世界中联中药分析专业委员会第十届学术年会
暨换届大会暨中药分析国际学术大会（2019·上海）

The 10th International Conference on TCM Pharmaceutical Analysis & Annual Meeting & Election of the Council of Specialty Committee of TCM Pharmaceutical Analysis, WFCMS（2019 · Shanghai）

2019年6月27-29日　中国·上海

日程册
Program Book

欢迎辞

尊敬的各位同仁：

我们作为本次大会的主席，谨在此诚挚的邀请您出席世界中联中药分析专业委员会第十届学术年会暨换届大会暨中药分析国际学术大会 (2019 · 上海)。

世界中医药学会联合会中药分析专业委员会于 2010 年 7 月正式成立，专委会秉承“与企业生产实际相结合、发展中药分析新技术与新方法、加强国际交流与合作、为提升药典标准服务”的指导思想，一直致力于促进中药材、饮片和中成药的生产、使用和管理的规范化、标准化，促进中药新药研发，推动中药产业发展。2019 年恰逢专委会成立 10 周年，兹定于 6 月 27 日 -6 月 29 日在上海市召开“世界中联中药分析专业委员会第十届学术年会暨换届大会暨中药分析国际学术大会 (2019 · 上海)”，届时将进行换届改选工作及相关庆祝活动。本次会议还将同时举行《中草药》杂志英文版全体编委会及办刊 10 周年高端论坛。热诚邀请中药分析专业委员会全体成员，从事中药及天然药物研发、生产、检验、临床应用以及从事中药分析教学、科研等方面的有关人员参加，并热烈欢迎尚未成为中药分析专业委员会大家庭一员的各位专家学者加入团队，共同谋划中药分析、标准以及相关研究的发展大计。

我们将以悉心的安排为您打造一个中药分析盛会，让我们在这个火热的夏天，齐聚上海，共襄盛举。

果德安 教授
世界中联中药分析专业委员会会长
第十届学术年会主席

陈万生 教授
第十届学术年会共同主席

Welcome

As chairs of the organizing committee, it is a great pleasure to welcome all of you as participants of The 10th Annual Meeting with 2019 International Conference on TCM Pharmaceutical Analysis, to be held in Shanghai.

The Specialty Committee of Traditional Chinese Medicine Pharmaceutical Analysis (WFCMS) was formally founded in July of 2010 with the basic concept of developing new technologies and methods for TCM analysis, strengthening international exchanges and collaboration, and serving for upgrading pharmacopoeia standards and TCM industrial healthy development. In order to promote TCM standardization, new TCM drug research and development, and TCM industrialization, the Specialty Committee is planning to held The 10th Annual Meeting jointly with 2019 International Conference on TCM Pharmaceutical Analysis in Shanghai on June 27-29th, 2019 to celebrate the 10th anniversary since its founding.

We will invite the renowned scientists and regulators in the field of herbal medicines around the world to deliver lectures on important issues such as new analytical techniques, quality monograph elaboration of TCM, comprehensive analysis and quality control of classic TCM recipes, granules etc. All the scientists, regulators and entrepreneurs who are interested in the topics are more than welcome to attend this unique-featured conference.

On behalf of the Organizing Committee, We hope, the conference is a global platform open to all researchers, who would like to present their studies and a great opportunity to exchange experiences of participants, particularly between the research workers for future collaboration. We look forward to your active participation and count on a successful conference.

Prof. Dean Guo
Chair of the Specialty Committee of Traditional Chinese Medicine Pharmaceutical Analysis, WFCMS

Prof. Wansheng Chen
Co-Chair of the10th Annual Meeting with 2019 International Conference on TCM Pharmaceutical Analysis

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主办单位

世界中医药学会联合会中药分析专业委员会

中药标准化技术国家工程实验室

承办单位

上海中医药大学

第二军医大学附属长征医院

安捷伦科技有限公司

上海植物生理与植物分子生物学学会

中国药学会临床中药学专委会

《Chinese Herbal Medicine》杂志编辑委员会

天津药物研究院

中国医学科学院药用植物研究所

上海市食品药品检验所

赞助企业

国药控股股份有限公司

广西梧州制药（集团）股份有限公司

安斯泰来制药（中国）有限公司

江苏康缘药业股份有限公司

四川新荷花中药饮片股份有限公司

北京赛科昌盛医药有限责任公司

南京圣和药业股份有限公司

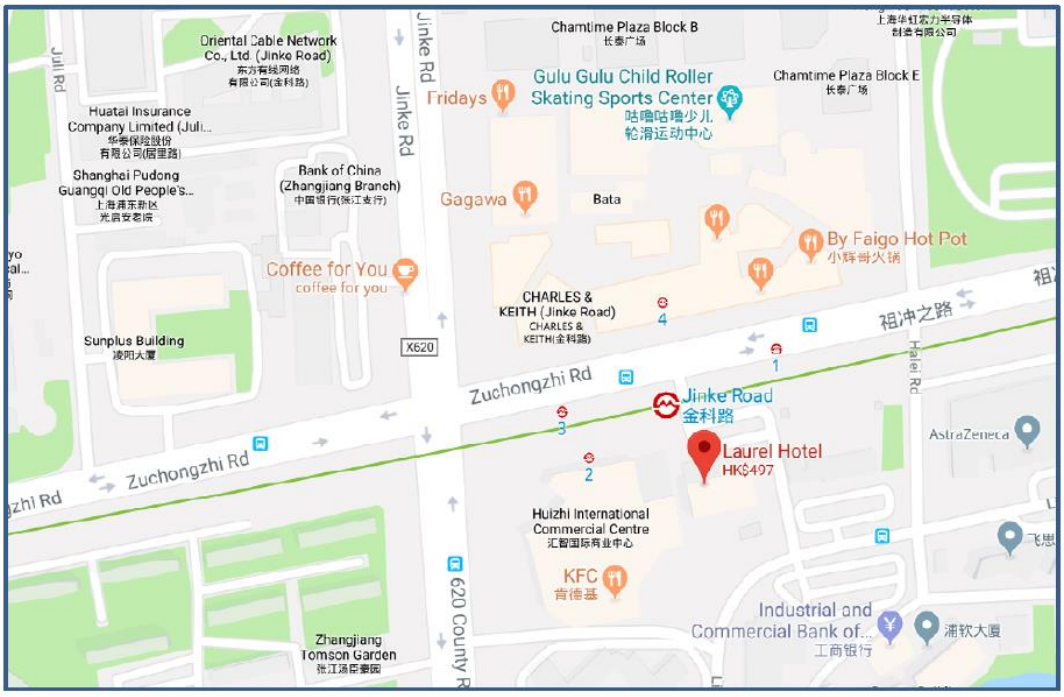
卫材（中国）药业有限公司

上海施丹德标准技术服务有限公司

会务信息 / Application Information

会场地址 Congress Address

上海长荣桂冠酒店（上海浦东祖冲之路 1136 号，近金科路地铁站）
Evergreen Laurel Hotel Shanghai
Address: 1136# Zuchongzhi Road, Shanghai 201203



交通 Traffic

公共交通 Public Transportation

虹桥枢纽出发：地铁 2 号线至金科路站

浦东机场出发：地铁 2 号线至金科路站

From Hongqiao Junction: Metro Line 2 to Jinke Road Station

From Pudong Airport: Metro Line 2 to Jinke Road Station

出租车费用 Taxi fare

虹桥枢纽出发：约 150 元　About 150 RMB from Hongqiao Junction

浦东机场出发：约 100 元　About 100 RM from Pudong Airport

会议注册 Conference Registration

6 月 27 日，12:00–20:00， 上海长荣桂冠酒店 一楼大堂

27th June，12:00–20:00， Lobby of evergreen Laurel Hotel Shanghai

代表证 Personized Badge

当您领到代表袋和大会文件时，您已经拿到了代表证。请在大会期间佩戴代表证，您凭此证得以进入会场和参与各项活动。

You have received a personalized name badge when collecting your delegate bag containing all documents. During the Congress, this badge must be worn and clearly visible at all times. The badge grants admission to the Congress session and official social events.

禁止吸烟 Non-smoking Policy

会场整个建筑物内禁止吸烟。

Smoking is not allowed anywhere inside the Central Hall Westminster.

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简要日程

2019 年 6 月 27 日

12:00–20:00	参会人员报到注册				
16:00–18:00	换届大会筹备会				

2019 年 6 月 28 日

08:30–09:30	开幕式	开幕致辞			
		换届大会			
		“中药分析与标准青年科学家奖”颁奖仪式			
		“中药分析与标准杰出贡献奖”颁奖仪式			
09:30–12:00	开场报告				
10:45–12:30	中药产业高质量发展论坛				
12:00–13:40	午餐（墙报阅读及评审）				
13:40–17:10	分场报告	中药分析新术、新方法会场	青年学者论坛	中药标准导向的基础研究会场	Chinese Herbal Medicines 办刊 10 周年国际编委会
18:30–21:00	十周年庆典活动及晚宴				

2019 年 6 月 29 日

08:40–12:30	分场报告	中药资源与生物技术研究会场	经典名方会场	中药标准导向的基础研究会场
12:30–14:00	午餐（墙报阅读及评审）			
14:00–16:45	大会报告			
16:45–17:10	优秀墙报颁奖仪式及闭幕式			

世界中联中药分析专业委员会第十届学术年会
暨换届大会暨中药分析国际学术大会（2019·上海）

The 10th International Conference on TCM Pharmaceutical Analysis & Annual Meeting & Election of the Council of Specialty Committee of TCM Pharmaceutical Analysis, WFCMS (2019-Shanghai)

大会日程

2019年6月27日 下午

12:00–20:00	参会人员报到注册
16:00–18:00	世界中联中药分析专业委员会换届大会筹备会 （参加人员：世界中联领导，中药分析专业委员会会长、副会长、秘书长、常务理事及理事）

2019年6月28日 上午

08:30–09:30	**开幕式、换届大会、颁奖仪式（地点：桂冠厅）**	
	主持人：陈万生 教授	
08:30–09:10	上海中医药大学领导致欢迎辞	
	世界中联中药分析专委会会长致辞	
	上海市科委领导致辞	
	安捷伦科技（中国）有限公司领导致辞（图谱库发布）	
	中国科学院上海药物所领导致辞	
	世界中医药学会联合会领导致辞	
09:10–09:20	世界中联中药分析专业委员会换届大会	
09:20–09:30	“中药分析与标准青年科学家奖” &“中药分析与标准杰出贡献奖”	
09:30–12:00	**大会报告（地点：桂冠厅）**	
	主持人：屠鹏飞 教授、马双成 教授	
09:30–09:55	刘昌孝 院士（天津药物研究院）	报告：中药质量标志物的发现与应用
09:55–10:20	岳建民 院士 （中科院上海药物研究所）	报告：Chemistry and Bioactivity of Natural Products from Medicinal Plants
10:20–10:45	茶 歇	
	主持人：张卫东 教授、李 萍 教授	
10:45–11:10	Rudolf Bauer 教授 （格拉茨大学，奥地利）	报告：HPTLC limit tests and a more holistic concept for quality control of herbal drugs
11:10–11:35	Satyajit D. Sarker 教授 （利物浦约翰摩尔斯大学，英国）	报告：Current Trends in Phytochemical Analysis
11:35–12:00	王喜军 教授（黑龙江中医药大学）	报告：基于中药有效性的质量标志物研究

10:45–12:30	中药产业高质量发展论坛（地点：上海厅）	
按姓氏拼音排序		主持人：果德安 教授
10:45–12:30	成金乐	中山中智集团副总经理
	关彦玲	黑龙江葵花药业执行董事
	江　云	四川新荷花中药饮片公司董事长
	兰青山	中国中药公司副总经理
	李　琦	上海市药材有限公司副总经理
	刘菊妍	广州药业集团副总经理
	欧阳静波	广西梧州制药公司董事长
	秦少容	重庆太极集团公司副总经理
	唐海涛	江苏苏中药业集团股份有限公司执行董事
	王　勇	南京圣和药业股份有限公司董事长
	解素花	同仁堂药业集团研究院院长
	谢天培	上海诗丹德标准技术服务有限公司董事长
	叶正良	天士力控股集团有限公司副总裁

2019 年 6 月 28 日　下午

13:40–17:10	中药分析新技术、新方法会场（地点：桂冠一厅）	
		主持人：季　申 教授、陆兔林 教授
13:40–14:00	杨　莉 教授（上海中医药大学）	报告：Quality and Safety Evaluation of Pyrrolizidine Alkaloids-Containing Herbal Medicine Using Hybrid Mass Spectrometry
14:00–14:20	A.A.Leslie Gunatilaka 教授（亚利桑那大学，美国）	报告：Discovery of Anticancer Agents from Plants Used in Traditional Medicine
14:20–14:40	Ikhlas Khan 教授（密西西比大学，美国）	报告：Stimulants in Weight loss and Pre-workout supplements
14:40–15:00	Giovanni Appendino 教授（皮埃蒙特东方大学，意大利）	报告：Champagne taste for beer price? The plague of adulterated herbal products
15:00–15:10	茶　歇	
		主持人：陈道峰 教授、蔡少青 教授
15:10–15:30	Ilkay Erdogan Orhan 教授（加齐大学，土耳其）	报告：Lead Molecules Inspired by Mother Nature and Folkloric Medicine: Enzymes on Target
15:30–15:50	Alexander Shikov 教授（圣彼得堡药物所，俄罗斯）	报告：Health effects and nutritional use of medicinal plants in Russia

15:50–16:10	Ha Minh Hien 教授 （越南药监局草药处）	报告：Extraction, Standardization and Product Development of Bioactives from Resin of *Calophyllum inophyllum* Nut Oil
16:10–16:30	马百平 教授 （北京放射医学研究所）	报告：超临界流体色谱在中药糖苷分析中的应用
		主持人：宣利江 教授、吕海涛 教授
16:30–17:10	短报告	

2019 年 6 月 28 日 下午

13:40–17:10	**青年科学家论坛（地点：桂冠二厅）**	
		主持人：林　羽 教授、孙连娜 教授
13:40–13:55	杨　华 教授（中国药科大学）	报告：Synergistic combination discovery from herbal medicines
13:55–14:05	乔　雪 副教授（北京大学）	报告：Effective Components and Their Glycosylation in licorice
14:05–14:20	赵　清 副教授（上海辰山植物园）	报告：药用植物黄芩的遗传信息解读
14:25–14:40	肖　莹 副教授（上海中医药大学）	报告：Precise Regulation of Lignans in *Isatis indigotica*
14:40–14:55	季莉莉 教授（上海中医药大学）	报告：Liver injury induced by pyrrolizidine alkaloids and its detoxification
14:55–15:10	茶　歇	
		主持人：刘志强 教授、杨　华 教授
15:10–15:25	袁　媛 教授（中国中医科学院）	报告：Archaeological evidence suggests earlier use of Ganoderma in Neolithic China
15:25–15:40	孙　洋 教授（南京大学）	报告：穿心莲内酯抗炎新机制的转化医学研究
15:40–15:55	高　雯 副教授（中国药科大学）	报告：Chemical characteristics-oriented standards establishment of herbal medicines
15:55–16:10	李兴旺 教授（华中农业大学）	报告：High-resolution 3D Genome Architecture and Transcriptional Regulation in Rice
16:10–16:25	宋月林 副教授（北京中医药大学）	报告：Advanced LC-MS for widely quantitative analysis of herbal medicines
		主持人：肖　莹 副教授、侯晋军 副研究员
16:30–17:10	短报告	

