetic Mice with Renal Injury

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One of the main pathological changes in diabetic nephropathy is the renal fibrosis, which includes glomerulosclerosis and tubulointerstitial fibrosis. In vivo and in vitro studies demonstrated that berberine could ameliorate renal dysfunction in diabetic rats with nephropathy and inhibit fibronectin expression in mesangial cells cultured under high glucose. However, the molecular mechanisms have not been fully elucidated. The purpose of the present study was to investigate the effects of berberine on the nuclear factor-kappa B (NF-κB) activation, intercellular adhesion molecule-1, transforming growth factor-beta1 and fibronectin protein expression in renal tissue from alloxan-induced diabetic mice with renal damage. The distribution of NF-κB p65 in glomerulus and the degradation of IκB-α in renal cortex were examined by immunohistochemistry and Western blot, respectively. The protein expression of intercellular adhesion molecule-1, transforming growth factor-beta 1 and fibronectin in renal cortex were also detected by Western blot. Our results revealed that in alloxan-induced diabetic mice, the nuclear staining of NF-κB p65 was increased in glomerulus, whereas renal IκB-α protein was significantly reduced. The protein levels of intercellular adhesion molecule-1, transforming growth factor-beta 1 and fibronectin were upregulated in kidney from diabetic mice. After berberine treatment, the immunostaining of NF-κB was decreased, and the reduced degradation of IκB-α level was partially restored. The protein levels of intercellular adhesion molecule-1, transforming growth factor-beta 1 and fibronectin were all downregulated by berberine compared with diabetic model group. In conclusion, the ameliorative effects of berberine on extracellular matrix accumulation might associate with its inhibitory function on NF-κB signal pathway.

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Effect of Emodin on Cell Proliferation, FN Expression and p38MAPK Pathway in Rat Mesangial Cells Cultured Under High Glucose

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Background: Diabetic nephropathy, one of the most serious microvascular complications of diabetes mellitus, is a major cause of end stage renal disease. Emodin, 3-methyl-1,6,8-trihydroxy anthraquinone, is an anthraquinone derivative isolated mainly from the Chinese herb, Rheum palmatum and giant knotweed rhizome. Previous studies have demonstrated that emodin plays a major role in improvement of renal function in diabetic nephropathy. Studies in vitro also have demonstrated that emodin is proposed as a potential agent exerting anti-proliferation and anti-fibrosis effect in mesangial cell. Although the evidence on the ability of emodin to counteract diabetic nephropathy is compelling, little is known about the molecule mechanisms. **Objective:** The purpose of our study is to investigate the effect of emodin on cell proliferation and fibronectin (FN) expression in mesangial cells cultured under high glucose, and then to explore the role of p38MAPK pathway in the protective effect of emodin in high glucose-induced mesangial cells. **Methods:** Cell proliferation was determined by MTT, cell cycle was determined by flow cytometry (FCM), and the protein levels of FN, p-p38MAPK, p-CREB, PPARγ, and CTGF in mesangial cells were detected by western blot. **Results:** The results showed that high glucose could induce cell proliferation, enhance protein expression of FN, phospho-p38MAPK, phospho-CREB and CTGF, and attenuate protein expression of PPARγ in rat mesangial cells compared with control group. Administration of emodin could inhibit those effects on rat mesangial cells which were produced by high glucose. **Conclusion:** We can draw a conclusion that high glucose treatment resulted in a higher cell proliferation and FN expression than control group, whereas emodin exerted an anti-proliferation and anti-FN expression effect in high glucose-induced mesangial cells, which is probably involved in inhibition of p38MAPK pathway, and subsequently regulation of CREB, PPARγ and CTGF expression.

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Development of High-throughput Yeast-based Activity-guided Screening Assay Targeting HMG-CoA Reductase Activity and Isolation of Active Constituents Inhibit HMG-CoA Reductase Activity from Total Triterpenoids Saponins of Gynostemma Pentaphyllum

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Gynostemma pentaphyllum (Gp), also called jiaogulan, is a rich source of dammarane-type triterpenoids and is used as a traditional Chinese herbal medicine for the treatment of various diseases including cancer and hyperlipidemia. In our laboratory, we have been investigating the anticancer and anti-hyperlipdemia activities of with Gp total triterpenoids (GpS). We found that GpS markedly reduced the numbers and sizes of polyps in *Apc*$^{min/+}$ mice, a commonly used mouse model for colorectal cancer, manifest both high number of intestinal polyps and hyperlipidemia. We also found that the GpS can effectively suppress the plasma triglycerides and cholesterol levels in *Apc*$^{min/+}$ and high-fat diet induced mice. The mRNA expression level of HMG-CoA reductase is significantly down-regulated upon GpS treatment in animals. Based on the above results, we have employed a knowledge-based drug discovery strategy to isolate the potential active constituents inhibit HMG-CoA reductase activity from GpS.

We have recently developed a reproducible, rapid and inexpensive yeast-based high-throughput (HTS) activity-guided fractionation assay to identity potential HMG-CoA reductase inhibitors. Our assay is based on the genetic interaction that *HMG1* and *HMG2* homozygous deletion strain is synthetic lethal in yeast cells; we can use this genetic interaction of yeast cells to screen for HMG-CoA reductase activity inhibitors. Among the nine isolated fractions from GpS, we have found one of the isolated fractions (YS57) has shown strong inhibitory effect in the yeast-based activity-guided fractionation assay. Then, we have further isolated 6 major constituents from YS57 fraction; we have found two of these active constituents have inhibitory effect. Results were validated by using the *in vitro* HMG-CoA reductase activity assay. In conclusion, we have demonstrated this yeast-based HTS activity-guided fractionation assay provides both rapid and low-cost routine assay to identify novel HMG-CoA reductase inhibitors. To our best knowledge, this is the first study to isolate the active constituents inhibit HMG-CoA reductase from the GpS using the yeast-based activity-guided assay.

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Catechins and Procyanidins in Extract of Ginkgo Biloba Show Protent Inhibitory Activity against β-Amyloid Peptide Aggregation

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The standard extract of *Ginkgo biloba* leaves (EGb 761) is clinically used for the symptomatic treatment of impaired cerebral function in primary degenerative dementia syndromes in Europe. Substantial *in vivo* and *in vitro* studies gave strong evidences to support the clinical use of EGb.

The abnormal production, aggregation of amyloid β peptide (Aβ) and deposition of fibrils in brain is regarded as a key step in Alzheimer Disease (AD). Therefore, to prevent Aβ from aggregation or disaggregate preformed fibrils is one of the approaches for prevention or treatment of AD.

Terpene trilactones and flavonoids are two main groups of constituents in EGb with the content 6% and 24%, respectively. In addition, procyanidins and catechins is another important group of compounds with the content of 9%. In our research, activities of these three categories of compounds on inhibition of Aβ aggregation and disaggregation of preformed fibrils were evaluated by using Thioflavin T (ThT) fluorescence method.

It was found that four main terpene trilactones, ginkgolides A, B, C and bilobalide exhibit little effect on the inhibition of Aβ42 aggregation even at very high concentrations (100μM). Seven main flavonoid glycosides (QCGR, QRG, QGR, KCGR, KRG, KGR and IRRG) were isolated and identified from EGb. The first three compounds showed medium inhibitory activities on Aβ42 aggregation in dose-dependent manner, however the other four flavonoid glycosides showed weak effect.

Catechins and procyanidins were identified in EGb761 by utilizing UPLC-MS method. Procyanidins B1 and B3, together with four catechins (C, EC, GC and EGC) were found to significantly inhibit Aβ42 aggregation (IC_{50} values: 3.3μM, 3.5μM, 14.9μM, 9.4μM, 17.5μM and 8.5μM). Furthermore, procyanidins B1 and B3, EC and EGC could disaggregate the performed fibrils (IC_{50} values: 3.5μM, 5.1μM, 6.0μM, and 7.8μM).

Therefore, catechins and procycnidins in EGb are important for inhibiting Aβ aggregation and disaggregating preformed fibrils.

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Cellular Lipidomic Study of β-Amyloid-induced Neurotoxicity and Intervention Effects of EGCG in Green Tea by Using UPLC-MS Based Glycerophospholipid Profiling and Multivariate Analysis

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β-amyloid (Aβ) aggregation plays a key role in the pathogenesis of Alzheimer disease (AD). Glycerophospholipid (GPL) metabolic networks have been suggested to be associated with the progress of AD. Epigallocatechin gallate (EGCG), a polyphenol in green tea, has long been recognized as a potent agent for its anti-neurodegenerative (anti-AD) activities. However, the molecular mechanisms of the AD process and potential anti-AD effects of EGCG are still unclear. In this study, we developed an ultra-performance liquid chromatography/time-of-flight mass spectrometry (UPLC/TOF-MS) based lipidomic approach to characterize the intracellular GPL profiles in the Aβ-treated PC12 cells with or without presence of EGCG. Multivariate statistical methods, including principle component analysis (PCA) and partial least squares-discriminant analysis (PLS-DA), were then used for visualizing the separation of different groups and screening of potential lipid markers. As a result, we found that the Aβ group is well separated with the control group, while EGCG group is more close to the controls in the scores plot. Several GPLs, including phosphocholines (PC), diacylglycerides (DG), and lysophosphocholine (LPC) or platelet activating factors (PAF), were elevated in Aβ-treated cells, and most of them were reset to normal levels with EGCG intervention. This study suggested that alterations in GPL levels may be involved in the neurotoxcity induced by Aβ. Moreover, EGCG exerts potential protective effects against such toxicity by regulating lipid metabolism. This work may bring further insights into the pathogenesis of AD, and may provide evidence for preventive effects of AD associated with the consumption of EGCG-containing botanic products.

Baicalein Inhibits Aggregation of Amyloidogenic Polypeptides and Prevents Protein Aggregation-induced Neurotoxicity

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Background: Abnormal protein aggregation in the brain is linked to the pathogenesis of neurodegenerative diseases including Alzheimer's disease (AD) and Parkinson's disease (PD). One of the strategies for the prevention or alleviation of degeneration process is to inhibit the abnormal protein aggregation process. Recent studies suggest that oligomeric form of aggregate is likely the most toxic specie and should be set as the direct therapeutic target. Baicalein is a flavonoid extracted from Chinese Herbal medicine *Scutellaria baicalensis* Georgi. (Huang Qin in Chinese) and has been shown to inhibit the fibrillation of alpha-synuclein (αsy) *in vitro*. **Methods:** To test the anti-oligomeric effect of baicalein on αsy in living cells, we established a bimolecular fluorescence complementation (BiFC) based cell model of visualizing the oligomeric alpha synuclein formation in cells. The anti-aggregation effect of baicalein in living cells and its neuroprotective activity were investigated by measuring intra cellular fluorescent signal and release of LDH from cell. In addition, inhibitory effect of baicalein on aggregation process of amyloid beta peptide (Aβ) was also studied by co-incubating or post-incubating baicalein with Aβ peptide. ThT assay and electronic microscope were used to monitor and observe the formation of Aβ fibril. Aβ oligomer specific antibody was used to observe the formation of Aβ oligomes in the presence/absence of baicalein. Neuroprotective effect of baicalein against Aβ fibril toxicity was further studied by MTT assay. **Results:** The data in this study showed that baicalein efficiently inhibits formation of oligomeric αsy in living cells, and significantly protected SH-SY5Y cells from oligomeric αsy-induced neurotoxicity. Besides, baicalein efficiently inhibited Aβ fibrillation with an IC50 value of approximate 3μM and disaggregated preformed Aβ fibril. In addition, baicalein inhibited Aβ oligomer formation and prevented Aβ fibril-induced toxicity in PC12 cell. **Conclusion**: Our study indicates that baicalein inhibits aggregation of amyloidogenic polypeptides and prevents protein aggregation-induced neurotoxicity, thus our data reveal the potential therapeutic effect of baicalein in the treatment of neurodegenerative diseases such as AD and PD.