13:40–17:10	中药标准导向的基础研究 会场 I（地点：桂冠三厅）	
		主持人：宣利江 教授、乔善义 教授
13:40–14:00	叶　阳 研究员 （中国科学院上海药物研究所）	报告：Bioactive compounds in Tong-Guang-San and its formulation
14:00–14:20	孙　蓉 教授（山东大学）	报告：基于效毒关联评价的有毒中药质量控制研究
14:20–14:40	孟宪生 教授（辽宁中医药大学）	报告：基于“质－量”双标的中药材质量控制方法研究
14:40–15:00	辛振强 总监（上海诗丹德标准技术服务有限公司）	报告：TCM-PCDL 技术在中药物质基础研究中的探索及应用
15:00–15:10	茶　歇	
		主持人：李晓波 教授、殷　军 教授
15:10–15:30	秦雪梅 教授（山西大学）	报告：Comparative study on quality of *Astragali Radix* with metabolomic analysis and pharmacodynamics
15:30–15:50	白　钢 教授（南开大学）	报告：Integrated Systems Biology and Chemical Biology Approach to Exploring Mechanisms of Traditional Chinese Medicines
15:50–16:10	张勇慧 教授（华中科技大学）	报告：Discovery of active natural products with new skeletons
16:10–16:30	杨　明 教授（江西中医药大学）	报告：中药挥发油的功效特点、品质特征与质量控制
16:30–16:50	谭　睿 教授（西南交通大学）	报告：利用干细胞筛选中药活性成分的新方法
16:50–17:10	余彦海 工程师 （安捷伦科技（中国）有限公司）	报告：液相阀方案在中药分析的应用

14:00–17:10	Chinese Herbal Medicines 办刊 10 周年国际编委会（圆桌会议） （地点：上海厅）

2019 年 6 月 28 日 晚

18:30–21:00	十年庆典活动及招待晚宴 （地点：桂冠厅）

2019 年 6 月 29 日 上午

08:40–12:30	中药资源与生物技术研究会场（地点：桂冠一厅）	
		主持人：唐克轩 教授、林 喆 教授
08:40–09:00	周景文 教授（江南大学）	报告：Production of complicated flavonoids by microorganisms
09:00–09:20	高 伟 教授（首都医科大学）	报告：中药活性成分合成生物学研究
09:20–09:40	戴均贵 教授（医科院药物所）	报告：Enzyme promiscuity and structural innovation of natural products and drug discovery
09:40–10:00	Mattheos A. G. Koffas 教授（伦斯勒理工学院）	报告：The road to animal-free glycosaminoglycan production using metabolic engineering of recombinant microorganisms
10:00–10:20	曾建国 教授（湖南农业大学）	报告：博落回资源系统研究与综合利用
10:20–10:30	茶 歇	
		主持人：张重义 教授、张 磊 教授
10:30–10:50	占纪勋 教授（犹他州立大学，美国）	报告：Microbial production of medicinally important plant natural products
10:50–11:10	王 勇 教授（中国科学院植物生理生态研究所）	报告：Pathway-specific Enzymes from the Leaves of Bamboo and Crops Biosynthesize the Antinociceptive Agent Isoorientin
11:10–11:30	高文远 教授（天津大学）	报告：Study on the preliminary process of medicinal plant materials
11:30–11:50	王 炜 教授（湖南中医药大学）	报告：Chemodiversity and Biodiversity of Hunan TCM and Ethnomedicine
		主持人：赵淑娟 教授、邸 鹏 副教授
11:50–12:30	短报告	

08:40–12:30	经典名方会场（地点：桂冠二厅）	
		主持人：刘红宁 教授、吴婉莹 教授
08:40–09:00	叶祖光 教授（中国中医科学院）	报告：中药经典名方研发的背景和要点
09:00–09:20	张保献 教授（中国中医科学院）	报告：经典名方共性问题的困惑与思考
09:20–09:40	张铁军 教授（天津医药研究所）	报告：基于质量属性辩识与表征的中药经典名方制剂一致性研发策略
09:40–10:00	梁鑫淼 教授（中国科学院大连化学物理研究所）	报告：中药经典名方质量分离分析方法
10:00–10:20	杨洪军 教授（中国医学科学院）	报告：经典名方——中医药传承发展的突破口
10:20–10:30	茶　歇	
		主持人：钱忠直 教授、屠鹏飞 教授
10:30–12:30	“经典名方”专家论坛	
	屠鹏飞 教授、叶祖光 教授、冯　怡 教授、余伯阳 教授、张保献 教授、梁鑫淼 教授	

08:40–12:30	中药标准导向的基础研究 会场 II（地点：桂冠三厅）	
		主持人：李　川 教授、Pulok Mukherjee 教授
08:40–09:00	Michael Heinrich 教授（伦敦大学，英国）	报告：Quality control and sustainable sourcing at the time of the blockchain technologies. What are the opportunities?
09:00–09:20	Anna Rita Bilia 教授（佛罗伦萨大学，意大利）	报告：Andrographolide from the ”King of Bitters”: strategies to overcome the blood–brain barrier
09:20–09:40	Krystyna Skalicka–Wozniak 教授（卢布林大学，芬兰）	报告：Liquids in discovery of natural products
09:40–10:00	马翠英 教授（美国药典委员会）	报告：Quality Control of Botanicals Using USP Monographs–HPLC and HPTLC Identify American Ginseng and Asian Ginseng, Distinguish Closely Related Species
10:00–10:20	李松林 教授（江苏省中医药研究院）	报告：Discovering characteristic chemical markers for inspecting sulfur–fumigated herbs and relevant products
10:20–10:30	茶　歇	

		主持人：胡立宏 教授、杨美华 教授
10:30–10:50	Yeong Shik Kim 教授 （国立首尔大学，韩国）	报告：A strategy for identification and structural characterization of sesquiterpenoids from *Tussilago farfara* L.by multiple scan modes of mass spectrometry
10:50–11:10	Xincong Li 教授 （密西西比大学，美国）	报告：Highlighting Fractionation in Natural Products Analysis and Drug Discovery
11:10–11:30	Aihua Liu 教授 （Dyne Co. Ltd. 美国）	报告：Innovation, Science and Research in a Contract Lab
11:30–11:50	秦路平 教授（浙江中医药大学）	报告：Antiosteoporotic investigation of traditional Chinese medicine for tonifying kidney, focusing on integrative mechanism
		主持人：吴　弢 教授、陈军峰 副教授
11:50–12:10	短报告	

2019 年 6 月 29 日（下午）

14:00–16:45	大会报告（地点：桂冠厅）	
		主持人：王峥涛 教授、石上梅 教授
14:00–14:25	吴婉莹 教授 （中科院上海药物所）	报告：《中国药典》2020 年版编制工作最新进展
14:25–14:50	庾石山 教授 （中国医学科学院药物研究所）	报告：题目待定
14:50–15:15	何跃辉 教授（中国科学院分子植物科学卓越创新中心）	报告：Seasonal control of flowering times
15:15–15:30	茶　歇	
		主持人：陈士林 教授、叶　阳 教授
15:30–15:55	宋　越 博士 （安捷伦科技（中国）有限公司）	报告：Agilent HRMS 天然产物数据库助力中药研究
15:55–16:20	Roy Upton 博士 （美国草药典委员会）	报告：Rebuilding the Foundation of herbal medicine in the United States
16:20–16:45	优秀墙报颁奖仪式及大会闭幕式（地点：桂冠厅）	
		主持人：果德安 教授

Conference Agenda

27 June, 2019

12:00-20:00	Conference Registration
16:00-18:00	Preparatory meeting for general conference of the special committee of TCM pharmaceutical analysis of WFCMS

Morning 28 June, 2019

08:30-09:30	**Opening Ceremony (Laurel Hall)**
09:30-12:00	**Plenary speaker & Keynote speaker**
	Chairman : Prof. Pengfei Tu **Prof.** Shuangcheng Ma
09:30-09:55	**Changxiao Liu , Academician** (Tianjin Institute of Pharmaceutical Research) **Topic:** Discovery and Application of TCM Q-Markers
09:55-10:20	**Jianmin Yue, Academician** (Shanghai Institute of Materia Medica, Chinese Academy of Sciences) **Topic:** Chemistry and Bioactivity of Natural Products from Medicinal Plants
10:20-10:45	Tea Break
	Chairman : Prof. Weidong Zhang **Prof.** Ping Li
10:45-11:10	**Prof. Rudolf Bauer** (University of Graz, Austria) **Topic:** HPTLC limit tests and a more holistic concept for quality control of herbal drugs
11:10-11:35	**Prof. Satyajit D. Sarker** (Liverpool John Moores University, England, UK) **Topic:** Current Trends in Phytochemical Analysis
11:35-12:00	**Prof. Xijun Wang** (Heilongjiang University of Chinese Medicine) **Topic:** Q-markers based on Effectiveness of TCM

Afternoon 28 June, 2019

13:40-17:10	Technological Innovation for Analysis of TCM (Venues 1)
	Chairman : Prof. Shen Ji **Prof.** Tulin Lu
13:40-14:00	**Prof. Li Yang** (Shanghai University of Traditional Chinese Medicine) **Topic:** Quality and Safety Evaluation of Pyrrolizidine Alkaloids-Containing Herbal Medicine Using Hybrid Mass Spectrometry
14:00-14:20	**Prof. A.A.Leslie Gunatilaka** (University of Arizona, USA) **Topic:** Discovery of Anticancer Agents from Plants Used in Traditional Medicine
14:20-14:40	**Prof. Ikhlas Khan** (University of Mississippi, USA) **Topic:** Stimulants in Weight loss and Pre-workout supplements
14:40-15:00	**Prof. Giovanni Appendino** (Università degli Studi del Piemonte Orientale, Novara, Italy) **Topic:** Champagne taste for beer price? The plague of adulterated herbal products
15:00-15:10	Tea Break
	Chairman : Prof. Daofeng Chen **Prof.** Shaoqing Cai
15:10-15:30	**Prof. Ilkay Erdogan Orhan** (Gazi University, Turkey) **Topic:** Lead Molecules Inspired by Mother Nature and Folkloric Medicine: Enzymes on Target
15:30-15:50	**Prof. Alexander Shikov** (St. Petersburg Institute of Pharmacy, Russia) **Topic:** Health effects and nutritional use of medicinal plants in Russia
15:50-16:10	**Prof. Ha Minh Hien** (Food and Drug Administration, Vietnam) **Topic:** Extraction, Standardization and Product Development of Bioactives from Resin of *Calophyllum inophyllum* Nut Oil
16:10-16:30	**Prof. Baiping Ma** (Beijing Institute of Radiation Medicine) **Topic:** The use of supercritical fluid chromatography for analysis of glycosides from TCM
	Chairman : Prof. Lijiang Xuan **Prof.** Haitao Lv
16:30-17:10	Short Reports

13:40-17:10	Youth Forum (Venues 2)
	Chairman : Prof. Yu Lin **Prof.** Lianna Sun
13:40-13:55	**Prof. Hua Yang** (China Pharmaceutical University) **Topic:** Synergistic combination discovery from herbal medicines
13:55-14:05	**A/Prof. Xue Qiao** (Peking University) **Topic:** Effective Components and Their Glycosylation in licorice
14:05-14:20	**Prof. Qing Zhao** (Shanghai Chenshan Botany Garden) **Topic:** Understanding the genetic information of a Chinese medicinal plant, *Scutellaria baicalensis.*
14:25-14:40	**A/Prof. Ying Xiao** (Shanghai University of Traditional Chinese Medicine) **Topic:** Precise Regulation of Lignans in *Isatis indigotica*
14:40-14:55	**Prof. Lili Ji** (Shanghai University of Traditional Chinese Medicine) **Topic:** Liver injury induced by pyrrolizidine alkaloids and its detoxification
14:55-15:10	Tea Break
	Chairman : Prof. Zhiqiang Liu **Prof.** Hua Yang
15:10-15:25	**Prof. Yuan Yuan** (China Academy of Chinese Medical Sciences) **Topic:** Archaeological evidence suggests earlier use of Ganoderma in Neolithic China
15:25-15:40	**Prof. Yang Sun** (Nanjing University) **Topic:** Translational Medical Research on New Anti-inflammatory Mechanisms of Andrographolide
15:40-15:55	**A/Prof. Wen Gao** **Topic:** Chemical characteristics-oriented standards establishment of herbal medicines
15:55-16:10	**Prof. Xingwang Li** (Huazhong Agriculture University) **Topic:** High-resolution 3D Genome Architecture and Transcriptional Regulation in Rice
16:10-16:25	**A/Prof. Yuelin Song** (Beijing University of Chinese Medicine) **Topic:** Advanced LC-MS for widely quantitative analysis of herbal medicines
	Chairman : A/Professor. Ying Xiao A/Professor. Jinjun Hou
16:30-17:10	Short Reports

Afternoon 28 June, 2019

13:40-17:10	Standard-oriented basic research of traditional Chinese medicine I (Venues 3)
	Chairman : Prof. Lijiang Xuan **Prof.** Shanyi Qiao
13:40-14:00	**Prof. Yang Ye** (Chinese Academy of Sciences Shanghai Institute of Materia Medica) **Topic:** Bioactive compounds in Tong-Guang-San and its formulation
14:00-14:20	**Prof. Rong Sun** (Shandong University) **Topic:** Quality Control of Toxic TCM Based on Relevant Evaluation of Effectiveness and Toxicity
14:20-14:40	**Prof. Xiansheng Meng** (Liaoning University of Traditional Chinese Medicine) **Topic:** Study on Quality Control of TCM Based on "Quality-Quantity" Integrated Standards
14:40-15:00	**Dr. Zhenqiang Xin** (Shanghai Standard Biotechnology Co., Ltd.) **Topic:** Exploration and Application of TCM-PCDL in the Study of Active Substance from TCM
15:00-15:10	Tea Break
	Chairman : Prof. Xiaobo Li **Prof.** Jun Yin
15:10-15:30	**Prof. Xuemei Qin** (Shanxi University) **Topic:** Comparative study on quality of *Astragali Radix* with metabolomic analysis and pharmacodynamics
15:30-15:50	**Prof. Gang Bai** (Nankai University) **Topic:** Integrated Systems Biology and Chemical Biology Approach to Exploring Mechanisms of Traditional Chinese Medicines
15:50-16:10	**Prof. Yonghui Zhang** (Tongji School of Pharmacy, Huazhong University of Science and Technology) **Topic:** Discovery of active natural products with new skeletons
16:10-16:30	**Prof. Ming Yang** (Jiangxi University of Traditional Chinese Medicine) **Topic:** Functional Characteristics, Quality Traits and Quality Control of Volatile Oil from Traditional Chinese Medicine
16:30-16:50	**Prof. Rui Tan** (Southwest Jiaotong University) **Topic:** A New Method for Screening Active Components from TCM by Stem Cells
16:50-17:10	**Dr. Yanhai Yu** (Agilent Technology (China) Co., Ltd.) **Topic:** The flexible application of HPLC valve for TCM analysis

14:00-17:10	Editorial Committee meeting & 10th Anniversary Forum of Chinese Herbal Medicines (Shanghai Hall)

Evening 28 June, 2019

18:30-21:00	Dinner (Laurel Hall)

Morning 29 June, 2019

08:40-12:30	Chinese Medicinal Resource & Biotechnology (Venues 1)
	Chairman : Prof. Kexuan Tang **Prof.** Zhe Lin
08:40-09:00	**Prof. Jingwen Zhou** (Jiangnan University) **Topic:** Production of complicated flavonoids by microorganisms
09:00-09:20	**Prof. Wei Gao** (Capital Medical University) **Topic:** Synthetic Biological Studies on active compounds in TCM
09:20-09:40	**Prof. Jungui Dai** (Institute of Materia Medica, Chinese Academy of Medical Science) **Topic:** Enzyme promiscuity and structural innovation of natural products and drug discovery
09:40-10:00	**Prof. Mattheos A. G. Koffas** (Rensselaer Polytechnic Institute) **Topic:** The road to animal-free glycosaminoglycan production using metabolic engineering of recombinant microorganisms
10:00-10:20	**Prof. Jianguo Zeng** (Hunan Agricultural University) **Topic:** Systematic Research and Comprehensive Utilization *Macleaya cordata*
10:20-10:30	Tea Break
	Chairman : Prof. Zhongyi Zhang **Prof.** Lei Zhang
10:30-10:50	**Prof. Jixun Zhan** (Utah State University , USA) **Topic:** Microbial production of medicinally important plant natural products
10:50-11:10	**Prof. Yong Wang** (CAS Center for Excellence in Molecular Plant Sciences/Institute of Plant Physiology and Ecology) **Topic:** Pathway-specific Enzymes from the Leaves of Bamboo and Crops Biosynthesize the Antinociceptive Agent Isoorientin
11:10-11:30	**Prof. Wenyuan Gao** (Tianjin University) **Topic:** Study on the preliminary process of medicinal plant materials
11:30-11:50	**Prof. Wei Wang** (Hunan University of Chinese Medicine) **Topic:** Chemodiversity and Biodiversity of Hunan TCM and Ethnomedicine

11:30-11:50	**Prof. Wei Wang** (Hunan University of Chinese Medicine) **Topic:** Chemodiversity and Biodiversity of Hunan TCM and Ethnomedicine
	Chairman : Prof. Shujuan Zhao **Prof.** Peng Di
11:50 -12:30	Short Reports
08:40-12:30	**Standard-oriented basic research of traditional Chinese medicine Ⅱ (Venues 3)**
	Chairman : Prof. Chuan Li **Prof.** Pulok Mukherjee
08:40-09:00	**Prof. Michael Heinrich** (University of London, England, UK) **Topic:** Quality control and sustainable sourcing at the time of the blockchain technologies. What are the opportunities?
09:00-09:20	**Prof. Anna Rita Bilia** (University of Florence, Italy) **Topic:** Andrographolide from the "King of Bitters" : strategies to overcome the blood–brain barrier
09:20-09:40	**Prof. Krystyna Skalicka-Woźniak** (University of Lublin, Poland) **Topic:** Liquids in discovery of natural products
09:40-10:00	**Prof. Cuiying Ma** (U.S. Pharmacopeial Convention) **Topic:** Quality Control of Botanicals Using USP Monographs-HPLC and HPTLC Identify American Ginseng and Asian Ginseng, Distinguish Closely Related Species
10:00-10:20	**Prof. Songlin Li** (Jiangsu Province Academy of Traditional Chinese Medicine) **Topic:** Discovering characteristic chemical markers for inspecting sulfur-fumigated herbs and relevant products
10:20-10:30	Tea Break
	Chairman : Prof. Lihong Hu **Prof.** Meihua Yang
10:30-10:50	**Prof. Yeong Shik Kim** (Seoul National University, Korea) **Topic:** A strategy for identification and structural characterization of sesquiterpenoids from *Tussilago farfara* L.by multiple scan modes of mass spectrometry
11:10-11:30	**Prof. Aihua Liu** (Dyne Co. Ltd., USA) **Topic:** Innovation, Science and Research in a Contract Lab
11:30-11:50	**Prof. Luping Qin** (Zhejiang Chinese Medical University) **Topic:** Antiosteoporotic investigation of traditional Chinese medicine for tonifying kidney, focusing on integrative mechanism

	Chairman : Prof. Hongning Liu **Prof.** Wanyin Wu
08:40-09:00	**Prof. Zuguang Ye** (Institute of Chinese Materia Medica China Academy of Chinese Medical Sciences) **Topic:** The Background and Key Points for the research and development of Classical Prescriptions of TCM
09:00-09:20	**Prof. Baoxian Zhang** (Institute of Chinese Materia Medica China Academy of Chinese Medical Sciences) **Topic:** Confusion and Consideration on the Common Issues of Classical Presentations
09:20-09:40	**Prof. Tiejun Zhang** (Tianjin Institute of Pharmaceutical Research) **Topic:** Research and Development Strategy for Consistency of Classical Presentations Based on Identification and Characterization of Quality Properties
09:40-10:00	**Prof. Xinmiao Liang** (Dalian Institute of Chemical Physics, Chinese Academy of Sciences) **Topic:** Separation and Analysis of Classical Prescriptions of TCM
10:00-10:20	**Prof. Hongjun Yang** (China Academy of Chinese Medical Sciences) **Topic:** Classical Prescriptions: Breakthrough for the Inheritance and Development of TCM
10:20-10:30	Tea Break
	Chairman : Prof. Zhongzhi Qian **Prof.** Pengfei Tu
10:30-12:30	Classic Prescription Forum

Afternoon 29 June, 2019

14:00-14:25	**Plenary speaker & Keynote speaker (Laurel Hall)**
	Chairman : Prof. Zhengtao Wang **Prof.** Shangmei Shi
14:00-14:25	**Prof. Wanying Wu** (Shanghai Institute of Materia Medica, Chinese Academy of Sciences) **Topic:** Progress of Compiling for Chinese Pharmacopoeia (2020 Edition)
14:25-14:50	**Prof. Shishan Yu** (Institue of Materia Medica, Chinese Academy of Medical Sciences) **Topic:** To be determined
14:50-15:15	**Prof. Yuehui He** (CAS Center for Excellence in Molecular Plant Sciences) **Topic:** Seasonal control of flowering times
15:15-15:30	Tea Break
	Chairman : Prof. Shilin Chen **Prof.** Yang Ye
15:30-15:55	**Prof. Yue Song**(Agilent Technology (China) Co., Ltd.) **Topic:** The Natural Products Database—Agilent HRMS powered the researches on TCM
15:55-16:20	**Dr. Roy Upton** (American Herbal Pharmacopoeia, USA) **Topic:** Rebuilding the Foundation of herbal medicine in the United States
16:20-16:45	**Excellent Poster Awarding Ceremony & Closing Ceremony**
	Chairman : Prof. Dean Guo

短报告 / Short Reports

Afternoon 28 June, 2019

Technological Innovation for Analysis of TCM

16:30–17:10	周婷婷 Tingting Zhou	海军军医大学 Second Military Medical University	New integrated technology for separation and preparation of active ingredients of TCM
	赵一懿 Yiyi Zhao	北京市药品检验所 Beijing Institute for Drug Control	2DLC–PDA/ELSD–QTOF–MS coupled with chemometric analysis to quantify and evaluate *Ginkgo biloba* leaves from different origins
	周姗姗 Shanshan Zhou	江苏省中医药研究院 Jiangsu Province Academy of Traditional Chinese Medicine	Integrating chemomics, metabolomics and gut microbiota genomics to investigate correlation between quality and efficacy of herbal medicine: Ginseng, a pilot study
	张建青 Jianqing Zhang	中科院上海药物所 Shanghai Institute of Materia Medica, Chinese Academy of Sciences	“Force iteration molecular designing–precursor ion list” (FIMD–PIL) strategy for systematic characterization of A. orientale and A. plantago–aquatica.
	毕启瑞 Qirui Zhao	中国药科大学 China Pharmaceutical University	A new multiple reaction monitoring strategy (PPCP–MRM) based on predicted precursor ions and characteristic fragment ions for global profiling Rubiaceae–Type cyclopeptides in Rubia podantha
	王洪达 Hongda Wang	天津中医药大学 Tianjing University of Chinese Medicine	Characterization and comparison of the metabolomes among three parts (root, stem leaf, and flower bud) of Panax quinquefolius by UHPLC/Q–Orbitrap–MS–based improved data–dependent MS^2 acquisition and metabolomics
	贾　丹 Dan Jia	海军军医大学 Second Military Medical University	Cardioprotective mechanism study of salvianic acid A sodium in rats with myocardial infarction using a proteome microarray approach combined with multi–omics analysis
	肖　尧 Rao Xiao	安捷伦科技（中国）有限公司 Agilent Technology (China) Co., Ltd.	Development and optimization of Comprehensive 2D–LC method for Ganoderic acid in *Ganoderma lucidum*

Afternoon 28 June, 2019

Youth Forum

16:30–17:10	贾艳喆 Yanzhe Jia	湖南中医药大学 Hunan University of Chinese Medicine	Phytochemical Investigation on the Fruits of Tujia Ethnomedicine “heilaohu”
	杨兴鑫 Xingxin Yang	云南中医药大学 Yunnan University of Chinese Medicine	Integrated Metabolomic Profiling of the Antilipidemic Effects of *Polygonatum kingianum* Extract on Dyslipidemia in Rats
	许盈芃 Yingpeng Xu	上海中医药大学 Shanghai University of Traditional Chinese Medicine	Synthetic biology-based exploration for alternateive resources of traditional Chinese materials
	瞿　城 Cheng Qu	中国药科大学 China Pharmaceutical University	Cellular lipidomics-based protective exploration of Safflower Injection for ischemic stroke
	汪志华 Zhihua Wang	南开大学 Nankai University	Integration of molecular network virtual screening with affinity mass spectrometry screening for the efficient discovery of ligands from natural herbs
	季宏建 Jianhong Ji	盐城市第三人民医院 Yancheng Third People’s Hospital	*Ginkgol Biloba* Extract as an adjunctive treatment for ischemic stroke: A systematic review and meta-analysis of randomized clinical trials with trial sequential analysis of recurrence rate
	王娜妮 Nina Wang	浙江省立同德医院 Zhejiang Tongde Hospital	Rapid screening anti-osteoporosis ingredients from Chinese medicine prescriptions by osteoblast membrane chromatography/ high performance liquid chromatography-time of flight mass spectrometry
	魏文龙 Wenlong Wei	中科院上海药物所 Shanghai Institute of Materia Medica, Chinese Academy of Sciences	Extension-mass defect filter combined with multidimensional data acquiring and metabolic network prediction for comprehensive characterization of metabolic profiles of bufadienolides in rats plasma

Morning 29 June, 2019

Chinese Medicinal Resource & Biotechnology

11:50–12:30	谭何新 Hexin Tan	海军军医大学 Second Military Medical University	Transcriptome analysis reveals novel enzymes for apo-carotenoid biosynthesis in saffron and enables heterologous production of crocetin in yeast
	吕宗友 Zongyou Lv	上海长征医院 Shanghai Changzheng Hospital	AaMYB2 negatively regulates *Artemisia annua* trichome initiation by interacting with the HD-ZIP transcription factor AaWOX1
	徐志超 Zhichao Xu	中药资源教育部工程研究中心 中国医学科学院药用植物研究所 The Institute of Medicinal Plant Development	比较基因组揭示黄芩属植物黄酮化合物生物合成进化机制 Comparative genomics reveals the evolutionary mechanism of flavonoid biosynthesis in *Scutellaria* plants
	张芳源 Fangyuan Zhang	西南大学 Southwest University	Molecular regulation of artemisinin biosynthesis under cold condition
	李　卿 Qing Li	上海长征医院 Shanghai Changzheng Hospital	Engineering the chloroplast genome of Datura innoxia mill. for hyperproduction of scopolamine
	刘京京 Jingjing Liu	浙江农林大学 Zhejiang Agricultural and Forestry University	Water soluble non-starch polysaccharide of *Dendrobium catenatum* cultivated in imitation wild and greenhouse
	郝小龙 Xiaolong Hao	浙江中医药大学 Zhejiang University of Traditional Chinese Medicine	Light-induced artemisinin biosynthesis is regulated by the bZIP transcription factor AaHY5 in *Artemisia annua*
	王如锋 Rufeng Wang	上海中医药大学 Shanghai University of Traditional Chinese Medicine	Structural insight into the elucidation on enhanced catalytic activity of glycosidase KfGH01 for the production of vina-ginsenoside R7