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Cryptotanshinone Decrease β-Amyloid Generation by Modulating Amyloid Precursor Protein Processing

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Background: Cerebral deposition of β-amyloid peptide (Aβ) plaques is now considered the central feature of Alzheimer's disease (AD). Thus reduction in levels of the potentially toxic Aβ has emerged as one of the most important therapeutic goals in treating AD. To find compounds that inhibit Aβ generation, we tested many compounds from traditional Chinese herbs. Among which cryptotanshinone (CTS) antioxidants extracted from the root of *Salvia miltiorrhiza* (Danshen in Chinese) showed positive effect on the modulation of APP processing. **Methods:** N2a cells expressing and Swedish mutant APP (N2a-SwedAPP) were treated with/without different concentration of CTS and the conditioned medium and cell lysate were collected to measure the Aβ1-40 and Aβ1-42 by ELISA. Extracellular secretion of sAPP-α in conditioned medium from different cell lines were evaluated using 6E-10 antibody and intracellular full length APP, CTF-α, ADAMs, phospho PKC-α, total PKC-α and β-actin were evaluated using respective antibodies using the Western blot analysis. **Results:** CTS at different concentration (1-2.5 μM) not only inhibited the extracelluar Aβ1-40 (IC_{50}: 0.18 μM) and Aβ1-42 (IC_{50}: 0.32μM) production but it also significantly reduced the intracellular Aβ1-40 (IC_{50}: 0.68 μM) and Aβ1-42 (IC_{50}: 0.86 μM) in N2SwedAPP. CTS significantly and dose-dependently increased the sAPP-α secretion without influencing the full length APP in N2a-SwedAPP, N2a-WildAPP and SHSY5Y cells. Moreover, CTS induced the phosphorylation of PKC-α and translocation of the PKC-α to the cell membrane indicating that PKC is involved in CTS-induced sAPP-α secretion. CTS also specifically increased the maturation of "a disintegrin and metalloproteinase-10" (ADAM-10), an α-secreatse candidate without influencing the ADAM-17. The involvement of ADAM-10 in the CTS-induced sAPP-α is confirmed by siRNA studies. Furthermore, treatment of N2a cells with CTS induced the translocation of ADAM-10 to the cell membrane, the site at which APP was cleaved, and this translocation was significantly reduced by the PKC-α inhibitor Go¨6976. **Conclusion**: These results suggest that CTS-induced sAPP-α secretion is regulated by a PKC-α and ADAM-10 cascade in neuroblastoma cells and may be involved in the lowering of Aβ production. Therefore, CTS is a likely candidate for lowering the Aβ production by modulating the abnormal APP processing.

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Astragaloside IV Protects Human Astrocytes in against High Glucose-induced Cell Death by Attenuating ROS Production

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Diabetes associated with chronic hyperglycemia was known to alter the integrity of the blood brain barrier (BBB) and thereby compromise the normal brain function. However, the underlying mechanism still remains unclear. Astrocytes are responsible for the physical support and regulation of brain microcirculation. Therefore, astroglial dysfunction in relation to chronic hyperglycemia may contribute to progressive neurodegeneration associated with diabetic cerebral micro-vasculopathy. In this study, we investigate the effect of astragaloside IV (AS IV), a single compound extracted from HaungQi (*Astragalus mongholicus* BUNGE), in protecting astrocytic cell death induced by high-glucose stress. Here, the effect of AS IV was evaluated by co-treating the human astrocytic cells (C6) with high-glucose medium in the presence of different dosages (low dose: 0.50 μM; medium dose: 5 μM; high dose: 50 μM) of AS IV. The level of ROS induction and astroglial reactivity were determined by using 2', 7'-dichlorofluorescein (DCF) method and Western blot analysis, respectively. In addition, cell viability was assessed by using Annexin-V flow cytometry. Our results indicated that AS IV treatment effectively ameliorated ROS induction, astroglial activation and astrocytic cell death triggered by high-glucose challenge. Our findings implicating that AS IV may exert strong anti-oxidative effect in against hyperglycemia in case of diabetes mellitus. This study warrants further mechanistic and therapeutic studies for the potential use of AS IV in treating diabetic cerebral microvasculopathy.

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Anti-hepatosteatotic Effect and Mechanism of Schisandrin B in Steatotic Cell Models

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Hepatic steatosis and oxidative stress play crucial roles in the development of non-alcoholic fatty liver disease (NAFLD), thus hepatic lipid lowering and antioxidant agents may be effective in the prevention and treatment of NAFLD. Schisandrin B, the main bioactive constituent of the fruit of *Schisandra chinensis* has been shown to exhibit hepatic lipid lowering and antioxidant effects in animals. In this study we investigated the anti-hepatosteatotic effect and mechanisms of schisandrin B using *in vitro* models. In methionine-and-choline-deficient (MCD) medium-induced steatotic AML-12 cells, schisandrin B (10-100 μM) dose-dependently decreased cellular triglycirides and lipid peroxide levels, and alanine aminnotransferase (ALT) release. In 1 mM free fatty acid (FFA) mixture (oleate/palmitate, 2:1 ratio)-induced steatotic L-02 cells, schisandrin B (10-100 μM) significantly inhibited cellular total lipid and triglyceride accumulation in a dose-dependent manner after 24 h concurrent treatment with the FFAs. In the FFAs-induced steatotic L-02 cells treated with 100 μM of schisandrin B, two-dimensional gel electrophoresis based proteomic analysis revealed 13 proteins including 78 KDa glucose-regulated protein precursor (GRP78) and 3-hydroxyacyl-CoA dehydrogenase type-2 (HADH II), and decreased GRP78 and elevated HADH II may be involved in lipid lowering action of schisandrin B by attenuating apolipoprotein B100 degradation and stimulating fatty acid mitochondrial β-oxidation, respectively; quantitative real-time PCR analysis showed that mRNA expression levels of ADRP and SREBP1-C were repressed, which may contribute to the lipid lowering activity of schisandrin B through impairing cellular FFAs uptake and *de novo* fatty acids synthesis, respectively. These findings demonstrated the anti-lipid peroxidation, hepatoprotective and lipid lowering activities, and uncovered the molecular mechanisms responsible for the lipid lowering effect of schisandrin B in cell models. Results of this study provide further basis for developing schisandrin B as an anti-NAFLD agent. [This work was supported by a grant, FRG/08-09/II-30 from Hong Kong Baptist University; 1, Equal contribution.]

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The Ginsenoside Protopanaxatriol Protects Endothelial Cells from Hydrogen Peroxide-induced Cell Injury and Cell Death by Modulating Intracellular Redox Status

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Ginsenosides, the active components of the famous Chinese herb ginseng, have been suggested to possess cardiovascular-protective effects. The mechanism of ginsenosides is believed to be associated with their ability to prevent cellular oxidative stress. The purpose of this study was to explore the cytoprotective effects of the ginsenoside protopanaxatriol (PPT) on hydrogen peroxide (H_2O_2)-induced endothelial cell injury and cell death. Pretreatment of human umbilical vein endothelial cells (HUVECs) with PPT for 24 h was able to protect the cells against H_2O_2-induced injury. In addition to cell death, pretreatment with PPT could also reduce H_2O_2-induced DNA damage, overactivation of the DNA repair enzyme PARP-1, and concomitant depletion of the intracellular substrate NAD^+. Furthermore, PPT could reverse the decrease in ATP/ADP ratio caused by H_2O_2. The metabolism of glutathione was also changed. H_2O_2 could induce a significant decrease in GSH level resulting in a decrease in the GSH/GSSG ratio. This could be prevented by pretreatment with PPT. The action was associated with increasing activities of the GSH-metabolizing enzymes glutathione reductase and glutathione peroxidase. These findings suggest that the ginsenoside PPT could protect HUVECs against H_2O_2-induced cell death via its action against oxidative stress, which may be responsible for the cardiovascular-protective action of ginseng.

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The Effect of Chinese Scorpion (Buthus Martensii Karsch) on Neuropathic Pain

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Background: Though Chinese Scorpion (*Buthus martensii* Karsch, Bmk) has long been used for the treatment of various neural diseases such as apoplexy, epilepsy, facial paralysis and chronic pains, its effect is still subject to controversy and its analgesic mechanisms remain to be delineated. Recent studies revealing the presence of ion-channel-modulating peptides in the venom of Bmk provided one possible mechanism for its analgesic effect. The current study **Aims** at studying the potential analgesic effect of Bmk and its mechanism in a rat model of neuropathic pain. **Methods:** One week after spinal nerve ligation (SNL), rats were fed daily with either the extract of Bmk or distilled water as control for 21 days. Behavioral test involved the application of von Frey filament to the hind-paws of the rats for mechanical hypersensitivity developed in the SNL rats. The Paw-withdrawal-threshold (PWT) of the rats was recorded in a regular basis throughout the experiment before and after the treatment by Bmk. **Results:** In comparison with the post-lesion baseline value of PWT measured 7 days after the SNL, Bmk could significantly increase the PWT of SNL rats, suggesting a reduction of the mechanical hypersensitivity developed in the SNL rats after Bmk treatment. **Conclusion:** This preliminary result suggests that the daily oral feeding of Bmk to SNL rats could significantly attenuate the mechanical hypersensitivity developed in the SNL rats, providing a basis for the further study of the underlying mechanism.

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COX-1 and COX-2 Upregulation in Spinal Dorsal Horn after Spinal Nerve Ligation

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Background: Cyclooxygenase (COX), a pain producing substance, is involved in the development of neuropathic pain. Recent studies suggested that the development of allodynia associated with neural injury may be partly due to upregulation of COX-1 and COX-2. However, the cellular source of COX-1 and COX-2 after nerve injury was unclear.

Aims: In this study, we investigated the temporal profile of glia cell (microglia and astrocytes) activation, and the cellular sources in the spinal cord of COX-1 and COX-2 in association allodynia following spinal nerve ligation (SNL).

Methods: Allodynia was induced by ligation of the left L5 spinal nerves in SD rats. Postoperative pain-related behavior was measured by the mechanical paw withdrawal thresholds (PWT). The expressions of glial fibrillary acidic protein (GFAP) and OX-42 in L5 spinal cord detected by immunostaining and COX-1 and COX-2 immunohistochemistry with co-labeling for cell types were examined in the spinal cord for cellular source determination.

Results: SNL rats displayed significant behavioral mechanical hypersensitivity ($p<0.001$). GFAP and OX-42 immunoreactivities were increased significantly on the ipsilateral side of spinal dorsal horn. There was an increase in both COX-1 and COX-2 immunoreactivity in the dorsal horn at 7 days post surgery on the ipsilateral side of surgery animals compared to the contralateral side. Double immunofluorescence labeling demonstrated that COX-1 immunoreactive cells co-localized with microglia and neurons and were predominantly expressed in nucleus whereas COX-2 was expressed in cytoplasm of neurons only.