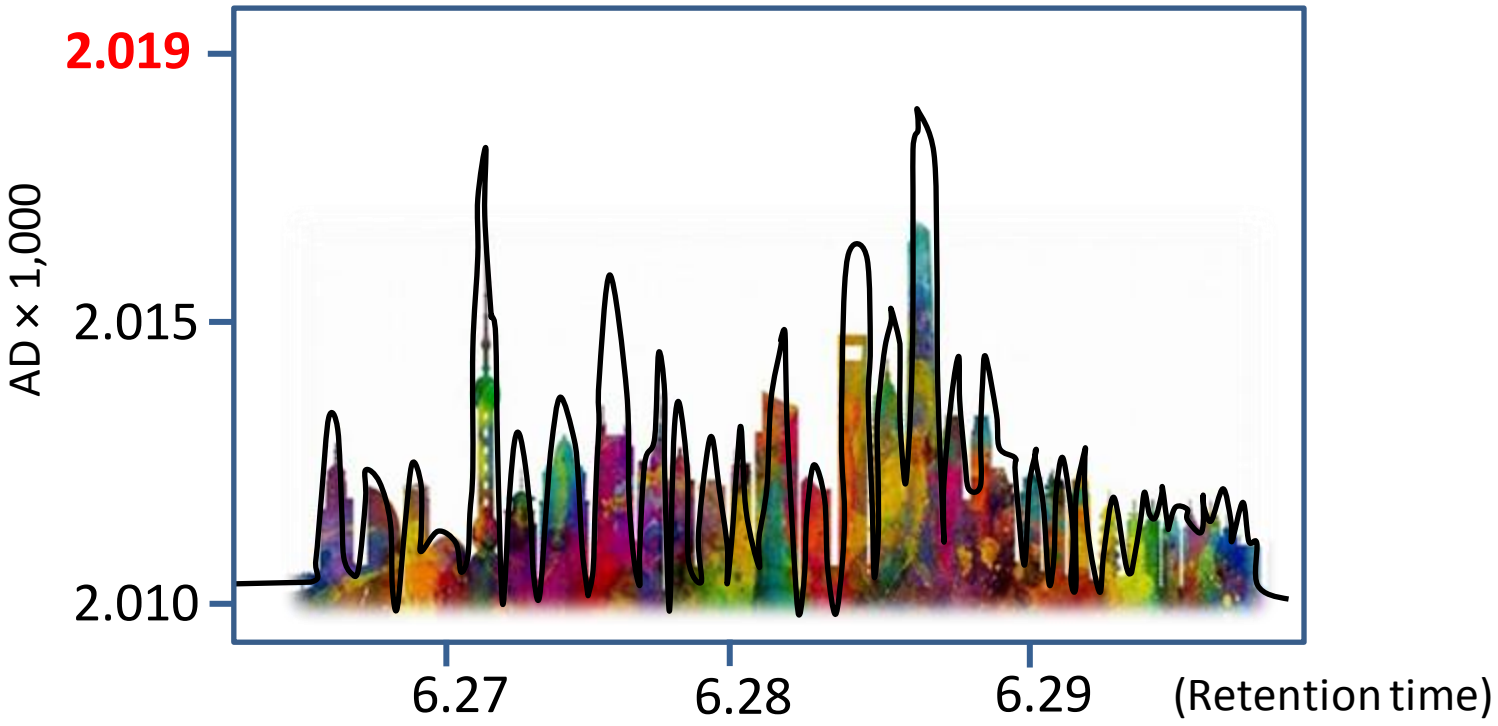
Morning 29 June, 2019

Standard-oriented basic research of traditional Chinese medicine II

11:50–12:30	邱　实 Shi Qiu	上海中医药大学 Shanghai University of Traditional Chinese Medicine	"Commercial-homophyletic" comparison-induced robust biomarkers discovery for the authentication of herbal medicines, *Panax ginseng* as a case study.
	赖长江生 Lai Chang jiang hseng	中国中医科学院中药资源中心 China Academy of Chinese Medical Sciences	Insight into the new challenge for quality control of *Ganoderma lucidum*
	范妙璇 Miaoxuan Fan	北京市药品检验所 Beijing Institute for Drug Control	Study on the effects Xiaojin preparation of Co-60 irradiation on endogenous components and exogenous pollutants of microorganisms and fungal toxins
	王玉丹 Yudan Wang	中国医学科学院 Chinese Academy of Medical Science	Occurrence and analysis of mycotoxins in domestic Chinese herbal medicines
	张光华 Guanghua Wang	药典会－沃特世联合实验室 Pharmacopoeia Society-Waters Joint Laboratory	Mmultiple components analysis of *Salvia Miltiorrhiza* decoction pieces by UPCC & -UPLC
	刘浩龙 Haolong Liu	北京市药品检验所 Beijing Institute for Drug Control	Simultaneous determination of prostaglandin and hormones in excreta of *Trogopterus xanthipes*
	陈啸飞 Xiaofei Chen	海军军医大学 Second Military Medical University	Preparation and application of novel transmembrane protein-liposome biological chromatography
	郑　伟 Wei Zheng	北京放射医学研究所 Institute of Radiation Medicine, Chinese Academy of Medical Sciences & Peking Union Medical College	Rapid characterization of chemical components by UHPLC-QTOFMS with full-composition database of traditional Chinese medicines

报告人信息

Speakers Information



大会报告

Plenary speaker & Keynote speaker

（桂冠厅/Laurel Hall）

2019-06-28，09:30-12:15

报告/Topic

中药质量标志物的发现与应用
Discovery and Application of TCM Q-Markers

刘昌孝，男，湖南人，1965 年毕业于北京医学院药学系（现北京大学医学部药学院）。2003 年当选中国工程院院士，现任天津药物研究院研究员，博士导师。天津药物研究院名誉院长和学术委员会主任，释药技术与药代动力学国家重点实验室主任。担任国家食品药品监督管理总局仿制药专家委员会副主任委员、国家科技奖审评专家、国家千人计划人才审评专家、中国药典委员会第 10 届执行委员、国际药代研究会（ISSX）中国办事处主任、中国药学会和中国药理学会常务理事、天津市药学会理事长、天津市药理学会理事长和天津市学会研究会理事长，担任 10 多家中外科技期刊的主编、副主编或编委。曾任国家科技部新药专家委员会委员（1987-2007）、国家 GLP 专家委员会委员（1993-2003）、国家新药审评专家委员会委员（1987-2007 等社会职务。曾获得湖南省先进工作者（1978 年）、天津市劳动模范（2000 年）、紫金花医学成就奖（2000 年）、全国劳动模范（2005 年）、北京大学杰出校友（2012 年）、国际药物代谢研究会特别贡献奖（2013 年）、全国优秀科技工作者（2014 年）、天津滨海突出成就奖（2016 年）等荣誉。我国药代动力学的学科开拓者和学科带头人之一。1968 年建立了国内第一个药代动力学实验室，1975 年在国内第一次将药代动力学研究用于新药评价，1980 年出版了国内第一本药代动力学专著，1995 年创建国内第一个部级药代动力学重点实验室，2003 年创建第一个药代动力学省部共建国家重点实验室，2010 年创建第一个药代动力学国家重点实验室。在国内首次提出中药代谢组学研究（2003 年）和首次提出中药质量标志物新概念（2015 年）。致力于新药和药物代谢动力学和药理学研究 50 多年。承担国家省部级重大科技项目、国家自然科学基金项目等 50 余项，承担 10 多项获得新药证书项目研究开发。获得国家部省级科技成果奖 50 余项和国际奖 5 项，发表中英文科研论文 460 多篇（SCI 论文 200 多篇），出版中英文专著 18 本。

报告/Topic

药用植物中天然产物的化学及生物活性研究

Chemistry and Bioactivity of Natural Products from Medicinal Plants

Dr. Jian-Min Yue, an eminent organic chemist and member of the Chinese Academy of Sciences, is currently Professor of Shanghai Institute of Materia Medica (SIMM), and Director of the Department of Natural Products, and Deputy Director of the Chinese National Compound Library.

He received his B.S. degree in 1984 from Lanzhou University where he also received his MS and Ph.D. in 1987 and 1990, respectively. He was a post-doctor in Kunming Institute of Botany (KIB), Chinese Academy of Sciences (CAS), and a post-doctor in School of Chemistry, University of Bristol, UK. He was an associate professor in KIB from 1994 to 1996. He joined the staff of Unilever Research SIOC as senior scientist, project leader from 1996-1999. He was then moved to Shanghai Institute of Materia Medica (SIMM), CAS, where he remains up to now as a professor. He was a visiting professor at Department of Chemistry, The University of Queensland, Australia (2001), and Novartis Pharma AG, Switzerland (2002).

摘要/Abstract

Chemical studies on a large number of Chinese medicinal plants (including TCM) have led to the identification of a big array of structurally interesting and/or bioactive components, e.g. anticancer, anti-HIV and immunosuppressive agents. Some compounds have been selected as lead structures for our drug development program, and over one hundred of modified chemical entities with significantly improved activities were also obtained; biological evaluation showed that some of the compounds exhibited remarkable anticancer (both cytotoxic and antiangiogenesis), immunosuppressive and anti-HIV activities; several groups of bioactive compounds showed very clear structure activity relationships; A few of structurally interesting and biologically important compounds have been synthesized. Our studies have provided good scientific background for drug development and understanding of the function and toxicity of the involved medicinal plants.

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报告/Topic

HPTLC limit tests and a more holistic concept for quality control of herbal drugs

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Prof. Dr. h.c. Rudolf Bauer is Full Professor of pharmacognosy and Head of the Institute of Pharmaceutical Sciences at University of Graz, Austria, amd since 2007 director of the TCM Research Center Graz (Med. Plant Research). He is expert in natural product chemistry, analysis, and activity-guided isolation of plant constituents with a major focus on traditional Chinese medicine since almost 30 years. He has been president of the International Society of Ethnopharmacology from 2015-2017, of the Society for Medicinal Plant and Natural Product Research (GA) 2002-2007, and founding president of GP-TCM Research Association. He has published 370 research papers with more than 6000 citations, and has edited several books. He is Associate Editor-in-Chief of the World Journal of Traditional Chinese Medicine and of the Chinese Journal of Natural Medicines, and chairman of the expert group on Chinese medicinal plants of the European Pharmacopoeia Commission. He has received several scientific awards. Only recently, he was awarded with the Honorary Doctorate of the Faculty of Philosophy of University of Helsinki.

摘要/Abstract

Pharmaceutical quality is the basis of efficacy and safety of synthetic as well as of herbal medicinal products (HMPs). Currently, quality control (QC) of HMPs is mostly based on single marker compounds, and determination is often accomplished with highly sophisticated methods. Because of the questionable relevance of low dosed single markers and the comparatively high costs of analysis, which are challenging the market in Europe, an alternative concept using HPTLC limit tests has been suggested and evaluated by the European Pharmacopoeia. Pilot studies have been performed for Corydalis rhizoma (延胡索), Fritillariae thunbergii bulbus (折贝母) and Leonuri herba (益母草). The HPTLC methods for the semi-quantitative test on the isoquinoline alkaloids tetrahydropalmatine and corydaline in Corydalis rhizome and that for the semi-quantitative determination of the cevane-type alkaloids peimine and peiminine in Fritillariae thunbergii bulbus have been successfully established. Leonuri herba is probably not a good candidate for this alternative approach because an assay for total flavonoids has to be replaced. Since herbal extracts are complex mixtures of many types of compounds, which may all contribute to activity of the herbal preparation, a more holistic approach for the QC of HMPs is needed for the future, which also considers antagonistic and synergistic effects. Fingerprint analyses and a metabolomics based approach should be evaluated. Chemometrics and multivariate data analysis allow the characterization of extracts in a targeted or untargeted way, depending on the knowledge on the therapeutically relevant compounds.

报告/Topic

Current Trends in Phytochemical Analysis

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Prof. Satyajit D Sarker, the Editor-in-Chief of Phytochemical Analysis, and the President of the Phytochemical Society of Europe, is the Director of School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University. He is a Pharmacy Professor and the Founding Head of the Centre for Natural Products Discovery, launched in January 2019. He is a Visiting Scientist (Guest Professor), recently awarded by the Chinese Academy of Sciences, and currently a Visiting Professor at the Taylor's University Malaysia.

He obtained BPharm and MPharm degrees from Dhaka University, and completed his PhD in Phytochemistry from Strathclyde University, Glasgow, UK. His research focuses on anticancer, anti-inflammatory, antimalarial, antimicrobial, chemopreventive and wound-healing properties of phytochemicals. He is the author of over 540 publications, and one of the most cited authors with over 13,400 citations by Goggle Scholar, an h-index of 52 and i-10 index of 322.

Prof Sarker is in the Editorial Board of 36 international journals including Biochemical Systematics and Ecology, Current Medicinal Chemistry, Current Trends in Medicinal Chemistry, DARU, Molecules, Pharmaceutical Sciences, Pharmacognosy Magazine and Pharmacognosy Research, and a reviewer for over 80 journals. He co-authored the popular textbook, Chemistry for Pharmacy Students (Wiley & Sons) in 2007, which was subsequently translated in Japanese, Greek and Portuguese languages. The second edition of this book is due to be published in 2019. He also is the co-author of the book, Steorid Dimers (Wiley & Sons), published in 2012.

He co-edited both the 2nd and the 3rd editons of Natural Products Isolation (Humana Press-Springer-Verlag), published in 2005 and 2012, respectively. Computational Phytochemistry (Elsevier; published in May 2018) is the latest contribution from Prof Sarker and Dr Lutfun Nahar. His scientific profile has been in the every edition of the Marquis Who's Who in the World since 2010.

摘要/Abstract

Soon after the introduction of various traditional medicinal systems, *e.g.*, Ayurveda and Chinese Traditional Medicine (TCM), the quest for determining the chemical entities that contribute to the medicinal properties and/or toxicities of medicinal plants began. Morphine, a well-known opioid painkiller, was the first medicinal phytochemical discovered from *Papaver somniferum* by a simple acid-based extraction method, about a couple of centuries ago. Since then, the search for bioactive compounds has continued its journey through application of various phytochemical analytical tools, which have evolved from traditional solvent-extraction/crystallization to *in silico* screening. During this journey, a distinct branch of research, called 'Phytochemical Analysis', has emerged, and it simply incorporates the analysis of plants and plant-derived compounds.

Over the years, several chromatographic separation techniques have been introduced for isolation and analysis of phytochemicals. Similarly, modern spectroscopic techniques, *e.g.*, NMR and MS, have been applied to analyze the structures of phytochemicals, and various *in vitro* assays have been established to assess bioactivity of phyto-products. However, over the last two decades, with the outstanding developments in computational arena, phytochemical research has embraced and applied various computational aids and mathematical models, leading to the introduction of 'Computational Phytochemistry', where computational tools, techniques and methods, artificial intelligence and mathematical modelling are incorporated to address various issues in phytochemical research. A significant shift from traditional ways of resolving phytochemical problems to computer-based modern approaches has been observed recently. This talk, based on the authors' own work, as well as various published literature on phytochemical analytical approaches and methods, will present an overview of the evolution of phytochemical analysis, and look into the current trend, especially the utilization of *in silico* methods

报告/Topic

基于中药有效性的质量标志物研究
Q-markers based on Effectiveness of TCM

王喜军，男，1961 年 12 月生人。1998 年获日本北海道药科大学药学博士，现为中药学教授，博士生导师，黑龙江中医药大学副校长。兼任国家药典委员会委员，世界中医药学会联合会中药鉴定分会主席;世界中医药联合会中药药理分会副主席；中华中医药学会中药鉴定分会副主任委员，国家药学专业教学指导委员会副主任。 主要从事有效性及药效物质基础研究，专注于中药血清药物化学及中医方证代谢组学研究。90 年代初，提出并建立了中药血清药物化学的理论及研究方法，2000 年代初期将中药血清药物化学与代谢组学技术整合，建立了中医方证代谢组学（Chinmedomics)的研究策略。主持完成的“中药血清药物化学研究方法的建立与实施”获 2002 年度国家科技进步二等奖、“人工种植药用植物病害的无公害防治技术”获 2009 年国家技术发明二等奖；并以第一完成人身份获省部级科学技术一等奖 6 项。发表学术论文 300 余篇，SCI 论文 170 余篇。

Prof. WANG Xi-Jun, male, born in December 1961, awarded PhD in the field of pharmaceutical science in Hokkaido College of Pharmacy, Japan, is professor of traditional Chinese medicines (TCM), vice president of Heilongjiang University of Chinese Medicine. His research focus on efficacy of TCMs and related effective constituents, especially on the studies of Serum Pharmacochemistry of TCM and Chinmedomics. He presided over the completion of the ‘Establishment and Application of Serum pharmacochemistry of TCM’ won the second prize of National Science and Technology Progress Award at 2002, ‘Prevention and Control Technology of Artificial Cultivation of Medicinal Plants’ won the second prize of National Technology Invention at 2009。 He published more than 300 papers, including 170 SCI papers. etc.

中药分析新技术、新方法会场

Technological Innovation for Analysis of TCM

（桂冠一厅/Laurel Hall I）

2019-06-28，13:40-17:10

报告/Topic

Quality and Safety Evaluation of Pyrrolizidine Alkaloids-containing Herbal Medicine Using Hybrid Mass Spectrometry

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YANG Li, Ph.D, Professor, acquired her Ph.D degree of Pharmacognosy from China Pharmaceutical University in 2006. As a visiting scholar, she worked in University of Toyama, Japan and City of Hope National Medical Center, USA, respectively. She was promoted to the full professor of Shanghai University of Traditional Chinese Medicine with a special merit. Prof. Yang dedicated to preserving knowledge on bioactive components and quality control of TCM. She has done a lot of work in quality evaluation and standardization of TCM products, especially in analysis and safety evaluation of toxin-containing medicinal herbs. She has established six TCM quality standards, such as *Dendrobii Caulis*, *Plantaginis Semen*, *Senecionis Scandentis* Hebra etc., which have been accepted and published in Chinese Pharmacopoeia. She has undertaken more than ten projects of Natural Science Foundations of China, National S&T Major Special Projects and so on. Her research has been rewarded with 2nd Prizes for China National Science and Technology Advancement. She was also rewarded with three 1st prizes of Natural Science Research of Ministry of Education. She received several talent programs including the National Natural Science Foundation of China outstanding youth funding, the Ministry of Education New Century Excellent Talents and Shanghai Shu-Guang scholar et al. She has published more than 150 papers including 98 papers in international journals, and 15 patents have been authorized.

摘要/Abstract

The quality and toxicity assessment of herbal medicines is important for the human health and appropriate utilization of these medicines. Pyrrolizidine alkaloids (PAs) are among the most hepatotoxic natural products, which produce irreversible injury to human beings via consumption of herbal medicine, tea preparations or honey, and over 8000 PA-induced liver injury cases have been reported worldwide so far. PAs are widely distributed in more than 6000 flowering plants, especially those from the family of *Asteraceae*, *Boraginaceae*, and *Fabaceae*. They are also reported to occur in many medicinal herbs in Europe and China, especially those from *Senecio* or *Gynura* genus (Asteraceae family), such as *Senecio vulgaris* L., *S. scandens* Buch.-Ham and *Gynura japonica*. Traditional techniques for analysis of toxic pyrrolizidine alkaloids-containing herbal medicine including HPLC, GC-MS require sophisticated operations and relatively long time. In this study, a study of quality and safety evaluation of these PAs-containing herbal medicines has been performed. First, a target profiling approach was established using UPLC-ESI Q/TOF mass spectrometry by combining the characteristic fingerprint analysis of herbal chemicals with potential toxicity and the target profiling analysis of biomarkers responsible for the toxicity. Then, to achieve rapid screening and determination of PAs in different matrices, we develop a novel strategy via direct analysis in real time mass spectrometry (DART-MS). The concentrations of PAs in samples were directly determined by DART ion source coupled with LTQ-MS. Moreover, novel purification and analysis methods including mass-directed auto purification or precursor ion scan-based mass spectroscopy techniques have been used for preparation of large amounts of PAs reference substances and then applied in the analysis of PAs-containing herbs. On the basis of the above studies, a PAs-containing herbs safety standard has been established and accepted in Chinese Pharmacopoeia (*Senecionis Scandentis* Hebra). All the results showed that hybrid mass spectrometry could have great potential for more applications in pharmaceutical analysis and quality control of Traditional Chinese Medicine.

报告/Topic

Discovery of Anticancer Agents from Plants Used in Traditional Medicine

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A. A. Leslie Gunatilaka is Director of Southwest Center for Natural Products Research, and Professor of Natural Resources and the Environment at the University of Arizona (UA), USA. He earned his B.S. in Chemistry from University of Sri Lanka and his Ph.D. in Organic Chemistry from Imperial College, University of London, under the guidance of the Nobel Laureate, Professor Sir Derek Barton. He is a Fellow of the Academy of Sciences for the Developing World (TWAS), Italy, and the National Academy of Sciences, Sri Lanka. He is a recipient of the Sri Lankan Presidents' gold medal for "creating a center of excellence in natural products research at the University of Peradeniya, Sri Lanka", CaPCURE award for "dedication to ending prostate cancer as a risk for all men and their families", Research Faculty of the Year Award of the UA College of Agriculture and Life Sciences, the UA Asian American Faculty, Staff and Alumni Association Outstanding Faculty Award, and UA Leading Edge Researcher Award for Innovative Research. He has published over 300 peer-reviewed papers with over 8,500 citations.

摘要/Abstract

Traditional medicine in many parts of the world utilized plants to treat a variety of diseases including cancer. Anticancer activities of these plants are associated with their constituent natural products (NPs) which represent a vast structural diversity not matched by any other source of small-molecules, and they remain the best reservoir and inspiration for drug discovery. According to the World Health Organization, cancer is the second leading cause of death globally and was responsible for ca. 9.6 million deaths in 2018, 70% of which occurred in low- and middle-income countries. Search for clinically-effective anticancer drugs is therefore considered a high research priority.

In our continuing efforts to discover anticancer agents, we have subjected 18,000 and 50,000-member libraries of NP-derived samples and synthetic molecules to a variety of high-throughput assays. These studies led to the identification of an extract of *Physalis crassifolia* (Nightshade Ground Cherry) and withanolide E, a constituent of *Physalis peruviana* (Cape Gooseberry), as the most promising leads. Bioactivity-guided fractionation of *Physalis crassifolia* extract provided its active constituent, physachenolide C, a 17 -hydroxywithanolide (17-BHW) structurally related to withanolide E. It is noteworthy that some *Physalis* species are employed in traditional medicine in Asia and South America to treat cancer. This presentation will focus on discovery of these 17-BHWs, their efficient production by the application of an innovative aeroponic technique for cultivation of *Physalis* species, and promising anticancer activities of 17-BHWs on a variety of cancers leading to a potential NP-based anticancer agent suitable for development as a clinical candidate.

报告/Topic

Stimulants in Weight loss and Pre-workout supplements

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Dr. Ihklas Khan is currently Director of the National Center for Natural Products Research University of Mississippi. Additionally, he is the Director for Sino-US TCM Research Center; Director, Center for Research of Indian Systems of Medicine; visiting Professor at Hunan University of Chinese Medicine, China; an Adjunct Professor, Chinese University of Hong Kong; visiting professor for King Saud University, Saudi Arabia since 2010; Soochow University, since 2010 and Heilongjiang University of Chinese Medicine, The People's Republic of China since 2010. His primary research interests include analytical fingerprinting for standardization of herbal products, and bio-analytical approaches to improvement of product quality and safety. He has made great strides in natural product research, which has gained him national and international recognition through numerous awards such as: "University of Mississippi's Distinguished Professor, 2018"; "The Wiley Award, Association of Official Agricultural Chemists International, 2018"; "Qihuang International Prize of China Association of Chinese Medicine, 2017"; "Outstanding Contributions in TCM Analysis & Quality Standards, 2017"; "Mark Blumenthal Herbal Community Builder Award, 2017"; and many more. Ikhlas has authored or co-authored over 700 original research articles, publications, or reviews. He has been invited to speaker at numerous national and international events

摘要/Abstract

Nutrition or dietary supplements can be found in any grocery store, pharmacy, or nutrition specialty store. Americans spend nearly 30 billion dollars on supplements and have a choice of over 85,000 products. Pre-workout supplement first introduced in 1982 gained popularity among those looking to increase stamina in the gym or on the field. The ingredient in the product responsible for this energy boosting effect is *Ephedra sinica*, also known as má huáng. It has been used for over 5,000 years to alleviate the symptoms of asthma and cough. It contains ephedrine and pseudoephedrine, which are similar structural analogs of methamphetamine. *Ephedra sinica* increases the alertness but also increases blood pressure, and heart rate thus causing adverse cardiac events. Therefore in 2004, the FDA banned all ephedra-containing supplements.

A modern dietary supplement that illustrates the product made by USPlabs called Jack3d, containing 1, 3-Dimethylamylamine (DMAA). DMAA is similar to ephedra since they both are sympathomimetics. DMAA was first manufactured and introduced as a nasal decongestant in the 1940's; however after reports of headaches and tremors in users of the medication, it was removed from the shelves in the 1970s. DMAA regained attention in 2006 when an organic chemist for USPlabs, synthesized in the laboratory for use in Jack3d. The only study since to find DMAA in geranium plants found only ng in a single geranium plant. That means, in order to produce a single serving of Jack3d, one would need 50,000kg of geranium. It was clear that DMAA was synthesized. The use of DMAA-containing dietary supplements is widespread in the military. Various literature using slightly different methodologies have yielded inconsistent and often contradictory evidence as to whether or not DMAA exists naturally in geranium oil. Despite the banning of ephedra and DMAA containing products, there continues to be pre-workout supplements on the market that contain dangerous sympathomimetic like compounds. DMHA, commonly known as octodrine (Dimethylhexylamine or 2-aminoisoheptane) is a psychoactive central nervous system stimulant

with a similar molecular structure to a number of illegal stimulants including AMP Citrate (DMBA), Ephedrine, and the ever popular DMAA. Both DMAA and DMHA are extremely potent stimulants which are often found in Pre-workout products.

Recently our group developed a new screening and quantitative method for stimulants in cocktails for 111 compounds based on liquid chromatography (LC) with electrospray ionization quadrupole time-of-flight mass spectrometry (ESI-QToF). Many of these supplements analyzed were found to contain stimulants, which were not claimed on the labels. Two-thirds of the supplements contained compounds that were not listed on the label. These include several phenethylamines (PEA) such as demelverine (*N*-methyldiphenethylamine), hordenine, *N*, *N*-dimethyl-phenethylamine, synephrine, *N*-methyl-β-phenethylamine, DMAA, DMHA, and methylsynephrine.

报告/Topic

Champagne taste for beer price? The plague of adulterated herbal products

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Giovanni Appendino is Professor of Organic Chemistry at Department of Pharmaceutical Sciences of the Università del PIemonte Orientale, Novara, Italy. His research activity takes inspiration from plant natural products to address problems in various realms of biomedical investigation, from pharmacology and nutrition (new drug leads and dietary ingredients) to organic/medicinal chemistry (new synthetic methodologies and optimization of natural product drug leads) and cell biology (novel mechanisms of activity). Author of over 350 peer-reviewed articles and 15 book chapters on the chemistry and bioactivity of plant natural products. Editor-in-Chief of the journal *Fitoterapia* and member of the Advisory Board of the some major journals in the field (*Natural Products Reports, Acta Pharmaceutica Sinica B*). Member of the Italian Academic of Sciences *(Accademia dei XL*) and recipient of the Quilico Medal from the Italian Chemical Society (2009) and the Bruker Prize from the Phytochemical Societies of Europe (2015).

摘要/Abstract

Nihil novum sub sole (nothing new under the sun)! Adulteration of expensive goods has always existed, and what is new is only its growing sophistication. Adulteration can sometimes be very smart, and difficult to detect using the molecular signature of a set of major marker compounds. Sometimes the need exists to go sub-molecularly at the level of isotopic composition and/or to focus on the global profile of the minor, rather than major, constituents. Metaphorically, one needs to recognize a forest not from the botany of its trees, but from the density of their wood or from the grass growing in their shadow. Examples of smart adulterations will be discussed, presenting cases where marker compounds from a cheaper source are added to a high value extract (bilberry, saffron, ginkgo) or when the whole profile of active ingredients is created ex-novo (Serenoa).[1,2] Cases of adulteration of natural products available by isolation with their cheaper synthetic versions (curcumin, resveratrol, cannabidiol) will also be presented, highlighting the growing relevance of isotopic analysis to authenticate naturally-originated materials. In this context, a pre-eminent role is played by the natural incorporation of atmospherically-generated ^{14}C in living organisms and by natural differences in carbon organication related to the photosynthetic mechanism of plants (C3 vs C4 plants). The geographic latitude of growth and climatic conditions underlie the relevance of measurements based on the ratio between oxygen isotopes and the deuterium-protium ratio. Overall, the isotopic fingerprint makes sometimes possible also to trace the origin of adulterants, and these concepts will be discussed in relationship to the adulteration of Serenoa extracts.[2]

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报告/Topic

Lead Molecules Inspired by Mother Nature and Folkloric Medicine: Enzymes on Target

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Prof. Ilkay Erdogan Orhan is currently Dean of Faculty of Pharmacy, Gazi Univ since 2016. She holds a Pharmacist degree (1993) from Gazi Univ (Ankara, Turkey), M.Sc. degree in Pharmacognosy at the same faculty in 1996 with young scientist scholarship. Then, she was awarded her second M.Sc. degree in Marine Natural Product Chemistry in 1998 at the Univ of the Ryukyus (Japan). She earned Ph.D. degree in Pharmacognosy at Gazi University (2002) and was visiting scientist at Univ of Winnipeg (Canada) in 2003 under NATO fellowship. She was promoted to Assoc.Prof. in 2004 and full Prof. in 2009. Dr. Orhan Dr. was appointed as "Dean" of Faculty of Pharmacy at Eastern Mediterranean University in the Northern Cyprus (2011-2014). She is member of TCM Experts Group in European Pharmacopeia, member of the International Scientific Board of Austrian Drug Screening Institute (ADSI) and member of pharmacy committee of Serra Hunter Program (Spain). She has 234 scientific papers in reputed journals and 2 books with over 4000 citations and owns 2 patents. Her h index is 33 (Web of Science) and 39 (Scopus). She received several awards such as ***Young Woman Scientist Award in Asia continent***, ***Science Award in Biology*** by COMSTECH (2010), ***Young Woman Scientist Award*** by L'Oreal & Turkish Academy of Sciences (2011), and ***Honor Award by Gazi University*** (2011), ***Innovation Award for Women in Turkey*** (2015), ***Science Award*** by Turkish Association of Pharmacists (2016), ***Golden Mortar Science Award*** (2017), ***Silver Medal for Patent in International Invention Fair*** (2017) as well as ***Best Academic Invention Medal*** by International Federation of Invention Associations (IFIA) (2018)