Conclusions: Our findings illustrated an activation of microglia and astrocyte in the spinal dorsal horn of SNL rats. Spinal dorsal horn neurons are the source of COX-2 as well as COX-1, whereas microglia is another important source of COX-1 up-regulation for neuropathic pain after spinal nerve injuries.

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Cardiovascular Tonic Herbal Medicine: Danshen And Gegen Decoction

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Danshen (root of *Salvia miltiorrhiza*) and Gegen (root of *Pueraria lobata*) are two traditional Chinese herbs which have long been used in China to treat cardiovascular diseases. Danshen-Gegen aqueous extract (DG) in 7:3 ratio had shown potent cardiotonic and anti-atherogenic effects in our previous studies, though the underlying mechanisms are still enigmatic. The objective of the present study was to examine the anti-atherosclerosis, anti-hypertensive and anti-stroke effects of DG.

The anti-inflammatory effect of DG was determined by lipopolysaccharides (LPS)-induced nitric oxide (NO) production which was measured using Griess reagent. In foam cell formation assay, the uptake of ac-LDL by macrophages (RAW 264.7) was quantified by flowcytometry. To evaluate the effects of oral administration of DG on anti-hypertension, spontaneous hypertensive (SHR) rats were used to test for preventive and therapeutic effects. The systolic blood pressure (SBP) was measured biweekly by tail-cuff method. Middle cerebral artery occlusion (MCAO) model was employed for mimicking ischemic stroke. DG was orally administered daily for 7 days before MCAO operation. The brain infarction percentage was assessed after 24 hours reperfusion and the neurological deficit was evaluated by scoring scale.

Our results showed that DG exhibited significant suppressive effect on NO production and inducible nitric oxide synthase expression at 500 and 1000 μg/ml. DG also had significant inhibitory effect on uptake of LDL at 250 - 1000 μg/ml. In addition, our results demonstrated for the first time the synergistic effect of DG on suppression of NO production. For the prevention of hypertension, DG at 90 and 300 mg/kg could significantly lower SBP to 180 mmHg as compared with control (210 mmHg). For the therapeutic study, DG at both dosages could also significantly lower SBP. In MCAO model, DG pretreatment at 0.3 and 3 g/kg was found to decrease the brain infarct significantly by 24.7% and 38.4%, respectively. DG treatment was also shown to improve the neurological deficit from 3 (control) to 2.81 and 2.33 at 0.3 and 3 g/kg, respectively.

In conclusion, DG was found to exhibit anti-inflammatory, anti-hypertension and anti-stroke activities. Our findings suggested that DG may be developed as a multiple-target herbal medicine in the prevention of cardiovascular events.

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Identification of a Compound from the Traditional Chinese Medicine with Antidepressant-like Property

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Depression is one of the common psychiatric disorders that affect more than 10% of world population. The existing antidepressants exert their therapeutic actions mainly through enhancing the neurotransmission of the monoamine system, e.g. through inhibition of the re-uptake or degradation of neurotransmitters serotonin (5-HT) and norepinephrine (NE). However, most of the existing medications for this psychiatric disorder have undesirable side effects. Therefore, development of new drugs is needed for safe and effective treatment of depression. In the present study, we identified a compound originated from a Chinese herb that exhibits an antidepressant-like effect in mice. Mice orally administered with this compound for 2 days exhibit an antidepressant response in forced swimming test, a widely used animal model for depression. Interestingly, we observed not only an increase in the level of both 5-HT and NE in the hippocampi of these treated mice, but also enhanced neurogenesis in the dendate gyrus. Preclinical studies are ongoing to evaluate the potential for further development of this compound

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Compound A2287 Rescues Primary Neurons against NMDA Excitotoxicity and Reduces Cerebral Infarct in a Rodent Stroke Model

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Ischemia stroke places great burden on the society due to the high economic loss and mortality rate of the disorder. Advances in understanding the pathophyisology of stroke reveal the involvement of glutamate excitotoxicity and inflammation, which result in extensive neuronal cell death. Currently, available medical treatment includes tissue plasminogen activator (tPA), which can be applied within a 3-hour time window after the incident. However, the safety and efficacy of tPA remains controversial. To this end, we have conducted screening for compounds the might be beneficial in the treatment and prevention of stroke. Among the compounds screened, A2287 exhibits neuroprotective effect on primary neurons against N-methyl-D-aspartate (NMDA) insult. We found that A2287 modulates NMDA receptor by reducing NMDA-induced calcium flux in primary hippocampal neurons. The effectiveness of A2287 in an ischemic stroke animal model – the middle cerebral artery occlusion (MCAO) – was investigated. MCAO is induced by transient filament insertion into the middle cerebral artery followed by reperfusion and assessment of behavioral performance, infarct volume and edema extent. Our results demonstrate that A2287 significantly decreases neurological deficits and cerebral infarction when administered at 6 hours after ischemia. These observations collectively suggest that A2287 may serve as a potential therapeutic treatment against stroke.

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Herba Cistanche Induces Mitochondrial Uncoupling and Glutathione Redox Cycling In H9c2 Cardiomyocytes

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Previous findings in our laboratory have demonstrated that Herba Cistanche, a Yang- invigorating traditional Chinese medicine, was capable of increasing ATP generation capacity in H9c2 cardiomyocytes. The measurement of mtiochodnrial respiration using Clark electrode revealed that Herba Cistanche treatment increased the mitochondrial state 3 respiration rate in H9c2 cardiomyocytes. In addition, mitochondrial uncoupling, as indicated by the decreases in the ratio of state 3 to state 4 respiration, was also observed in Herba Cistanche pretreated cardiomyocytes. The inhibition of Herba Cistanche-induced increase in state 4 respiration by GDP suggested the involvement of uncoupling proteins in mitochondrial uncoupling.

Given the abilities of Herba Cistanche to enhance both mitochondrial ATP generation and mitochondrial uncoupling, it is postulated that Herba Cistanche can also increase mitochondrial reactive oxygen species (ROS) production. The increased amount of ROS serves as a cellular signal for up-regulating antioxidant mechanisms such as the glutathione antioxidant system. We therefore investigated the time course of Herba Cistanche-induced changes in cellular reduced glutathione (GSH) level in H9c2 cardiomyocytes. The results indicated that Herba Cistanche treatment caused a time driven cyclic variation of cellular GSH level in cardiomyocytes. The cyclic variation of cellular GSH reflects a dynamic interplay between ROS-induced glutathione oxidation and enzyme-mediated glutathione recovery. The co-treatment with rotenone, a complex I inhibitor, was found to abrogate the Herba Cistanche-induced cyclic change in cellular GSH, suggesting the involvement of mitochondrial electron transport chain in triggering the cyclic process.

In conclusion, Herba Cistanche treatment can induce mitochondrial uncoupling and glutathione redox cycling in H9c2 cardiomyocytes, which may confer cytoprotection against oxidant-induced injury.

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The Holistic Approach of Anti-Aging Lycium Barbarum (Wolfberry) in the Protection against Pathological Factors Related to Alzheimer's Disease

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Lycium barbarum (Wolfberry) is a traditional Chinese medicine herb which can be used for both disease treatment and as functional food. For a long time, it is believed that *L. barbarum* has anti-aging properties, but there is little scientific evidence to support the statement. Alzheimer disease (AD) is an aging-associated neurodegenerative disease that leads to dementia. We hypothesized that Wolfberry could utilize a holistic approach to protect neurons against pathological factors of AD. Our findings showed that polysaccharides from *L. barbarum* (LBA) could protect primary cultured cortical neurons against beta-amyloid (A✩) peptide, glutamate, and homocysteine (Hcy) induced neuronal damages. These pathological factors are involved in different stages in the pathogenesis of AD. Hyperhomocysteinaemia is a risk factor for AD. Our data showed that LBA could attenuate Hcy-induced neuronal cell death, tau phosphorylation and cleavage, thus suggesting a potential preventive role of *L. barbarum* for the disease. A✩ peptide neurotoxicity is believed to play a key role in AD development. LBA treatment significantly reduced the level of apoptosis induced by A✩, therefore providing more evidence to support its use for AD treatment or prevention. Furthermore, LBA attenuated the neuronal damages induced by glutamate, which is involved in the progression of AD. We found that LBA could suppress the activation of stress kinases such as JNK and ERK, however, LBA is unlikely to act as an anti-oxidant. Taken together, our findings showed that LBA from *L. barbarum* protected neurons against multiple AD-related pathological changes and this can partly explained the holistic concept of using anti-aging herbs.

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Neuroimmune Responses of Polysacharides from Lycium Barbarum (Wolfberry) in Retina after Experimental Glaucoma

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Retinal macroglia (astrocytes and Müller cells) undergo an activation process in glaucoma, they may have intrinsic protective or detrimental effects on survival of the retinal ganglion cell (RGC). In the rat model of glaucoma, *Lycium barbarum* polysaccharide (LBP) has been proved to be neuroprotective. In this study, we investigated whether LBP acts as a neuro-protectant by modulating activation of retinal macroglia cells. Since astrocytes and Müller cells have long been known to produce trophic factors and anti-inflammatory cytokines, we were particularly interested in examining insulin like growth factor 1 (IGF-1) and interleukin-10 receptor (IL-10R) expression on retina. Ocular hypertension (OH) was induced by laser photocoagulation, activated phenotypes of retinal macroglia were identified by morphologic assessment and immunostaining for the cell markers glutamine synthetase (GS) as well as glial fibrillary acidic protein (GFAP). Cellular localization of IGF-1 and IL-10R were studied by immunohistochemical staining. Four groups of rats including normal, OH model, control, OH with PBS-feeding and LBP-feeding were analyzed. Retinal astrocytes and Müller cells exhibited a hypertrophic morphology and increased immunostaining for GFAP in the OH retinas. LBP suppressed up-regulated GFAP expression. In normal retina, IGF-1 and IL-10R were detected in the cells in the retina ganglion cell layer. LBP restored the decreased immunoreactivity of IGF-1 and IL-10R in the RGCs compared to PBS group. These findings provide evidence that LBP can modulate activation of macroglia in fine tune anti-inflammatory responses and expression of trophic factor in retina. This study also provides insights of the significant of anti-inflammatory responses in glaucoma.

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Effects of Buyang Huanwu Decoction on Modulating Cellular Growth Signals and Improving Neural Stem Cells Proliferation and Differentiation for Post-Stroke Treatment

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Buyang Huanwu Decoction (BHD), a classic traditional Chinese medicine (TCM) formula, has been used for recovering neurological dysfunctions and treating post-stroke disability in China for about 200 years. The molecular mechanisms are still unknown. In order to explore the molecular mechanisms of the formula for stroke treatment, we investigated the effects of BHD on modulating cellular growth signals and improving neural stem cells proliferation and differentiation in the experimental rat stroke model by the occlusion of middle cerebral artery (MCAO). BHD was orally administrated to the rats for 14, 28 and 36 days after MCAO. We detected the proliferation-promoting effects by immunofluorescent staining of thymidine analog 5-bromo-2'-deoxyuridine (BrdU). The results showed that the formula stimulated the proliferation of the neural stem cells at dentate gyrus of hippocampus in the ischemic brains. We also detected the differentiation-promoting effects by immunofluorescence double staining of doublecortin (DCX) and neuron-specific nuclear antigen (NeuN). BHD was showed to increase the amount of double staining positive cells. To understand its mechanisms, we investigated the expressions of p-stat3 and hes1 which are important signaling molecules to maintain the neural stem cells at the early stage and improve neurogenesis on the later period. We found the formula remarkably up-regulated the expressions of p-stats3 and hes1 at day 14.28, but inhibit their expressions at day 36. These result indicated that BHD can improve the neural stem cell proliferation and differentiation, and the underlying mechanism are related to activate Jak/p-Stat3 –hes1 pathway.

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A Non-competitive JAK2 Inhibitor from Ginkgo Biloba

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Janus kinases (JAKs) play an important role in signal transduction *via* cytokine and growth factor receptors. In mammals, the Janus kinase/signal transducers and activators of transcription (JAK/STAT) pathway is the principle signaling mechanism for cell proliferation, differentiation, cell migration, and apoptosis. Deficiencies in JAK signaling have been implicated in the pathogenesis of myeloprofilerative disorders (MPDs), namely polycythaemia vera (PV), essential thrombocythaemia (ET), and primary myelofibrosis (PMF). A point mutation in JAK2, V617F, results in constitutive kinase activity and this mutation has been identified in 95% of PV cases, and 50% of ET and PMF cases.

We have performed a high-throughput molecular modeling screen using natural product database, and have identified compound B03, from Chinese plant *Ginkgo biloba*, to be a promising lead inhibitor of JAK2. Preliminary results have indicated that B03 is an inhibitor of JAK2, with an IC_{50} value in the low micromolar range in a cell-free kinase assay. According to a competitive ATP assay, B03 was found to bind non-competitively to JAK2 and a K_i value of approximately 20–30 μM was determined.

Parallel Activation of Nrf2 and PI3K/Akt Pathways by z-ligustilide Enhances the Survival of Neuronal PC12 Cells under Oxygen and Glucose Deprivation: A Role for Heme Oxygenase-1

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Oxidative stress is implicated in the pathogenesis of ischemia reperfusion injury in stroke patients. Heme oxygenase-1 (HO-1) is an inducible enzyme that degrades prooxidant heme into three potent antioxidant and antiapoptotic products: biliverdin, carbon monoxide and free iron. Our recent effort to characterize the HO-1 induction by herbal medicine *Rhizoma Chuanxiong* resulted in the identification of senkyunolide-H and -I as novel HO-1 inducers. We also found that senkyunolide-H and -I attenuated hydrogen peroxide-induced cell death via the induction of HO-1. In this study, we investigated HO-1 induction by a related phthalide z-ligustilide (z-LIG), the main component in the essential oil of *Rhizoma Chuanxiong*. We found that z-LIG was a more potent HO-1 inducer than senkyunolide-H and -I. We attempted to elucidate the molecular mechanism underlying the HO-1 induction by z-LIG in a rat neuronal-like pheochromocytoma cell line PC12. According to our results, z-LIG induced the nuclear accumulation of nuclear factor-E2-related factor 2 (Nrf2) in a time and dose-dependent manner. Nrf2 is a transcription factor that binds to the antioxidant response element (ARE) and induces the expression of phase 2 detoxifying and antioxidant enzymes including HO-1. On the other hand, z-LIG transiently induced the activation of Akt/protein kinase B. Interestingly, two phosphatidylinositol 3-kinase (PI3K) inhibitors, LY294002 and wortmannin, could abolish the activation of Akt and partially attenuate HO-1 induction by z-LIG. In contrast, neither of these PI3K inhibitors affected the nuclear accumulation of Nrf2 induced by z-LIG. Moreover, a thiol antioxidant N-acetylcysteine (NAC) largely attenuated HO-1 induction and the nuclear accumulation of Nrf2 by z-LIG. LY294002 and NAC in combination could completely inhibit HO-1 induction by z-LIG. Importantly, HO-1 induction appeared to be a key antioxidant mechanism underlying the neuroprotective effect of z-LIG in a cell model of ischemic stroke generated by oxygen glucose deprivation. These results suggest that z-LIG could simultaneously activate Nrf2 and PI3K/Akt pathways conferring HO-1 induction and subsequent protection of neuronal cells against oxidative injury.

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Drug Discovery from Herbal Medicine: Where we are? Where we go? - A Lesson from a Classic Formula Study for Post-stroke Treatment

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Traditional Chinese Medicine (TCM) is a unique medical system different from "conventional" western medical system. In western medicine, therapeutic drugs and approaches are generally developed from the prevalent "one drug, one target" dogma, whereas in TCM, therapeutic approaches are designed by using mixed herbal formulae, which contain multiple chemical components and are formed with particular TCM principles and theories. Recent progress in systemic biology, analytic chemistry and functional imaging greatly facilitates to clarify the roles of TCM formulae. Drug discovery from herbal medicine can be achieved from 3 different strategic directions: (1) Developing leading compounds with bioactivities; (2) Seeking chemically well-defined active fractions with certain bioactivities; (3) Developing standardized TCM formula. We will use a classical TCM formula named BHD-01 as an example to discuss the strategy for drug discovery. BHD-01 is a representative TCM formula with potential for improving functional recovery of stroke-induced disability. To understand the therapeutic basis of BHD-01, we used multiple comprehensive approaches and conducted a series of chemical, molecular and cellular and animal studies to understand its therapeutic principles and seek for active fractions and compounds for drug discovery: (1) the chemical fingerprint analysis and genome-wild biological fingerprint analysis for quality control study; (2) the neurological behavior study for evaluating the effects of BHD-01 for neurological deficit treatment in a rat ischemic stroke model with middle cerebral artery occlusion; (3) the pharmacological studies on improving neuronal proliferation and differentiation and related signal pathways in the post-stroke brains, (5) seeking for active fractions and compounds for promoting neuronal development of neuronal progenitor cells. The results indicate that (1) quality control for BHD-01 is feasible; (2) BHD-01 can improve the recovery of neurological functions in post-stroke treatment; (3) BHD-01 can stimulate the regeneration of neural stem cells, which is related to regulate growth factors and several transcription factors; (4) Several active fractions and compounds from the formula can promot neurogenesis. Therefore, integrating the comprehensive technologies including systemic biology, analytic chemistry, molecular pharmacology and immunofluorescent imaging technology, etc, can be a bridge for understanding therapeutic principles of Chinese medicinal formula and develop new potential drug candidate.

Facilitation of Male Sexual Behavior by Lycium Barbarum (Wolfberry) Polysaccharide

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According to the *Bencao Gangmu, Lycium barbarum* (wolfberry) is a Chinese medicine with anti-aging property. It has been considered to have facilitative effect on male sexual behavior without much concrete scientific evidence. Therefore, we investigated the effect of *Lycium barbarum* polysaccharide (LBP) on male rat copulatory behavior. Sexually naïve, adult male Sprague-Dawley rats were divided into two groups (n=8 for each group): the control group received oral feeding of 0.01M phosphate-buffered saline and the experimental group received feeding of LBP at 1mg/kg daily. The experiment continued for 21 days, and copulatory tests were conducted at 7, 14 and 21 days after of the first day of treatment. Compared to control group, experimental group showed (a) higher copulatory efficiency (i.e. higher frequency to show intromission rather than mounting during the test), (b) higher ejaculation frequency, and (c) shorter ejaculation latency. The differences were found at all time points (Two-tailed Student's *t*-test, $p<0.05$). There is no significant difference in mount/intromission latency between two groups, which indicates that the time required for initiation of sexual activity is the same between two groups. Additionally, no difference in mount frequency and intromission frequency was found. Therefore, the results support scientifically by showing that wolfberry has facilitative effect on male sexual behavior. In this notion, LBP may provide therapeutic effects for disorders related to ejaculatory difficulty.

Keywords: wolfberry, sexual behavior, Lycium barbarum polysaccharide

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Effect of Erxian Decoction and its Bioactive Fractions on Lipid Profile of Menopausal Rat Model

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Introduction: The prevalence of cardiovascular disease (CVD) increased after menopause. It is suggested that the adverse lipid profile after menopause increases the risk factors of CVD and is related to the deprivation of estrogen. Er-Xian Decoction has been used to relief menopausal syndromes and proved to stimulate ovarian estrogen biosynthesis through activation of ovarian aromatase expression, but the effects of EXD on lipid profiles have not been reported.

Aim: Our study aimed at elucidating the effects of EXD and its bioactive fractions [butanol fraction (BU), ethyl-acetate fraction (EA), aqueous fraction (WA) and polysaccharide fractions (PS)] on the serum lipid profile [total cholesterol (TC), total triglyceride (TG), HDL-cholesterol (HDL-C) and LDL-cholesterol (LDL-C)] of twenty-year-old menopausal SD-rat model.

Results and Discussion: After oral administration of EXD and the bioactive fractions, the serum TC level of EXD-treated group decrease significantly compared to control but not the other fractions. This indicated EXD displays synergistic effects on serum TC level. The serum TG level after EXD treatment did not change significantly, while the EA, BU and WA group demonstrated significant increase in TG level. Though EXD did not have beneficial improvement on serum TG level, it avoided the increase of TG by its bioactive fractions which may lead to increase in CVD risk. EXD, BU and WA did not increase HDL-C level after treatment, but the HDL-C level decrease after EA treatment. This suggests synergistic effect of EXD exist in preventing the worsening of lipid profile by its fractions. LDL-C level decrease significantly in EXD-treated group but not its bioactive fractions, demonstrating synergistic effect of Chinese medicine. As LDL-C promotes atherogenesis and regarded as an important risk factor of CVD, EXD exhibits protective effects in lipid profile of our menopausal rat model.

Summary: Our study unveiled the protective effects of EXD in lipid profile of menopausal rat model by reducing the level of serum TC and LDL-C level in a synergistic manner, while the HDL-C and TG level were unaltered. Our study provided insight in the feasibility of EXD as cardiovascular protective supplement for menopausal female.

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Chrysotoxine, a Novel Bibenzyl Compound Isolated from Dendrobium Species, Inhibits 6-hydroxydopamine Induced Apoptosis in SH-SY5Y Cells via Mitochondria Protection and NF-□B Modulation

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Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting about 2% of the population over the age of 60 years. The Chinese herbs and herbal extracts have shown potential clinical benefit in attenuating the progression of PD in human beings by multiple mechanisms. Bioactive bibenzyl compounds isolated from Dendrobium species have been shown to exert potent antioxidant activity. However, the neuroprotective effect of bibenzyl compounds has not been reported so far. In the present study, five structurally similar bibenzyl derivatives isolated from medicinal Dendrobium species were tested for their neuroprotective effect against 6-hydroxydopamine (6-OHDA)-indcued apoptosis. The signaling pathways involved in mitochondria dysfunction and nitric oxide (NO) release were investigated. We found that one bibenzyl derivative, namely chrysotoxine, significantly reversed 6-OHDA induced SH-SY5Y cell death for the first time. The mechanism study indicated that chrysotoxine strikingly inhibited 6-OHDA-induced intracellular generation of reactive oxygen species (ROS), activation of p38 MAPK and ERK1/2, and mitochondrial dysfunctions, including lowered membrane potential, increase in intracellular free Ca^{2+}, the release of cytochrome c, the imbalance of Bax/Bcl-2 ratio and caspase-3 activation. Meanwhile, chrysotoxine counteracted NF-κB activation by blocking its translocation to the nucleus, thereby blocking up-regulation of inducible nitric oxide synthase (iNOS) and intracellular nitric oxide (NO) release. Taken together, our results suggest that chrysotoxine may be further investigated as a novel candidate for protection against neurodegeneration in PD.