摘要/Abstract

Discovery of new drugs are becoming more tedious and costlier. In fact, drugs have so far discovered generally by ascertaining the active substance(s) from traditional remedies or through unforeseen discoveries as with penicillin. Mother nature mother has been always a fruitful source for new drugs. Not only plants, but also animals, fungi, algae as well as microorganisms have afforded numerous compounds, which later on became clinically available drugs, *e.g.* quinine, morphine, aspirin, artemisinin, metformin, captopril, galantamine, exenatide, acyclovir etc. On the other hand, it is not easy to get a lead molecule in pre-clinical phase to proceed into clinical phases. New drug discovery is such a complicated procedure that requires multidisciplinary collaboration of many basic and applied scientific branches including physical and organic chemistry, cellular and molecular biology, biochemistry, pharmacology, computational chemistry, medicine, toxicology, etc. It is also well-know that there are too many fatal diseases threatening human health with complex pathophysiological mechanisms, which are connected with multiple targets for research. Thus, a good target for research towards any disease needs to be efficient, cost-effective, and safe, and also meet clinical needs and choice of molecular targets based on disease mechanism is a principal paradigm in drug discovery process. In this regard, our research has focused on enzymatic mechanism *via* their inhibition relevant to various diseases. Up to date, we have identified many natural molecules targeting a number of

enzymes such as cholinesterase, tyrosinase, xanthine oxidase, elastase, collagenase, phosphodiesterase, HMG-CoA reductase, etc. One particular plant secondary metabolite group that we highly focused was coumarins, which are quite promising lead molecules especially for their selective butyrylcholinesterase effect as we have shown in our ongoing *in vivo* and *in silico* studies as along with accompanied lately by cell culture experiments (Figure 1).

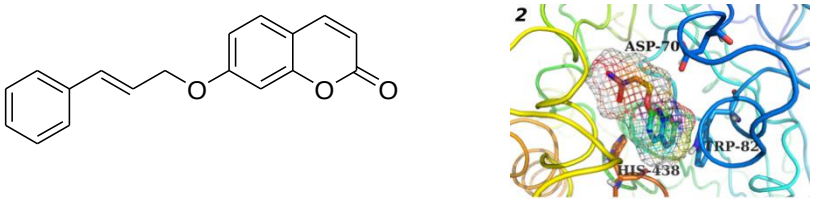

Figure 1. 7-Styryloxycoumarin and its molecular interactions with butyrylcholinesterase

报告/Topic

Health effects and nutritional use of medicinal plants in Russia

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Professor Dr. Alexander Shikov studied pharmacy at the Saint-Petersburg State Chemical Pharmaceutical Academy; 1995 graduation as Ph.D. at the same Academy; 1995 –1998 Associate Professor at the Saint-Petersburg State Chemical Pharmaceutical Academy; Independent expert of Institute of Standardization of Scientific Center of Expertise and Governmental Control of Medicinal Preparation of the Ministry of Public Health of Russian Federation in 2002 – 2003, 2004 he is full professor of pharmaceutical science at Saint-Petersburg State Chemical Pharmaceutical Academy, Russia and since 2008 he is deputy of G eneral Director of Saint-Petersburg Institute of Pharmacy, Russia. His research interests are in the natural product chemistry, pharmacology, and pharmaceutical formulations with natural products. He has published over 20o research papers. Currently he is Associate Editor of Journal of Ethnopharmacology and member of editorial board of Phytomedicine; Chinese Herbal Medicines; Chinese Journal of Natural Medicines; Synergy, and World Journal of Traditional Chinese Medicine. Prof. Shikov is expert of Russian Academy of Science and member of Specialty Committee: Society for TCM Pharmaceutical Analysis (WFCMS-World Federation of Chinese Medicine Societies) from 2010.

摘要/Abstract

Plants are excellent sources of active phytochemicals with importance in the prevention of different diseases and are gaining rapid recognition globally. Many medicinal plants may also have direct nutritional benefits of which we know little.

The multinational population of Russia has used plants both in daily diet and for self-medication however these traditions has remained mostly unknown in other regions. The State Pharmacopoeia of the USSR (11th edition) includes 83 individual monographs for plants describing 119 species [1]. The large majority of species referred in the Russian Pharmacopoeia are known to have been used as food by local population in Russia. These edible plants have a wide range of pharmacological properties: expectorant (9 spp.), diuretic (8 spp.), bitterness and choleretic (7 spp.), astringent (6 spp.), haemostatic (6spp.), anti-inflammatory (4 spp.), adaptogens (4 spp.), diaphoretic (3 spp.), sedative (2 spp.), spasmolytic (2 spp.), polyvitamin (2 spp.), cardiovascular (1 sp.), and anti-helminthic (1 sp.). These plants are used in next food categories: beverages, wild berries and fruits, tea and coffee substitutes, seasonings and spices, sweets, bread surrogates, green vegetables and potherbs, plants used for preserves [2]. The improvement of economic and living standards has changed people's concept of lifestyle and they pay more attention to health food. This type of food not only serves to provide nutrition but also can be a source for prevention and cure of various diseases and become a large popularity.

The utilization of knowledge about beneficial pharmacological effects of edible plants is one of probably safe and effective way for development of new health food. The wild Russian species monographed in pharmacopeia have a great potential for developing new functional foods (the foods that not only serve to provide nutrition but also can be a source for prevention and cure of various diseases).

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Extraction, Standardization and Product Development of Bioactives from Resin of *Calophyllum inophyllum* Nut Oil

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Institute of Drug Quality Control-Ho Chi Minh City, Vietnam

Dr. HA Minh Hien is currently working at the Institute of Drug Quality Control in Ho Chi Minh City (IDQC-HCMC), Vietnam and is the Head of Traditional - Herbal Medicine Analysis Department. He is a member of Vietnamese Pharmacopoeia Commission as well as Western Pacific Regional Forum for the Harmonization of Herbal Medicines (FHH). He has focused his research on Drug Discovery, Medicinal/Pharmaceutical Chemistry and Quality Control of Traditional-Herbal Medicines. In 2007, he participated in the Study Programme on Manufacturing and Quality Control of Traditional Medicine held and sponsored by Japan International Corporation of Welfare Services (JICWELS) in Japan. In 2010, he was awarded a Pre-Doctoral Scholarship granted by the Nagai Foundation Tokyo to pursue his research work in GEA-NUS Pharmaceutical Processing Research Laboratory-Department of Pharmacy-National University of Singapore. He was awarded the best poster award (Pharmaceutical Chemistry/Drug Discovery) at Asian Association Schools of Pharmacy (AASP) conference in Singapore in 2013. Dr HA Minh Hien has published several international articles in the field of Pharmaceutical chemistry/Quality control and is an invited speaker at conferences. He is also a visiting lecturer at universities.

Abstract Content

摘要/Abstract

To exploit the resin from *Calophyllum inophyllum* L. oil which demonstrated antimicrobial and antioxidant properties for production of quality herbal medicinal products by introducing the appropriate methodology and tools to enhance its quality control aspect. Thus, an objective was to extract and isolate bioactive from crude herbal materials as this allowed the quantification of bioactive in the herbal extract. The GC-MS methodology for the determination of a bioactive, namely calophyllolide is firstly proposed. From the standardized extract, the second objective was to develop herbal products of quantifiable quality. Pellets containing herbal extract were developed and coated for the design of controlled release multi-particulate drug delivery system. Dissolution runs were carried out and the *in vitro* release data analyzed under different release rate controlling conditions to better understand the release kinetics of the botanical components.

The use of supercritical fluid chromatography for analysis of glycosides from traditional Chinese medicines

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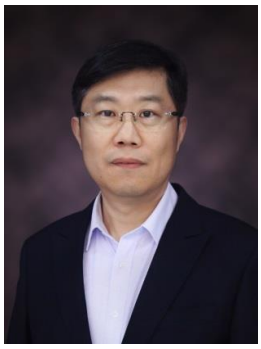

Dr. Baiping MA is a Professor in Natural Products Chemistry at Pharmaceutical Department in Beijing Institute of Radiation Medicine, China. He is the Head of Herbal Chemistry Laboratory. His research specialized in the fields of separation and structural elucidation of active ingredients from TCM, profiling and characterization of chemical compositions of herbs, and biotransformation of natural products. He also works in drug research and development from TCM. He is in charge of R&D of an anti-dementia steroidal saponin, Timosaponin BII, as an innovatory pharmaceutical which has been in clinical trials stage. He also finished preclinical studies of TSA, a purified saponin fraction from an herb, as anti-platelet drug. Six patent families have been filed and 34 patents have been granted all over the world. Baiping MA has published over 180 scientific articles, review papers and book chapters.

摘要/Abstract

Supercritical fluid chromatography (SFC) is becoming a mainstream chromatographic technique complimentary to RP-HPLC for both chiral and achiral molecules. Traditional Chinese medicines (TCM) usually consist of complex matrices of phytochemical compounds, including diverse structures and lots of isomers, responsible for their efficacy. Polar glycosides, such as saponins and flavonoids, are important compositions in water decoction of TCM for the traditional usage in clinic.

Steroidal saponin chemically consists of a steroidal aglycone and the linked oligosaccharide moieties. Among them, furostanol saponin contains two sugar chains at positions C-3 and C-26 generally, and spirostanol saponin has one sugar chain at position C-3 and a closed F ring. The mixed 10 similar structures of furostanol saponins were separated in 22 min on the Diol column at temperature of 40 ◦ C. The mobile phase was CO_2 (mobile phase A) and methanol (containing 0.2% $NH_3 \cdot H_2O$ and 3% H_2O) (mobile phase B). SFC was found to be effective in separating the furostanol saponins that shared the same aglycone but varied in sugar chains. By comparison of UHPSFC and UHPLC, we found that UHPSFC is effective in separating the spirostanol saponins which share the same aglycone and vary in sugar chains, and is very sensitive to the number and the position of hydroxyl groups in aglycones.

Comprehensive analysis and quality assessment of Herba Epimedii mainly containing flavone glycosides from multiple botanical origins were carried out based on UHPSFC-QTOF/MS and UHPSFC-PDA. 51 flavonoids were characterized, and 28 potential markers enabling the differentiation of *E. wushanense* from other four species, *E. brevicornum*, *E. sagittatum*, *E. pubescens*, and *E. koreanum*, were discovered by UHPSFC-QTOF/MS combined pattern recognition multivariate statistical analysis. Additionally, an UHPSFC-PDA was developed and validated for simultaneous quantification of 7 predominant flavonoids in five Epimedium species, and remarkable variation in their contents was observed.

The integrated UHPSFC approach has potential applications in analysis and quality evaluation of TCMs containing hydrophilic glycosides.

青年论坛
Youth Forum

（桂冠二厅/Laurel Hall II）

2019-06-28，13:40-17:10

Synergistic combination discovery from herbal medicines

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Dr. Hua Yang is Full Professor at State Key Laboratory of Natural Medicines, School of Traditional Chinese Pharmacy, China Pharmaceutical University (Nanjing, China) and assistant director of Department of Pharmacognosy. Dr. Yang's research mainly focused on discovering bioactive components of herbal medicines and exploring their mechanism.

摘要/Abstract

Disease is recognized as an integration of multiple pathological factors, and its complexity determines the efficacy limit of single drug therapeutics, which therefore addresses development of new therapies as an important issue. Compared with single drug, synergistic combinations are more compelling for their better efficacies, less side effects, and slimmer chances of drug resistance. Herbal medicines are complex mixture of multiple chemical compounds that might work synergistically. A challenge is that how to rapidly identify synergistic combination in herbal medicines. Our research team has previously devised several novel strategies for screening synergistic combinations, and these strategies were efficiently applied in screening of effective combinations from herbal medicines or herbal formulas.

Effective components and their glycosylation in licorice

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Dr. Xue Qiao is currently an associate professor in the School of Pharmaceutical Sciences, Peking University. Her research focused on chemical analysis and biosynthesis of effective components in traditional Chinese medicines. She has published more than 40 SCI-cited papers in *Anal. Chem.*, *J. Chromatogr. A*, *Org. Lett.*, etc., as the (co-)first or (co-)corresponding author. Her work was supported by Beijing Natural Science Foundation as Beijing Distinguished Young Scholars, CAST Young Elite Scientists Sponsorship Program, and National Natural Science Foundation of China

摘要/Abstract

Traditional Chinese medicines (TCMs) usually have complex chemical composition, and unknown effective components. These have been major hurdles for the modernization of TCM. Herein, we integrated chemical analysis, *in vivo* metabolism, and bioactivity evaluation to systematically elucidate the effective components of licorice. We then discovered their tailoring enzymes to synthesize these compounds and increase their structural diversity.

Firstly, 311 compounds were detected in licorice by using comprehensive 2DLC/MS. In total 257 compounds were isolated from three medicinal *Glycyrrhiza* plants (*G. uralensis*, *G. glabra*, *G. inflata*), including 44 new compounds. Chemical difference among the three species was revealed by quantifying 151 secondary metabolites in 95 samples using LC/MS/MS. Successively, the purified compounds were screened using 11 cell- and enzyme-based bioassays. Furthermore, the *in vivo* metabolites of licorice were analyzed, where 90 metabolites were detected and 55 were monitored by multi-component pharmacokinetic analysis. Finally, compounds with potent bioactivity and high plasma exposure were confirmed for their bioactivities using animal models. For example, glycycoumarin showed hepatoprotective effect to chronic and acute alcoholic liver injuries.

We then identified the glycosyltransferases (GT) from licorice and other plants to modify the effective components. In total 13 GTs were characterized from licorice. For example, GuGT2 catalyzes the C-30/29 regio-specific glycosylation of pentacyclic triterpenoids, which generated the esterified licorice saponin A3. GuGT10 catalysed the glycosylation of liquiritigenin and isoliquiritigenin. Moreover, Sb3GT1 utilizes five different sugar donors to catalyze 3-*O*-glycosylation of 17 flavonols. TcCGT1 efficiently and regio-specifically catalyzes 8-*C*-glycosylation of 36 flavones and other flavonoids. These enzymes provide effective approaches to synthesize natural and unnatural glycosides *in vitro*, and increased their chemical diversities.