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Peony-Glycyrrhiza Decoction (PGD), an Herbal Preparation, Suppresses Synthesis and Secretion of Prolactin in Pituitary Adenoma Cells – Implication for the Treatment of Hyperprolactinemia

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One notable side effect of antipsychotic therapy is hyperprolactinemia (hyperPRL), a condition with abnormally high levels of prolactin (PRL) in the blood. Our recent study found that an herbal preparation called Peony-Glycyrrhiza Decoction (PGD) which is prepared from peony and glycyrrhiza radices could suppress antipsychotic-induced hyperPRL and reduce associated symptoms in female patients with schizophrenia. The purpose of the present study was to further examine the effects of individual and combined preparation of PGD on synthesis and secretion of PRL in MMQ cells, an exemplary model of hyperPRL that is derived from pituitary adenoma cells. Treatment with PGD (0.5-5 mg/ml) for 36 h resulted in a significant decrease of PRL concentration in the cultured medium in a dose-dependent manner compared to controls. Similar inhibitory effect was also observed on the expression of PRL in MMQ cells using Western blotting detection. Peony preparation alone and pooled together with glycyrrhiza preparation, but not glycyrrhiza preparation alone, also displayed equivalent effects in inhibiting PRL in both cultured medium and cells. Theses results suggest that PGD possesses suppressive effects on synthesis and secretion of PRL in vitro, and peony appears to play a predominant role in this suppression. The data provide an additional piece of evidence in the support of PGD as adjunct for the treatment of hyperPRL.

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Eriocaulon Buergerianum Extract Protects against 6-hydroxydopamine-induced Neuron Death on PC12 Cells In Vitro and Zebrafish In Vivo

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Ericaulon buergerianum (Gu-Jing-Cao) is a traditional medicinal herb used as ophthalmic, anti-inflammatory and antimicrobial agents in China. The present study aims to investigate the neuroprotective effect of *Ericaulon buergerianum* ethanol extract (EBE) and to elucidate its underlying mechanism of action.

Pretreatments of EBE (25, 50, 100, 200 μg/ml) increased the viability of 6-OHDA-damaged PC12 cells in a dose dependent manner. Protections against 6-OHDA-induced *nuclear fragmentation and* accumulation of apoptotic bodies were also observed in EBE pretreated cells. Moreover, EBE exhibited significant neuroprotective activity against 6-OHDA-induced dopaminergic (DA) neuron loss in zebrafish at which the viability of dopaminergic (DA) neuron was examined by ant-tyrosine hydroxylase (TH) immunostaining. Mechanistic study showed that neuroprotective effect of EBE probably involved inhibition of NO production and iNOS expression, as well as modulation of PI3K/Akt pathways.

The present study, for the first time, demonstrates the neuroprotective activity of EBE *in vitro* and *in vivo*, and our results suggest that *Ericaulon buergerianum* has potential to be developed as a therapeutic agent for Parkinson's disease.

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Characterization of (+)-praeruptorin A Metabolism in Human Liver Microsomes

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Background Radix Peucedani (Chinese name Bai-Hua Qian-Hu), is the dried root of *Peucedanum praeruptorum* Dunn. and noted for its benefitial effects in the treatment of respiratory diseases and pulmonary hypertension. (+)-Praeruptorin A (*d*PA) is one of the main bioactive constituents of this herb, yet it's metabolic stability and hence disposition in the body remains to be addressed. The present study reported, for the first time, the metabolic stability of *d*PA in human liver microsomes (HLMs). The major enzymes involved in *d*PA metabolism were also characterized. **Method** *In vitro* metabolic studies of *d*PA in human liver microsomes and seven recombinant CYP enzymes (CYP3A4, 2C19, 2B6, 1A1, 2C8, 1A2 and 2D6) were performed in the presence/absence of the NADPH-regenerating system. In the inhibitory study, eight chemical inhibitors for CYP1A1/1A2 (α-naphthoflavone), CYP3A4 (ketoconazol), CYP2C9 (sulfaphenzole), CYP2C19 (omeprazole), CYP2D6 (quinidine), CYP2E1 (chlorzoxazon), CYP2A6 (coumarin) and CYP2C8 (quercetin) were examined. The metabolites were qualitatively and quantitatively determined using rapid resolution electrospray ionization mass spectrometry (RRLC/ESI-MS). **Results** Totally six metabolites (M1-M6), three (M1-M3) generated via hydrolysis and three (M4-M6) via mono-oxidation, were detected. Formations of M1-M6 were NADPH-dependent. α-Naphthoflavone, ketoconazole, sulfaphenzole, omeprazole, quinidine and chlorzoxazon showed inhibitory effect on *d*PA metabolism. Both ketoconazole and quercetin exhibited potent inhibitory effects on formations of all metabolites. Five recombinant human CYPs showed activity of M1-M6 formation with higher activities achieved by CYP3A4, CYP2C19 and CYP2B6. **Conclusion** *d*PA was extensively metabolized in human liver microsomes via hydrolysis and oxidation. Preliminary studies revealed CYP3A4 as the primary isozyme involved in hepatic metabolism of *d*PA.

Keywords: (+)-praeruptorin A; human liver microsomes; hydrolysis; oxidation; CYP3A4.

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Identification of the Major Urinary and Fecal Metabolites in Rats Dosed with Radix Peucedani Extract by RRLC/ESI-MS

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Background: Radix Peucedani, the dried root of *Peucedanum praeruptorum* Dunn. (Bai-hua Qian-hu), is a famous Chinese herbal medicine commonly used for the treatment of respiratory disease and pulmonary hypertension. The present study aimed to reveal the drug-related forms of this herb in the rat. **Method**: Three extraction methods, including ultrasonication, circumfluence extraction and leach after circumfluence were compared to get a standard extract of this herb. The chemical profile of the standard extract was characterized using rapid resolution liquid chromatography with electrospray ionization mass spectrometry (RRLC/ESI-MS). Then, the standard extract was orally administered to rats at 1 g/kg and urine and feces samples collected at appropriate time intervals for RRLC/ESI-MS analysis. **Results**: Among the 3 extraction methods, circumfluence thrice with 10 volumes of 95% ethanol at 80 ℃ for 60 min yielded an extract with the highest peak areas of praeruptorin A (PA), praeruptorin B (PB) and praeruptorin E (PE), three main therapy-related constituents in the herb. Totally 41 peaks in the standard extract were identified using RRLC/ESI-MS with 6 unambiguously identified using authentic compounds. All 41 components belong to coumarins, either angular-type or linear-type. PA, PB, PE, peucedanocoumarin II, peucedanocoumarin I and *cis*-3′, 4′-disenecioylkhellactone appeared to be the main constituents of the extract. After oral dosing, the 6 main constituents from the herb and 12 glucuronidated metabolites were detected in urine, while all 21 compounds detected in feces were highly lipophilic constituents from the herb. **Conclusion**: The main coumarins in Radix Peucedani are also the main components present in the blood. Some coumarins may not have good absorption due to their high lipophilicity.

Keywords: Peucedanum praeruptorum; courmarins; RRLC/MS; feces; urine; rat

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Dose-Dependent Effects of Betel Nut on Cardiovascular Risk Factors in a Rat Model

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Areca nut (commonly known as betel nut) chewing has been shown to be associated with metabolic syndrome and cardiovascular disease (CVD). The mechanism by which betel nut ingestion could lead to development of CVD is not precisely known, however, dyslipidemia and hyperhomocysteinemia and hypertriglyceridemia could be some of the potential risk factors. Present study was undertaken to investigate the effects of different dosages of betel nut on components of metabolic syndrome, such as hypertriglyceridemia, low HDL-cholesterol, obesity, fasting hyperglycemia, inflammation, and hyperhomocysteinemia in a rat model.

Twenty-five adult female Sprague-Dawley rats, aged 10-12 weeks were divided into four equal groups, with the exception of group-1. Group-1 served as the control group (n=7) and received water, whereas groups 2, 3 and 4 were given water suspension of areca nut orally in dosages 30mg, 60mg and 90mg, respectively for period of 5 weeks. At the end of 5 weeks, animals were sacrificed and blood was collected.

Plasma/serum were analyzed for glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides homocysteine, folate, vitamin B12 and N-acetyl-β-D-glucosaminidase (NAG). When the mean concentration values in four groups were compared using one way ANOVA followed by Tukey's HSD-test, there was a significant increase in the concentrations of total cholesterol ($p=0.038$) and triglycerides $p=0.05$ in the group receiving 30mg/day betel nut compared to the control group. However, administration of higher doses of areca nut had no significant effect on the serum levels of glucose, HDL-cholesterol, LDL-cholesterol, and NAG (a marker of inflammation).

Plasma homocysteine concentration in the group-4 receiving 90mg/day areca nut was significantly decreased compared to the control group ($p=0.036$) and this appeared to be due to increased level of folate in this group. Mean vitamin B12 levels were not found to be significantly different in all the groups. Low dosages of betel nut are associated with greater risk of hypercholesterolemia and hypertriglyceridemia.

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Quantitation by UPLC-MS\MS of Endogenous Estrogens and Monoamine Neurotransmitters and its Application on Bioactivities Evaluation of Qing'e Formula

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Qing'e Formula is a famous compound preparation recorded in ChP (2010) consisting of four ingredients, Eucommiae Cortex (Duzhong), Psoraleae Fructus, Juglandis Semen and Bulbus Allii. Qing'e Formula is commonly used clinically for treatment of osteoporosis, chloasma and heart disease, particularly in postmenopausal woman.

Hot flash, depression and sleep disorder are all disorders of menopause, most of which are related to the decreased estrogen levels in the body of women in perimenopausal period. In order to investigate the potential regulation effect of Qing'e Formula on estrogen level and neuroendocrine function, the quantitative analysis methods of endogenous estrogens and monoamine neurotransmitters based on UPLC-MS^2 were established.

Trace analysis method of steroid hormones including 17β-estradiol, estriol, estrone, progesterone and testosterone in serum with dansyl chloride pre-column derivatization by isotope dilution UPLC-MS^2 was established. Compared with control, the levels of progesterone of aging rat after oral administration of Qing'e Formula for two months were increased.

The determination method of monoamine neurotransmitters in rat brain tissue by UPLC–MS^2 was established including serotonin (5-HT), L-tryptophan (Trp), L-5-hydroxytryptophan (5-HTP), 5-hydroxyindole acetic acid (5-HIAA), norepinephrine (NE), L-dopamine (DA), epinephrine (E) and 3,4-dihydroxy-L-phenylalanine (DOPA). Compared with control, the brain tissue levels of 5-HTP, 5-HT, 5-HIAA, DA and NE of aging rat after oral administration of Qing'e Formula were increased significantly. The Trp, 5-HTP, 5-HT, 5-HIAA, E and DA levels in ovariectomized mice brain tissue were significantly decreased compared with the sham operated group. And the active compounds psoralen, corylin, psoralidin and bavachinin could antagonize these decreasions.

The regulative effects of Qing'e Formula and its active components on estrogens and monoamine neurotransmitters suggested that Qing'e Formula could be used in the treatment of hot flash, depression, and sleep disorder in menopausal women.