Understanding the genetic information of a Chinese medicinal plant, *Scutellaria baicalensis*

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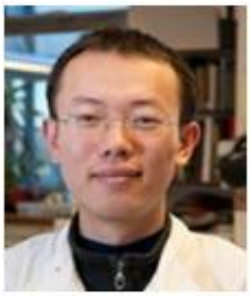

Dr. Qing Zhao is currently the executive group leader of Medicinal Plant and Health Group, Shanghai Chenshan Plant Science Centre, CAS. He has focused his research on the synthesis, regulation and evolution of flavonoids in Scutellaria baicalensis and related species. His study has elucidated that a specific flavone synthesis pathway exists in the root of Scutellaira baicalensis, which is responsible for wogonin and baicalein. His team completed full genome sequencing of Scutellaira baicalensis, offering a foundation for comparative genomic analysis between members of the family *Lamiaceae* and will facilitate elucidation of metabolic pathways, as well as molecular breeding, for this important medicinal plant. He is the project leader of a National Key R&D Program, two programs from National Natural Science Foundation and several from Chenshan Special Funding. He is a fellow of Youth Innovation Promotion Association, CAS.

摘要/Abstract

Scutellaria baicalensis Georgi is important in Chinese Traditional Medicine where preparations of dried roots, 'Huang Qin', are used for liver and lung complaints including complementary cancer treatments. We report a high quality reference genome sequence for *S. baicalensis* where 93% of the 408.14 Mb genome has been assembled into 9 pseudochromosomes with a super-N50 of 33.2 Mb. Comparison of this sequence to those of closely related species in the order Lamiales, *Sesamum indicum* and *Salvia splendens*, revealed how the specialised metabolic pathway for the synthesis of 4'deoxyflavone bioactives evolved in the genus, *Scutellaria*. The gene encoding a specific cinnamate CoA ligase assumed its new function following recent mutation, and four genes encoding enzymes in the 4'deoxyflavone pathway exist in tandem repeats. Gene duplications, segmental duplication, gene amplification and point mutations coupled to gene neo- and sub-functionalisations were involved the evolution of 4'deoxyflavone synthesis in the genus, *Scutellaria*.

Precise Regulation of Lignans in *Isatis indigotica*

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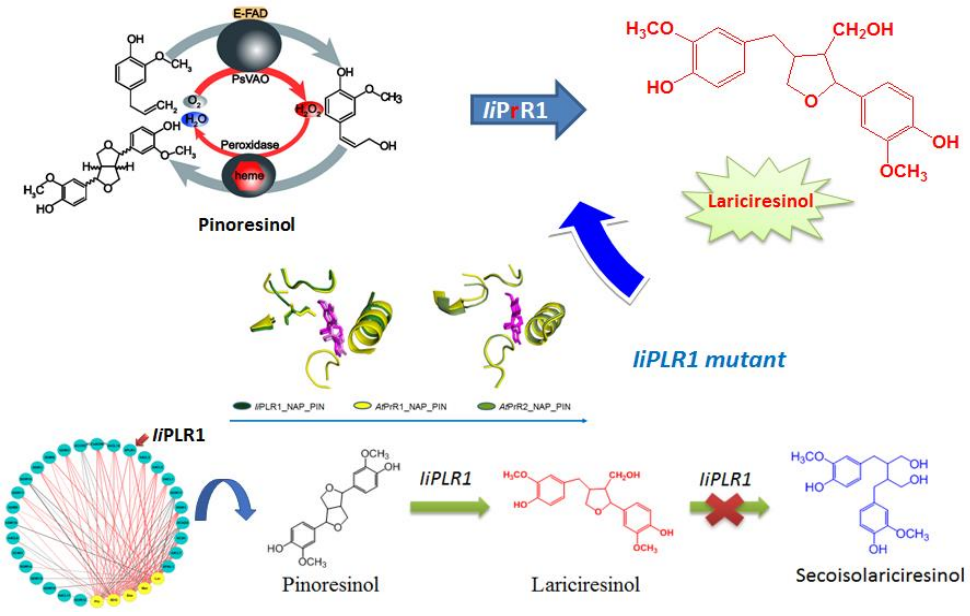
摘要/Abstract

Isatis indigotica is a widely used herb for the clinical treatment of colds, fever, and influenza in Traditional Chinese Medicine. Lignans, such as lariciresinol and its derivatives, have been identified as effective antiviral ingredients of *I. indigotica*. A molecular description of lignan biosynthesis in *I. indigotica* displaying its synthetic characteristics and regulatory mechanism is of great importance for the improvement of the production of this class of active compounds. Although some enzymatic steps have been proposed to be particularly important for activating the lariciresinol biosynthetic pathway, the specific roles of gene family members in regulating this metabolic flux have rarely been investigated. In our study, a correlation analysis between the RNA sequencing (RNA-Seq) expression profile and lignan content by using *I. indigotica* hairy roots treated with methyl jamonate (0.5 μM) at different time points as a source implicated that *I. indigotica* pinoresinol/lariciresinol reductase 1 (*Ii*PLR1), but not *Ii*PLR2 or *Ii*PLR3, contributed greatly tolariciresinol accumulation. Since the lower substrate specificity of *Ii*PLR1 (It catalyzes pinoresinol to form lariciresinol, and also catalyzes lariciresinol to secoilariciresinol) hampers the biosynthetic efficiency of antiviral component lariciresinol, the crystal structure of *Ii*PLR1 was elucidated using structural biology approach. The structure-guided mutagenesis successfully switches the substrate specificity of *Ii*PLR1, leading to overproduction of lariciresinol. In conclusion, our study sheds light on how to engineer the production of target metabolites effectively and precisely using more suitable intervention points or by more refined strategies.



Liver injury induced by pyrrolizidine alkaloids and its detoxification

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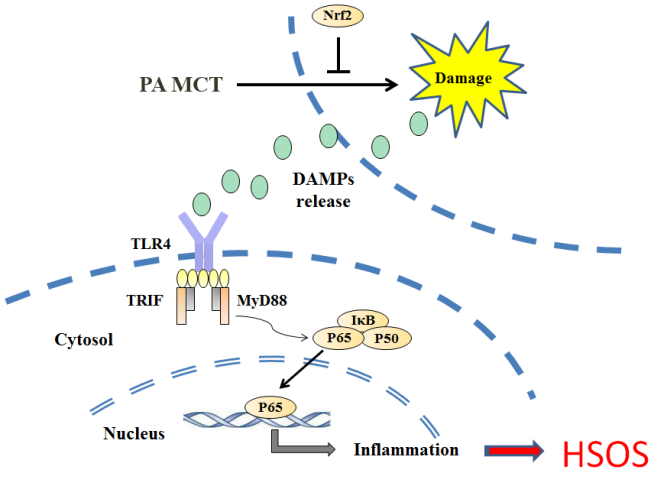
Prof. Lili Ji is currently as the Professor at The MOE Key Laboratory for Standardization of Chinese Medicines, Shanghai Key Laboratory of Compound Chinese Medicines and The SATCM Key Laboratory for New Resources and Quality Evaluation of Chinese Medicines, Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine. She focused her research on pharmacology and toxicology of traditional Chinese medicines (TCMs). She elucidated the novel toxic mechanism involved in liver injury induced by hepatotoxic PAs, which widely distributed in a variety of TCMs such as *Senecionis Scandentis* Hebra. She also found the hepatotoxic and anti-cancer active compounds in Airpotato yam, and set up the safe range for the usage of Airpotato yam. These above results laid scientific foundation for the establishment of safety standards and clinical safe application of those TCMs and their preparations. Based on the compatibility of TCMs and the combined usage of TCMs and western medicine, she found that some TCMs and active compounds had protection from the liver injury induced by representative hepatotoxic drugs. These results enriched the theory of compatibility of TCMs. Those works received two 1st prize of Natural Science Research of Ministry of Education. She was selected into National Natural Science Foundation--Excellent Youth Foundation (2013) and the third group of national high level talents special support plan (Ten Thousand Plan)-Scientific and Technological Innovation Leader (2018). She has published over 96 papers in SCI cited journals with about 1130 SCI citations.

摘要/Abstract

Pyrrolizidine alkaloids (PAs) are natural hepatotoxins with worldwide distribution in more than 6000 high plants including medicinal herbs or teas. Dietary ingestion of PAs-containing medicinal herbs or foods including teas, milk and honey is a major cause for the development of hepatic sinusoidal obstruction syndrome (HSOS). In the world, about thousands of HSOS clinical cases due to PAs-poisoning have been documented since 1920. In particular, in china over 400 clinical cases reported the HSOS induced by a traditional herbal medicine *gynura segetum* (Tusanqi), which contains abundant PAs. The pathophysiology of PAs-induced liver injury is complicated and its concrete mechanism is still not very clear.

We found that mitochondrial-dependent apoptosis, cellular glutathione (GSH) antioxidant system, phagosome-mediated innate inflammation, and liver inflammatory injury initiated by damage-associated molecular patterns (DAMPs)-toll-like receptor 4 (TLR4)-nuclear factor κB (NFκB) signaling pathway are all involved in PAs-induced liver injury. Moreover, some natural products like quercetin, chlorogenic acid, liquiritin, liquiritigenin and (-)-epicatechin attenuated PAs-induced liver injury via inducing the activation of nuclear factor erythroid 2-related factor 2 (Nrf2) to attenuate liver oxidative injury and inhibiting the activation of NFκB inflammatory signalling pathway to combat liver inflammatory injury.



Archaeological evidence suggests earlier use of Ganoderma in Neolithic China

Prof. Yuan Yuan is currently as the Professor and deputy director of National resource center for Chinese material medica, Chinese academy of traditional Chinese medicine. She has focused his research on the investigation of biological principles and key technologies in process of the quality formation of traditional Chinese medicine. She is now responsible for the revision of several Chinese pharmacopoeia standards, including PCR identification of Chinese medicinal materials and ELISA analysis of aflatoxin.

摘要/Abstract

Herbs and fungi, which have always been the principal form of medicine in developing countries, have regained popularity in the developed world as people strive to stay healthy in the face of chronic stress and pollution and treat illnesses with medicines that work in concert with body's defense. There are several age-old books originating from various countries that record diversified herbal medicine. In China, the earliest text to record medicinal herbs and fungi is the "Shennong's Herbal Classic", which appeared more than 2500 years ago. The saying "Shennong tasted one hundred herbs" comes from the ancient China and the famous "Divine Husbandman" known as "Shennong" who is said to be the first to collect and use medicinal plants in China. Shennong is esteemed for transmission and emergence of ancient China's agricultural practices dating back to 4000–5000 BC, although there is evidence for the use of medicinal plants dating back up to 60000 years before present. However, owing to the lack of reliable archaeological evidence, it has been highly debated when prehistoric farmers began utilizing wild herbal medicine and how long it took for this practice to spread. Here, we examined the morphology of spores excavated from 5 *Ganoderma* samples (G1−G5) in three archaeological sites located in Tianluoshan, Yuhangnanhu, and Qianjintadi that date back to the Neolithic era. Dating using 14C isotope revealed that the use of G1sample began about 6817±44 years BP in the Hemudu society, G2 sample began about 5379±59 years BP and G5 sample began about 4508±50 years BP in the Hemudu society and liangchu society. The comparison of morphological characteristics of spores from the prehistoric samples and spores of the present-day, modern *Ganoderma* species confirmed that the G1–G5 samples belong to the genus *Ganoderma*. Hemudu society is one of the birthplaces of Chinese civilization, and people had started using reed mats and planted tea and rice. The prehistoric *Ganoderma* was unearthed with the cultural relics, such as wood carving headornaments, jade articles, and so on. It was speculated that the witch had been using *Ganoderma* at that time. The earliest dates for the lower Yangtze River areas Neolithic indicate that it expanded the archaeobotanical records of herbal medicine (*Ganoderma*) exploitation in China to 6800 years BP. With the formation of early agriculture, people have continued exploration and utilization of fungi with *Ganoderma* appearance. In the course of the history, the ancient Chinese people gradually documented its value and extolled its purpose. This opinion is related to the legendary events of "Xuanyuan gifted with *Ganoderma*" and "Shennong gathers Ganoderma" in the mythological era of China. Further research in this region should help clarify the trajectory of herbal medicine origination in China.

报告/Topic

Mechanism and clinical application of anti-inflammatory TCM component andrographolide

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Yang Sun received his Bachelor (2000), Master in Pharmacology (2003) from China Pharmaceutical University and Ph.D. in Physiology (2006) from Nanjing University. He joined the Faculty of School of Life Science, Nanjing University since Aug 2006. Yang was awarded Outstanding Youth Science Foundation by NSFC in 2014. From 2015 to 2016, Yang did his visiting scholar research at School of Medicine, UCSD. His research interests focus on uncovering the molecular mechanisms of inflammatory diseases and inflammation-related cancer and identifying target protein of small-molecule compound with unique activity. He is now a professor of pharmacology and a principal investigator in State Key Laboratory of Pharmaceutical Biotechnology, Nanjing University.

摘要/Abstract

Small molecule andrographolide (Andro), is a natural diterpenoid from *Andrographis paniculata* which has anti-bacterial, anti-antiviral and anti-inflammatory activities in clinic. However, its detailed molecular mechanism is still unclear. Here we show that Andro inhibits NLRP3 inflammasome activation, as indicated by reduced expression of cleaved Caspase-1, disruption of NLRP3-ASC-pro-Caspase-1 complex assembly, lower IL-1β secretion in macrophage and protecting mice against azoxymethane/dextran sulfate sodium-induced colitis-related carcinogenesis. Moreover, Andro is found to trigger mitophagy in macrophages via targeting P110, which in turn inactivates the NLRP3 inflammasome. Furthermore, Andro enhances the anti-tumor activity of 5-fluorouracil (5FU) and reverses the resistance due to the NLRP3 inflammasome activation. On this basis, clinical trials on colonic cancer is carried out in People's Hospital of Jiangsu Province (Ethics committee approval number 2013-SR-131), and it is also registered on the website of clinical trials (http://clinicaltrials.gov) in NIH (registration number NCT01993472). As is expected, combination 5FU with Andro significantly attenuates the tumor fever as well as tumor size, and ameliorates the related biochemical markers of the colonic cancer patients. Taken together, our findings demonstrate that Andro induces mitophagy-mediated NLRP3 inflammasome inhibition via targeting P110 and reverses 5FU resistance in human colorectal cancer. Our data may help to guide decisions regarding the use of Andro in patients with inflammatory bowel diseases, and provide a rationale for novel combination treatment strategies, especially for patients with 5FU-resistant tumors.