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Schwann Cell Migration Induced by Earthworm Extract via Activation of PAs and MMP2/9 Mediated through ERK1/2 and p38

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The earthworm, which has stasis removal and wound healing functions, is a widely used Chinese herbal medicine in China. Schwann cell migration is critical for the regeneration of injured nerves. Schwann cells provide an essentially supportive activity for neuron regeneration. However, the molecular migration mechanisms induced by earthworms in Schwann cells remain unclear. Here, we investigate the roles of MAPK (ERK1/2, JNK and p38) pathways for earthworm-induced matrix-degrading proteolytic enzyme (PAs and MMP2/9) production in Schwann cells. Moreover, earthworm induced phosphorylation of ERK1/2 and p38, but not JNK, activate the downstream signaling expression of PAs and MMPs in a time-dependent manner. Earthworm stimulated ERK1/2 and p38 phosphorylation was attenuated by pretreatment with U0126 and SB203580, resulting in migration and uPA related signal pathway inhibition. The results were confirmed using small interfering ERK1/2 and p38 RNA. These results demonstrated that earthworms can stimulate Schwann cell migration and upregulate PAs and MMP2/9 expression mediated through the MAPK pathways, ERK1/2 and p38. Taken together, our data suggests the MAPKs (ERK1/2, p38) -PAs (uPA, tPA) - MMP (MMP2, MMP9) signaling pathway of Schwann cells regulated by earthworms might play a major role in Schwann cell migration and nerve regeneration.

Lipid Metabolism Of Curcuma Longa on High-hat-diet Induced Obesity Mice with Hepatic Steatosis

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Background and Aim: Nonalcoholic fatty liver disease (NAFLD) has become increasingly recognized as the most common cause of chronic liver disease. Curcuma is known to exert potent anti-inflammatory and antioxidant effects. The present study was to test the efficacy of curcuma, for it's ability to modulate pathways implicated in obese mice that develop hyperlipidemia and fatty livers.

Methods: To evaluate this possibility, mice with fatty livers were treated with curcuma (30 or 100 mg/kg, po) in diet induced obesity mice, an agent that possessed lipid lowing and anti-inflammation properties. At the end of the experiment, serum biochemical parameters, liver histology and lipid profile were analyzed. In the liver, the SREBP-1 and PPAR gamma protein levels were determined by Western blot and messenger RNA levels of some enzymes involved in lipogenesis were examined by real time polymerase chain reaction.

Results: Following a 4 week protocol, curcuma suppression of hepatomegaly and steatosis was reflected by a 18% lower liver average triglyceride content as compared with obese controls. In addition, curcuma simultaneously decreased hepatic fatty acid synthesis (SREBP-1c) and increased beta-oxidation genes expression of obesity mice. Reduction of SREBP-1 protein level in livers of obesity mice by curcuma treatment modestly improves fat drop deposition, and completely normalizes the increased expression of CB1-mediated effects. Curcuma also suppressed systemic inflammation by reducing the serum level of tumor necrosis factor alpha. Moreover, obesity mice display decreased senescence marker protein-30 in liver that is normalized by curcuma, this in turn, helps to restore GSH concentrations and viability.

Conclusions: Obese subjects in the persistent inflammatory states may have up-regulated CB1-mediated signaling leading to up-regulation of fatty acid synthesis expression and increased oxidative stress in liver. Thus, curcuma may play an modulation role in pathogenesis of the hepatic steatosis by it's biological effects of antioxidant and anti-inflammation properties.

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Evaluation for the Impact of Penta-O-galloyl-glucopyranose Isoforms (PGG) on Each Stages of Adipocyte Life Cycle

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Background: Obesity nowadays is linked with various diseases including diabetes, hypertension, cardiovascular dysfunction and even cancer. One of the therapeutic approaches for tackling obesity could be modulating the size and number of fat cells via acting on key stages of adipocyte life cycle. The insulin mimetic action and inhibition of adipogenesis by tannin acids, including Penta-O-galloyl-glucopyranose (PGG), have been shown previously.
Objective: The aim of our investigation is overall evaluate the action of PGGs, including the synthetic form of α-PGG and nature product dominant form of β-PGG., on each stage of adipocyte life cycle.

Methods: human mesenchymal stem cells were used to resemble the stage before pre-adipocyte. By using 3T3-L1 fibroblast, the whole adipocyte life cycle were generated by using differentiation induction medium. After PGG treatment for 48hr or 6 days, the viability coupling with cell cycle analysis, TG accumulation measured by Oil-Red-O staining, glycerol release and free fatty acid release were further carried out.

Results: Firstly, insulin mimetic action of both PGGs was confirmed by using H4IIE cells. The administration of PGGs could reduce the viability of hMSC and pre-adipocytes while the viability of adipocytes was modestly affected. Cell cycle analysis further confirmed the induction of apoptosis PGG treatment in pre-adipocytes. In addition, PGG administration leads to cytotoxicity during adipogenesis. Differentiation process appeared to be affected by the PGG treatment indicated by reduction of TG content, glycerol release the morphology. α-PGG is more effective then β form. In addition, α-PGG also resulted in promotion of glycerol release in differentiated adipocytes.

Conclusion: Both PGGs have similar effects on the cytotoxicity of hMSC and pre-adipocytes via induction of apoptosis. Both PGGs could also inhibit adipogenesis. However, α-PGG is overall better than β-form and it also additionally promote glycerol release in adipocytes.

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Andrographolide Inhibits LPS, IFNγ and Oxygen-glucose Deprivation-induced Microglial Activation through Modulation of PI3K, ERK, and Nuclear Factor-κB Activation

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Andrographolide (Andro) is one of the active components of *Andrographis paniculat,* a Chinese official herbal medicine used as an anti-inflammatory and hypoglycemic drug. Andro is known to display anti-inflammatory activity in peripheral neutrophils and macrophage, but its effects on CNS and mechanisms of action are not clear. In the present work, we examined the effects of Andro on LPS- and IFN-γ-stimulated microglial cells (BV-2) and in oxygen-glucose deprivation (OGD)-activated microglia and neurons. Andro concentration-dependently reduced iNOS and nitric oxide (NO) production in LPS- and IFN-γ-stimulated BV-2, possibly through inhibition of nuclear factor-κB (NFκB) by suppressing IκB activation and extracellular signal-regulated kinase (ERK) activation. Andro also inhibited LPS-induced reactive oxygen species (ROS) and cytokines (TNF-α and IL-1β) production in BV-2 through modulation of intracellular calcium mobilization. Furthermore, Andro decreased OGD-induced protein nitrotyrosine in BV-2 by reducing the iNOS expression. Besides, OGD triggered a mitochondria dysfunction-dependent ROS production leading to neuronal cell death. Andro significantly prevented OGD-induced neuronal death. We conclude that Andro is a potent anti-inflammatory drug by modulating NFκB activation to compromise microglia activation during inflammatory and hypoxic conditions that confers Andro to be beneficial for the treatment of inflammation-related CNS diseases.

Tanshinone II A Stimulates Endothelial Cell Growth and Angiogenenis by Up-repulating the Levels of Endothelial Nitric Oxide Synthase and Phosphatidylinositol 3-Kinase

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Background: The vessel stenosis caused by atherosclerosis is linked to various ischemic diseases including Coronary Heart disease (CHD). One of the strategies for the alleviation of ischemia is to promote the formation of collateral circulation using drugs. Tanshinone II A (Ts II A) is a effective liposoluble constituents extracted from Chinese Herbal medicine *Salvia miltiorrhiza* Bge (Dan Shen in Chinese) and has been confirmed that has various cardiovascular pharmacological activities. Recent studies suggest that Ts II A sulfonic sodium could promote the formation of collateral circulation in vivo. In addition, our previous study has demonstrated that Ts II A could promote angiogenesis of the chick emobryo chorioallantoic membrane (CAM).However, the molecular mechanism underlying the effects of Ts II A remained unknown.

Methods: Firstly, the human umbilical vein cells were incubated with Ts II A for 24h or 48h.Next, the effect of Ts II A on the endothelial cell proliferation was investigated by Sulforhodamine B assay. Finally, the potential involvement of signaling pathways was investigated by immunoblot analysis.

Results: The data in this study showed that the proliferation of vessels in experimental groups is more obvious than that is in physiological saline group and menstruum group. Besides, the groups treated by Ts II A have a concentration-dependent effect. And the proliferation of vessels in the Ts II A 10mmol/l Group is more obvious than that in the Ts II A 5mmol/l Group, but the Ts II A 15mmol/l Group did not have a noticeable difference compared with the Ts II A 10mmol/l Group. In addition, Ts II A could up-regulate the levels of endothelial nitric oxide synthase and phosphatidylinositol 3-kinase.

Conclusion: Ts II A could promote endothelial cells proliferation, and then promote angiogenesis of the chick embryo chorioallantoic membrane.The effects of the monomers on angiogenenis is mediated by phosphatidylinositol 3-kinase,and is probably related to the generation of endogeneous nitric oxide. The results show that Ts II A plays an important role in angiogenenis and endothelial protection.

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Comparison Study on Cardiac Toxic Reaction of White Prepared Lateral Root of Aconite to Normal rats and Traditional Chinese Medicine Indication Model Rats

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Objective: to evaluate cardiac toxic reaction difference of white prepared lateral root of aconite to normal rats and pertinent indication model rats and explore scientific evidences on using TCM indication animal model to assess poisonous Chinese herb toxicity.

Methods: eighty male Sprague-Dawley (SD) rats were randomly and averagely divided into normal group and model group. After establishing TCM indication model by injecting hydrocortisoni natrii succinas, normal and model group rats were respectively divided into four treatment groups and blank control group, with eight rats in each group. Treatment group rats were administered different concentrations white prepared lateral root of aconite solution for two weeks. Cardiogram was recorded in 12nd day. Serum adrenocorticotrophic hormone (ACTH), cyclic adenosine monophosphate (cAMP), cyclic guanosine monophosphate (cGMP), aspartate aminotransferase (AST), creatine Kinase (CK) and lactate dehydrogenase (LDH), besides cardiac tissue homogenate succinate dehydrogenase (SDH) and Na^+-k^+–ATPase were detected after the last administration.

Results: compared with normal rats, model blank group rats' ACTH and cAMP level decreased, but cGMP level rose. With dosage adding, both group rats' heartbeat rate quickened and quickening extent of model rats was smaller than that of normal rats, and both group rats' the occurring rate of arrhythmia increased and model rats' increasing extent was lower than normal rats'. White prepared lateral root of aconite caused normal rats' CK increase and Na^+-k^+ ATPase descend, but not made that of model rats change. In addition, both group rats' LDH level rose, SDH level descended, and change extent of those of normal rats was much greater with dosage adding.

Conclusion: Compared with normal rats, cardiac toxic reaction of white prepared lateral root of aconite in pertinent indication model rats was always lighter. This study provided objective evidence for the thought of evaluating Chinese herbs toxicity based on TCM indication animal model.

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The Experimental Study on Hepatic and Renal Toxicity of Rats Induced by *Fructus Gardeniae* and Pharmacokinetics of Geniposide

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Fructus Gardeniae is widely used in the Chinese medicine practice and health food industry. Our previous related study showed that the compound Chinese drug comprised of *Fructus Gardeniae* could induce severe hepatic and renal toxicity. It is necessary and urgent to take systematic and profound research about the toxicity induced by *Fructus Gardeniae* and the mechanism of the toxic action. To trace the toxic substances, the SD rats were administrated the extract of *Fructus Gardeniae* and geniposide for 3 days, observing the change of appearance, behavior and organ index , detecting the serum level of ALT, AST and TBIL. The results indicate that the extract of *Fructus Gardeniae* and geniposide has hepatic and renal toxicity, and geniposide is the main toxic ingredient of the *Fructus Gardeniae*. Geniposide is transformed by the bacterium in the intestinal tract, which is related to the tissue dyeing and the color of the urine and feces.

To illustrate the intracorporal process of geniposide, the SD rats were administrated geniposide in dosage of 280mg•kg^{-1}.The concentrations of geniposide and its metabolite in rat plasma, hepar and nephros tissue, urine and feces were detected. The main Pharmacokinetic parameters were described as follows: Cmax (3.23±0.37) μg•mL^{-1}, $t_{1/2}$ (1.00±0.35) h, MRT (2.39±0.18) h, AUCi (11.23±2.18) h•μg•mL^{-1} for geniposide. Cmax (17.41±5.27) ng•mL^{-1}, $t_{1/2}$ (4.86±2.55) h, MRT (7.86±3.61) h, AUCi (90.60±13.44) h•ng•mL^{-1} for genipin. Geniposide was metabolized and eliminated rapidly. Only 4.25% and 2.82% geniposide were excreted with urine and feces respectively in the original form, 0.50% and 23.38% geniposide were excreted with urine and feces respectively in the form of genipin. Most of Geniposide was transformed into the blue pigment, then eliminated with urine and feces.

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Hepato-toxicity or Protection? Pattern Recognition for the Paradoxical Effect of a Phytomedicine (Rheum Palmatum L.) to Treat Liver Injury

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Recently, the voice doubted the safety of phytomedicines was magnified with the consecutive occurrences of hepatotoxic adverse effects of a series of herbs. Rhubarb is a common used herb worldwide and has nowadays been well used to treat chronic hepatic diseases in oriental medicine. However, recent reports had revealed that rhubarb anthraquinones had hepatotoxic effects on rats. Hence, increasing attention has been focused to fully assess the benefits and risks of rhubarb. In this study, the total extracts of rhubarb at different dosages were oral administrated to both normal rats and CCl4-injured rats for 12 weeks with biochemical and histopathological tests. The results suggested that the curative effect of rhubarb to treat liver injury was much related to protecting hepatic cells away from free radical damage through anti-oxidation; while the hepatotoxic potential was much related to liver fibrosis. By factor analysis, the bio-indices were abstracted into a comprehensible visual pattern using only two latent factors, namely fibrosis factor and cellular injury factor. We also found that the hepatotoxic effect of the herb could be attenuated by steam-processing, an ancient method recorded in traditional Chinese medicine. And the protective effect of processed rhubarb was better than crude herb. Conclusion: The findings of this study firstly illustrated the bidirectional potential of rhubarb on CCl4-injured and normal rats as well as demonstrated the feasibility of using factor analysis for studying the dosage-response relationships of traditional herbal medicines in a holistic way.

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Attenuation of Oxidative and Nitrosative Stress by Pure Constituents of Traditional Chinese Remedies

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Sulfamethoxazole hydroxylamine (SMX-HA), a reactive metabolite of Sulfamethoxazole, plays a critical role in the pathogenesis of adverse drug reactions and generates cellular oxidative and nitrosative stress. Baicalein (BE), Crocetin (Cro), Resveratrol (Res) and Schisanhenol (Sal) are found in natural herbs used in traditional Chinese medicine. Purified BE, Cro, Res and Sal are reported to have many biological activities including antioxidant effects. We investigated their effects on oxidative and nitrosative stress mediated by SMX-HA in cultured Jurkat *E* 6.1 cells.

We studied lipid hydroperoxide formation, protein carbonylation and oxidative changes in the disulfide proteome (by redox two-dimensional polyacrylamide gel electrophoresis (R2D- PAGE)) in lysates of Jurkat *E* 6.1 cells treated with 400 μM SMX-HA.

SMX-HA increases lipid hydroperoxide in Jurkat *E* 6.1 cells ($P<0.01$) and this increase is significantly attenuated ($P<0.05$) with 5 or 20μM of each chemical; 5μM of BE, Cro, Res or Sal treatment reduced lipid hydroperoxide formation by approximately 40%, 55%, 55%, and 40%, respectively. Protein carbonylation is also significantly increased by SMX-HA treatment in Jurkat *E* 6.1 cells ($P<0.01$) which was significantly attenuated ($P<0.05$) by pre-treatment with BE, Cro, Res or Sal (5 or 20μM). Cro showed the best chemoprotective effect, reducing SMX-HA induced protein carbonylation by 60% at 5 μM. The minimal effective concentration of a 1:1:1:1 mixture of these compounds was 1 μM ($P<0.05$) which reduced protein carbonylation by approximately 40%. R2D-PAGE experiments were consistent with results for lipid peroxidation and protein carbonylation.

Our results suggest that defined mixtures of known antioxidants and immunomodulants of natural origin with complementary mechanisms of action are likely to provide more chemoprotection against SMX-HA oxidative stress than eqimolar concentrations of single antioxidants.

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Inhibitory Effects of *Radix isatidis* Extract on Attachment of Influenza A and B Virus to MDCK Cells

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Radix isatidis boiling water extract (RIE) is a clinically applied antiviral agent. To elucidate its antiviral mechanism, influenza viruses A/Beijing/95-262 (H1N1) and B/Shanghai/93-1, and Madin-Darby Canine Kidney (MDCK) cell were respectively treated by RIE, and the influences of these treatments on viral infection were investigated by MTT assay, plaque reduction assay and scanning electron microscopy (SEM). RIE inhibited the infection of influenza viruses *in vitro* while viruses were inoculated at the presence of RIE. A very low cytotoxicity of RIE was observed by evaluating the cell survival rates. CC_{50} of RIE in MDCK cells was higher than 100 $mg \cdot ml^{-1}$. Furthermore, when cells were incubated with RIE prior to viruses inoculation, their survival rates were 63.4 ± 5.6% and 65.1 ± 14.1% in influenza virus A and B, respectively, suggesting a remarkable protection effect of RIE. In contrast, either of inoculating cells with viruses prior to RIE treatment, or incubating viruses with RIE prior to viruses inoculation, did not improve the cell survival rates significantly, which indicating no antiviral effects of both treatments. Moreover, much less virus particles were spotted by SEM in the RIE-treated cells than the cells without RIE treatment. These results indicate RIE's antiviral effect is attributed to its host cell protection effect but not actions on viruses or after infection interruption. A novel antiviral mechanism of RIE is proposed: RIE compositions bind to and subsequently modify the host cell plasma membrane to block attachment of viruses.

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Binding and Interaction of Anti-diabetic MRPs to Pancreatic ß-Cell Plasma Membrane

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The antioxidant and antidiabetic effects of the decoction of bitter melon (*Momordica Charantia Linn.*) pulps has been proven *in vitro* and *in vivo*, particularly on Type II diabetic subjects. The major active component of the decoction is Maillard reaction products (MRPs), namely 'MCE MRPs' here. MCE MRPs showed protective effects on cell oxidization damages induced by superoxide anion radicals donor, alloxan. The effects of MCE MRPs on pancreatic cells' plasma membrane and phosphoglycerol lipids (DOPG) monolayer were studied in order to illuminate the mechanism of MRPs' antioxidant and anti-diabetic effects.

MCE MRPs doubled the cell survival rates of HIT-T15 pancreatic cells at 2 mg/mL (W/V), incubating with cells prior to the exposure to alloxan (1 mM, 1 h). Furthermore, once Cell plasma membrane was broken down, Green Fluorescence Protein (GFP) could freely traveled into these damaged cells. The degree of oxidative damage to integrity of membrane could be directly examined by measuring the intensity of green fluorescence in cellular plasma with fluorescent microscopy. Only very weak fluorescence was observed in the MCE MRPs protected cells while a strong green light was excited in the control. The interaction of MCE MRPs with membrane lipids was examined with Langmuir balance on phospholipids monolayer. MCE MRPs significantly decreased the surface tension of DOPG monolayer, and caused lipid packing less rigid. Furthermore, MCE MRPs formed a film at the water-air interface. It is assumed that MCE MRPs contain amphipathic compounds, which can integrate into monolayer and interact with hydrophobic hydrocarbon chains.

To conclude, MCE MRPs protected cells from free radical damage by binding to the cellular plasma membrane. Its capacity of stabilizing the lipid films and subsequently maintaining the integrity of plasma membrane is proposed as a mechanism of MCE's cellular protection activities.

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Emodin inhibits current through SARS-associated coronavirus 3a protein

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Severe acute respiratory syndrome (SARS) first appeared in 2002 in China. In mainland China about 50% of patients were treated with Chinese herbal medicine as adjunct therapy, and some positive effects in SARS patients had been reported. Previously (Ho et al. 2007) identified emodin as an effective component of *Polygonaceae* to block the interaction of the SARS-coronavius spike protein (SARS-CoV S protein) with the angiotensin-converting enzyme 2 (ACE2) and the infection by S protein-pseudo-typed retrovirus. The 3a protein of SARS-CoV had been demonstrated to form an ion-permeable channel in infected cells that can influence virus release (Lu et el. 2006). Here we investigated the effect of emodin on the function of the 3a protein as an ion channel. To measure the current mediated by 3a protein, we used the *Xenopus* oocytes as an expression system and applied two-electrode voltage clamp to determine steady-state current-voltage dependencies.

Oocytes expressing 3a protein exhibited large additional Ba2+-sensitive currents that were considered as the current mediated by 3a protein. Oocytes not expressing 3a protein also exhibited Ba2+-sensitive currents, but they were smaller than in oocytes that were injected with cRNA of the 3a protein by a factor of 2. The endogenous Ba2+-sensitive current was not affected by emodin. In 3a-protein expressing oocytes part of the Ba2+-sensitive current could be inhibited in dose-dependent manner by emodin. Assuming that this current component is mediated by 3a protein, 50% inhibition was estimated at about 15 μM. At similar concentration virus release from infected cells became strongly reduced.

We suggest that emodin may contribute through inhibition of the current mediated by 3a protein to reduce virus release from the SARS-CoV-infected cells and may form the basis for a new therapeutic agent in treatment of SARS.

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YiNaoKang's Effect on the AS Based AIS SD Mice's Brain VEGF Expression and Brain Pathological Change

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Objective: To study how the YiNaokang affect the AS and AS based AWAS SD mices' brain VEGF expression and brain pathological changes, so as to explain its mechanism.

Method: 115 SD rats weighted 180g±20g were randomly divided into six groups which were A group (normal) 15 ; B to F group (model) 100 among which group C was AS group, group D was composite group, group B was Yi Naokang prophylactic group, group E was YiNaokang group and group F was lipitor group. On the 8th day the B to F group were given intraperitoneal injection of VD_3 one-time and then began to feed them with high fat feed to copy the AS models, and on the 65th day , 4 groups except group C were injected with ET-1 near the MCA area to duplicate the AIS model. On the 74th day, 3 rats would be picked out randomly to test their brain VEGF expression and HE stained to observe the brain pathological changes.

Result: The VEGF expression in the YiNaokang group was ++ while the lipitor group was +, the expression of VEGF in the YiNaokang group was stronger than the lipitor group.

Conclusion: The effect of YiNaokang's on AIS maybe was related with its function of upregulating VEGF expression in the ischemic brain.

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Effect of Oral *Schisandra Sphenanthera* Extract on the Pharmacokinetics of Paclitaxel in Rats

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Backgrounds: Paclitaxel is a substrate of the efflux transporters such as P-glycoprotein, and is mainly metabolized by the liver. The extract of Schisandra sphenanthera (Sch E) has been reported to be able to inhibit the activity of P-gp and CYP3A in our previously published report. It might be possible that Sch E would alter the pharmacokinetic behavior of paclitaxel. Therefore, the purpose of this study was to investigate the effect of Sch E on the pharmacokinetics of paclitaxel administered orally and intravenously in rats. **Methods:** Paclitaxel was administered to rats orally (30 mg/kg) or intravenously (0.5 mg/kg) with or without the concomitant administration of SchE (0.25 g/kg). Concentrations of paclitaxel in rat plasma were determined using our previously developed UPLC-MS/MS method. Pharmacokinetic parameters were calculated by non-compartmental model. **Results:** After the oral administration of paclitaxel to rats pretreated with SchE, there were significant increases in $AUC_{0\text{-}24h}$ of paclitaxel (from 280.8 ± 97.3 to 543.5 ± 115.2 h*ng/mL; $P < 0.05$) and Cmax (from 44.6 ± 16.4 to 86.8 ± 16.1 ng/mL; $P < 0.05$). The pharmacokinetic data for i.v. paclitaxel with SchE showed a relatively small (when compared with that of oral paclitaxel) but still significant increase in $AUC_{0\text{-}24h}$ (from 163.6 ± 22.1 to 212.7 ± 17.7 h ng/mL; $P < 0.05$) and decrease in clearance (from 3.2 ± 0.6 to 2.2 ± 0.3 L/h/kg; $P < 0.05$). **Conclusion:** The results indicated that the presence of SchE can improve the systemic exposure of paclitaxel in rats. The pharmacokinetic interaction between these two drugs should be taken into consideration in clinical use.

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Study of Biological Activities and Molecular Mechanism of Herbal Formula (*Radix Rehmanniae* and *Radix Astragali*) on Human Skin Fibroblast Cell Line HS27

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A Chinese herbal formula comprising Radix Rehmanniae (RR) and Radix Astragali (RA) has been demonstrated to improve the healing of diabetic foot ulcer through enhancing the viability of primary fibroblasts in diabetic patients suffering insulin resistance. In this study, biological activities of herbal formula (RA-RR) in human skin fibroblast HS27 were investigated by evaluating factors such as cell viability and proliferation, cell cycle analysis, fibroblast cell migration, adhesion and contraction. Moreover, the expression of ECM proteins and cytokines was examined by western blot or protein array techniques, which provided information for the effects of RA-RR on cell growth, cell migration, angiogenesis, fibrogenesis as well as inflammatory response. Additionally, gene expression profile of HS27 fibroblast cells stimulated by RA-RR was studied by using a human cDNA microarray containing 10,000 genes. 126 genes with significant changes in expression level upon RA-RR treatment were identified, in which 102 genes were up-regulated and 24 genes were down-regulated. Two signaling pathways were shown to play important roles on RA-RR effects, i.e., Wnt signaling and angiogenesis pathway. These pathways are directly related to cell proliferation, angiogenesis, ECM formation and inflammation in the process of wound healing. Our results provide the molecular basis for biological effects of RA-RR on skin fibroblasts, which may provide insights for the mechanism of RA-RR herbal formula and serve as new therapeutics for wound healing.

Up-regulation of L-type Calcium Channels in Colonic Smooth Muscle Cells is Involved in Colonic Motility Dysfunction Induced by NMS

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Aims: Irritable bowel syndrome (IBS) is characterized by colonic motility disorder. L-type calcium channels play an important role in the colonic smooth muscle contraction. This paper aimed to investigate the relationship between up-regulation of L-type calcium channels and altered motility disorder in a rat model of IBS.

Material and Methods: Male Sprague-Dawley rats were subjected to daily maternal separation (NMS) from postnatal day 2 to 14 or normal handling (NH), and used when weighted 250 - 300 g. Colonic smooth muscle contractions was studied in an organ bath system. L-type Ca^{2+} channel α_{1c} subunit expression in smooth muscles from rat colon were studied by immunofluorescence and Western blotting analysis. The intracellular calcium concentration ($[Ca^{2+}]_i$) of enzymatically isolated single colonic smooth muscle cell was studied with laser confocal fluorescent microscopy.

Results: The fecal pellets during one hour water avoidance stress (WAS) were significantly increased; the amplitude of spontaneous contractions and contractions induced by Bay K 8644 (10 nM - 1 μM), KCl (10 - 60 mM) and ACh (100 nM - 10 μM) were significantly increased in NMS rats, when comparing with that of NH rats. $[Ca^{2+}]i$ induced by Bay K 8644 (1 μM), KCl (40 mM) and ACh (10 μM) significantly increased in muscle cells of NMS rats than NH rats. Further, α_{1c} protein expression was significantly up-regulated in colonic smooth muscle of NMS rats than NH rats.

Conclusion: These results suggest that NMS lead to up-regulation of L-type Ca^{2+} channels expression in the colon, which contributes to the colonic motility disorder. Our findings provide direct evidence to help understanding the underlying mechanism of chronic stress-induced colonic motility disorder in IBS.

Keywords: neonatal maternal separation; L-type Ca^{2+} channel; motility disorder; irritable bowel syndrome

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Inhibitory Effect of Magnolol on Colonic Motility is Mediated through Down-regulation of Voltage-dependent L Type Ca^{2+} Channels of Colonic Smooth Muscle Cells in Rats

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Aims: The aim of this study is to investigate the effect of magnolol (5,5′-Diallyl-2,2′-biphenyldiol) on colonic contraction in rats and the underlying mechanism.

Material and Methods: The effects of magnolol on distal colonic segments contraction in rats were tested by using an organ bath system. The effects of magnolol on the currents of voltage dependent L-type Ca^{2+} channels in enzymatically isolated single colonic smooth muscle cells were investigated by using whole-cell patch-clamp techniques. L-type Ca^{2+} channel α_{1c} subunit expression in smooth muscles from rat colon were studied by Western blotting analysis.

Results: The results showed that the spontaneous contractions and ACh (10 μM)-induced contractions of colonic smooth muscle segment were dose-dependently inhibited by magnolol (3–100 μM). And magnolol (30 – 100 μM) inhibited the colonic smooth muscle contraction induced by 100 nM Bay K 8644. In the presence of Bay K8644 (100nM), magnolol (10 – 100 μM) inhibited the contraction induced by 10μM ACh. Further, tetrodotoxin (TTX 100 nM) and N_{ω}-nitro-L-arginine methyl ester (L-NAME 100μM), the nitric oxide (NO) synthase inhibitor, didn't change the inhibitory effect of magnolol (10 μM). In addition, magnolol (3 – 100 μM) inhibited the L-type Ca^{2+} channels currents of colonic smooth muscle cells dose-dependently and decreased the expression of L-type Ca^{2+} channel α_{1c} subunit on colonic smooth muscle of rat.

Conclusions: The results indicate that magnolol can inhibit the colonic muscle contraction in vitro, and the mechanisms involved is related with the inhibitory effect on L-type Ca^{2+} channels of colonic smooth muscles cells.

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Magnolol Regulates the Colonic Motility Dysfunction through Inhibiting l-type Calcium Channels in Colonic Smooth Muscle in Neonatal Maternal Separation Rats

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Aims: Irritable bowel syndrome is a common disease of lower gastrointestinal functional disorder. The aim of this study is to investigate the effect of magnolol (5,5′-Diallyl-2,2′-biphenyldiol) on colonic motility in neonatal maternal separation (NMS) rats and the underlying mechanism.

Material and Methods: The effects of magnolol on distal colonic motility in vivo were tested by recording the fecal pellets in 1 hour water avoidance stress (WAS). The effects of magnolol on colonic segments contraction in rats were tested by using an organ bath system in vitro. The effects of magnolol on the intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) in enzymatically isolated single colonic smooth muscle cells were investigated with laser confocal fluorescent microscopy.

Results: The results showed that administrated with magnolol can decrease the number of fecal pellets in 1 hour WAS in vivo with NMS rats at the dose of 2mg/kg, 10mg/kg, and 50mg/kg. magnolol also inhibit the increased number of fecal pellets pretreatment with Bay K 8644, an L-type calcium channel activator, under 1 hour WAS in vivo with NH rat. Furthermore, the results in vitro study demonstrated that magnolol at the concentration of 10 μM, 30 μM, and 100 μM inhibit the colonic smooth muscle spontaneous contraction and contractile effect induced by different stimuli in vitro in NMS rats in a time-dependent and dose-dependent manner. Finally, 30 μM, and 100 μM magnolol decreased the $[Ca^{2+}]_i$ induced by high K^+ with colonic smooth muscle cells in NMS rats.

Conclusions: The results demonstrate that magnolol can inhibit the colonic motility disorder in NMS rats in vivo and in vitro which provide the evidence that magnolol could be applied to treat abnormal colonic motility. The effect may be associated with the inhibitory effect on activity of voltage-sensitive L-type $[Ca^{2+}]_i$ channels.

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Magnolol Attenuates the Colonic Smooth Muscle Contraction by Decreasing the Activities of MLCK/myosin Light Chain 20 in Colonic Smooth Muscle

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Aims: Protein kinase C(PKC)/Myosin light chain kinase(MLCK)/MLC20 pathway plays an important role in the colonic smooth muscle contraction. The aim of this study is to investigate the effect of magnolol (5,5′-Diallyl-2,2′-biphenyldiol) on PKC/MLCK/MLC_{20} pathway in colon smooth muscle contraction with rats.

Material and Methods: The colonic smooth muscle contraction induced by activation PKC and the effect of magnolol on PKC activation were observed by using organ bath. The effect of magnolol on PKC/MLCK/MLC_{20} pathway was performed by using western blotting methods.

Results: Magnolol at the concentration of 10 μM - 100 μM inhibited smooth muscle contractility after activation of PKC in the presence of Ca^{2+} but have no inhibitory effect in the absence of Ca^{2+}. The results of western blotting showed that magnolol could inhibit the expression of MYL9 (MLC_{20}) on smooth muscle but could not affect the expression of MLCK and CPI-17 on colonic smooth muscle.

Conclusions: The present results demonstrate that magnolol inhibit the colonic smooth muscle after activation PKC. This effect is involved in the Ca^{2+} dependent PKC pathway. Furthermore, the effect is accompanied by a reduction of MLC_{20} on the colonic smooth muscle.

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The Analgesic Effect of JCM-16021 on Trinitrobenzene Sulfonic Acid (TNBS)-induced Postinfectious Irritable Bowel Syndrome Rats

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JCM-16021, a revised traditional Chinese herbal formula, has been proved to relieve symptoms of IBS patients and attenuate neonatal maternal separation -induced visceral hypersensitivity in rats. This study aimed to investigate whether JCM-16021 had analgesic effect on postinflammatory visceral hyperalgesia. Postinfectious irritable bowel syndrome (PI-IBS) model was induced by TNBS intracolonic administration in male Sprague-Dawley rats. When TNBS-induce inflammation had completely recovered 4 weeks after TNBS instillation, the rats which had been proven to have visceral hyperalgesia were administered with JCM-16021 orally at the dose of 1.2, 0.9, and 0.6g/kg, individually, once a day. After 14 days' treatment, pain threshold pressure in response to colorectal distention was tested using abdominal withdrawal reflex test. JCM-16021 treatment can significantly and dose-dependently increase the pain threshold pressure when compared to that before treatment and in the model group (water treated), suggesting JCM-16021 has analgesic effect on TNBS-induced postinflammatory visceral hyperalgesia rats. The results also indicate that JCM-16021 may have the potential to attenuate visceral hyperalgesia in PI-IBS patients.