报告/Topic

Chemical characteristics-oriented standards establishment of herbal medicines

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Dr. Wen Gao is an associate professor, doctoral supervisor at China Pharmaceutical University. Her research focused on using modern analytical methods to screen and analyze active/ characteristic components of traditional Chinese medicines (TCMs), and quality control of TCMs. She has authored over 30 papers in SCI cited journals. She is also the invited reviewer of *Phytomedicine*, *Journal of Separation Science*, etc.

摘要/Abstract

The key issue for quality control of traditional Chinese Medicines (TCMs) is to select appropriate marker compounds. Generally, highly abundant compounds, active compounds, and characteristic compounds are selected as chemical markers. Nobody could have failed to notice that TCMs are complex mixtures and integrative function. The quality marker of TCM formulation should be relevant to its therapeutic effects. However, for herbal raw materials, the authentication may be more important to ensure their safety and efficacy. Some herbs belonging to closely related species but differing in medicinal properties, and some others show the similar chemical profiles but do not always exhibit the expected equivalent efficacies. Therefore, we conducted the untargeted/targeted metabolomics strategy couple with multivariate statistical analysis to discover the characteristic compounds for closely species identification. Those strategies have been successfully applied to the quality control of *Lonicera* species Flower, *Sophora* Flower/Flower-bud, *Paeonia suffruticosa* Bark and its processed, etc.

报告/Topic

High-resolution 3D Genome Architecture and Transcriptional Regulation in Rice

Lun Zhao†, Shuangqi Wang†, Zhilin Cao†, Weizhi Ouyang, Qing Zhang, Liang Xie, Ruiqin Zheng, Minrong Guo, Meng Ma, Qifa Zhang, Guoliang Li & Xingwang Li**
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Dr. Xingwang Li joined in Huazhong Agricultural University three years ago and has been focused on rice 3D genome structure research including 3D genome mapping technologies development and mechanism of 3D genome structure on transcription regulation as well as cis regulatory element identification and characterization. Dr. Li was trained in biochemistry and molecular biology and perused his Ph. D. of rice functional genomics from National Key Laboratory of Crop Genetic Improvement. Then, he continued his research on rice male gametocyte developments as a Research Associate in the same group.

After that, he decided to join in Dr. Yijun Ruan's lab at The Jackson Laboratory for Genomic Medicine as a postdoctoral associate, leading the 3D genome mapping technologies development, getting involved in research on mechanism of 3D genome structure on transcription and initiated the potential effects of genetic variations and epi-genomic modification on dynamics of 3D genome structure in human and mouse. Currently, Dr. Li had started his own lab at Huazhong Agricultural University and his group is extending their knowledge and experiences on 3D genome to rice and other crops.

摘要/Abstract

High-resolution three-dimensional genome organization and its effect on transcription remain elusive in plants. Here, using an improved ChIA-PET approach, we mapped H3K4me3- and RNA polymerase II (RNAPII)-associated promoter-promoter interactions and H3K9me2-marked heterochromatin interactions at nucleotide/gene resolution in rice. The chromatin architecture was separated into different independent spatial interacting modules with distinct transcriptional potential and covered approximately 82% of the genome. Compared with inactive modules, active modules possessed the majority of active loop genes with higher density of active genes that contributed to the most of transcriptional activity in rice. In addition, promoter-promoter interacting genes tended to be transcribed cooperatively. By contrast, heterochromatin-mediated loops played structural roles in chromatin configuration and had no significant effect on gene transcription. Furthermore, we revealed the impact of genetic variation on chromatin interactions and transcription and identified a spatial correlation between the genetic regulation of eQTLs and e-traits. In summary, our strategy reveals hierarchical and modular 3D genome architecture for transcriptional regulation in rice.

报告/Topic

Advanced LC-MS for widely quantitative analysis of herbal medicines

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Dr. Yuelin Song is currently as an associate professor in School of Chinese Materia Medica, Beijing University of Chinese Medicine. He received bachelor and master degrees in School of Pharmaceutical Sciences in Peking University at 2007 and 2009, respectively, and he completed his Ph.D. education in biomedical science from Institute of Chinese Medical Sciences in University of Macau at Sept. 2013. He has authored 90+ SCI articles with 1000+ SCI citations. His H-index is 19. He won Second prize of 2015th National Science and Technology Progress Award (Rank 10) and First prize of 2016th Science Technology Improvement Award of Science Research Famous Achievement Award in Higher Institution (Rank 12). Dr. Song has been selected into "Young Elite Scientists Sponsorship Program (2017-2019)" by China Association for Science and Technology. Now, Dr. Song acts as a peer review for several journals, such as Anal Chem, Anal Chim Acta, Brit J Pharmacol, J Chromatogr A, *etc*.

摘要/Abstract

Liquid chromatography–tandem mass spectrometry (LC–MS/MS) integrates the merits from both LC and MS/MS. On one side, LC is able to fractionate a given complicated sample into single peaks, and on the other side, MS/MS enables the qualitative and quantitative detection of the substances in the LC effluent. LC–MS/MS is currently the most popular analytical tool towards the chemical composition characterization of complex matrices (e.g. herbal medicines), in particular the employment of high resolution MS/MS. It is still challenging, however, to build the entire structures *via* linking those substructures because isomers usually yield extremely similar mass spectral patterns. In recent years, our efforts have been devoted to configure advanced LC–MS/MS platform to fit for the requirements from widely quantitative analysis of herbal medicines. Because of our continuous work, serial new techniques (Fig. 1) have been developed in our group aiming to promote all steps such as sample preparation, chromatographic separation, mass spectrometry, and database construction, involved for LC–MS/MS analysis. Owing to the new techniques such as online pressurized liquid extraction, dried spots of herbal medicines, serially coupled RPLC-HILIC, RRCEC matching, online parameter optimization, LC–MS/MS binary code, NMR barcode, QSRR, QSCR, quasi-content, and so on, direct analysis comprehensive retention, confident measurement and rapid data processing have been almost achieved for herbal medicines.

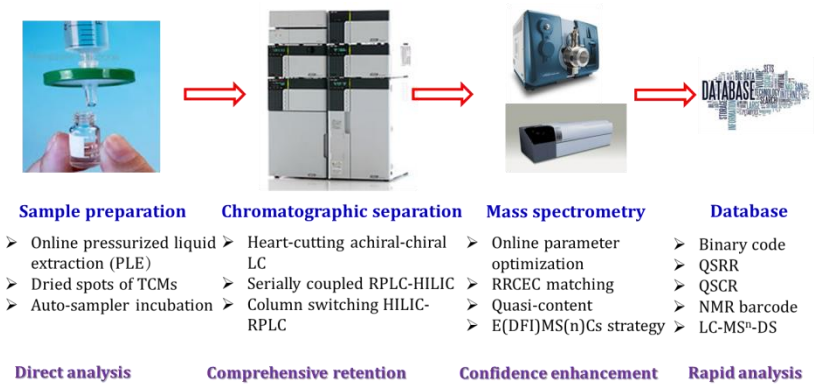

Fig. 1 Advanced LC–MS/MS platform for widely quantitative analysis of herbal medicines

中药标准导向的基础研究会场 I

Standard-oriented basic research of traditional Chinese medicine I

（桂冠三厅/Laurel Hall III）

2019-06-28，13:40-17:10

报告/Topic

Bioactive compounds in Tong-Guang-San and its formulation

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Prof. Yang Ye is currently as the deputy party secretary and principal investigator at Shanghai Institute of Materia Medica, Chinese Academy of Sciences. He has focused his research on the extraction and isolation, structural elucidation, structural modification of natural products, and the investigation of chemical base of therapeutic usages of traditional Chinese medicines (TCMs) In recent 5 years, more than 800 compounds were isolated and structurally elucidated from over 20 medicinal herbs, including around 300 new compounds and 20 new skeletons. He has published 4 academic books including Natural Products Chemistry. Besides, he has applied 12 China patents and 1 international patent, with 4 approved. In 2009, he won the National Science Fund for Distinguished Young Scholars. Thanks to his academic contribution, he has been invited to give lectures in some important international conferences, and to be in the editorial boards of some important journals. He also established two joint labs with the Chinese University of Hong Kong in 2011, and with the Griffith University in 2014, for promoting globalization of TCMs and drug discovery.

摘要/Abstract

Multidrug resistance (MDR) is a major obstacle for the successful chemotherapy of cancer, which is often mediated by overexpression of ATP-binding cassette (ABC) transporters that remove substrates out of the cell against a concentration gradient. Among 48 human ABC transporters discovered, three, namely P-glycoprotein (P-gp or ABCB1), multidrug resistance-associated protein-1 (MRP-1 or ABCC1), and breast cancer resistance protein (BCRP or ABCG2), are most often associated with MDR.

Marsdenia tenacissima (Roxb.) Moon. (Asclepiadaceae) distributes mainly in the southwest of China. Its dried rhizomes and roots have been used for the treatment of cancer in compound formulation of traditional Chinese medicines for a long time. Its formulation, Xiaoaiping Injection, was approved for the treatment of cancer, or to be used as the adjuvant drug in chemotherapy in clinical. Due to unknown for the chemical base for its anti-cancer application, a systematic investigation on the chemical constituents from *M. tenacissima* has been conducted and totally 37 polyoxypregnane steroids were obtained including 12 new. Interestingly, 4 novel and 10 known compounds showed positive effects to circumvent MDR in different cancer cell lines with overexpression of the aforementioned three ABC transporters. Moreover, 3 most abundant compounds were proven to be prodrug for MDR reversal agents in vivo. In vitro study indicated that active steroids could significantly reverse the cytotoxicity of DOX and Taxol against drug-resistant cell lines SW620/Ad300 and LCC6/MDR1 when in combined with these anti-cancer drugs. On the basis of above results, qualitative and quantitative method of Tong-Guang-San and its formulation have been developed and Quality control standard was recommended for Tong-Guang-San.

报告/Topic

基于效毒关联评价的有毒中药的质量控制研究

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孙蓉教授主要从事中药药理研究评价与创新药物发现，构建基于中药“疾病—证候—功效”的药理学研究方法和药效学评价技术，有效成分群与功效关联评价技术，中药方剂结构及配伍规律研究，中医病证动物模型建立和基于病证的中药创新药物发现与新药研发；中药毒理学研究与临床合理用药控制。阐明近 20 味有毒中药“毒性—功效—证候”发生机制和关联特性，构建毒性在功效-证候背景下的现代表征体系和科学认知标准；“中药肝毒性早期发现与合理评价技术平台建设及其科学应用”获得 2015 年度山东省科技进步一等奖。2016 年提出“基于毒效相关的 Q-marker 合理辨识与科学控制”的理念，并率先开展吴茱萸毒性标志物研究。

报告/Topic

基于“质-量”双标的中药材质量控制方法研究

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孟宪生 教授 主要从事药效物质基础及作用机制方面的科学研究，在研究中首次提出了中医证是体内部分变化的内源性物质组理论，及从整体到组分再到整体的创新中药研究思路。

摘要/Abstract

2016 年国务院发布《关于促进医药产业健康发展的指导意见》中重点提出“完善质量标准体系，健全以《中国药典》为核心的国家药品标准体系”的要求，该要求的提出为今后完善中药质量控制标准，提高标准的科学性、合理性及可操作性指明了方向。但由于化学成分复杂、有效成分不是单一物质、多种化学物质共同作用达到药效等问题，导致中药质量差异悬殊。寻找适合于中药复杂体系的质量评价方法，一直是中药研究的关键科学问题，同时也是制约中药现代化、产业化和国际化进程的瓶颈问题。

中药质量评价方法是中药质量控制的关键，也是保证中药药效的必须手段。随着现代科技手段的进步与中药领域的深入研究发展，结合中药多成分、多靶点发挥功效的作用特点，中药的质量评价方法逐渐由“单一成分质量控制”向“多指标成分质量控制”转变，逐渐由“指标性成分”向“有效成分”转变。近年来，中药指纹图谱研究、谱效关系研究、一测多评法、生物效价法及中药质量标志物等等方法与概念的提出，为更加科学、合理地控制中药质量做出了积极的贡献。但仍然难以解决部分中药化学对照品制备困难且价格昂贵、中药化学成分“整体性”与“清晰性”难以兼顾等实际问题，从而造成多指标、多成分、整体性的中药质量控制模式面临巨大挑战。经统计，现行 15 版药典中单指标质量控制的中药材有 277 种，多指标质量控制的有 133 种（多为 2 个指标），无含量测定指标的有 210 种，有指纹图谱评价的仅有 2 种，标准的提高仍存在很大空间。

为此，课题组总结多年中药质量控制方法研究经验，突出中药指纹图谱、一测多评、多波长融合等技术方法优势特色，结合研究现状与实际，提出了基于“质-量”双标的中药材质量控制方法。即以对照药材为基准，建立同一基原药材不同产地特征图谱，实现药材整体化学成分“质”的清晰；在特征峰与活性成分基本指认明确的基础上，以某一单一成分或添加内标的方式为参照，结合全时段等基线多波长覆盖融合技术，进行其它化学成分的相对定量，实现药材特征成分“量”的明确，从而更加全面、合理地控制中药材质量。旨在通过廉价易得的对照药材和单一对照品，实现多成分、多指标，定性、定量相结合的中药材整体质量控制，从实用性和推广性角度出发，为中药质量标准研究关键科学问题的解决提供探索性方法。

报告/Topic

TCM-PCDL技术在中药物质基础研究中的探索及应用

Shanghai Standard Biotechnology Co., Ltd.

Mr. Zhen-qiang Xin is currently as the CTO and Vice General Manager at Shanghai Standard Technology Co. Ltd. He has focused on research and development of chemical reference standards (CRS) of TCM for more than 10 years. In recent years, on the basis of high resolution mass spectrometry database of CRS, the technical services of his team mainly cover the establishing quality standard of TCM related functional products and non-clinical pharmaceutical research services for new drug registration.

摘要/Abstract

Rapid and accurate analytical methods are necessary to develop with the increasing demand of quality control of TCM related products. The high resolution mass spectrometry database of chemical reference standards (CRS) of TCM, featuring positive and negative MS^2 resulting from respective 7 levels of collision energy, enables the efficiency of research on establishment of quality standard of products derived from TCM.

报告/Topic

Comparative study on quality of Astragali Radix with metabolomics analysis and pharmacodynamics

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Prof. Xue-mei Qin is currently as the Professor at Shanxi University, Director of Modern Research Center for Traditional Chinese Medicine of Shanxi University (CTCMS) and the Shanxi Key Laboratory of Active Constituents Research and Utilization of TCM. Meanwhile, she is the Chair of the Shanxi Pharmacology Society. Prof. Qin is mainly engaged in quality control and evaluation of TCM, metabonomics of TCM, as well as the innovative drug research. She has been in charge of 6 projects of National Natural Science Foundation of China (NSFC), 2 projects of Key International S&T cooperation, 2 National Science and Technology Major Projects for "Major New Drugs Innovation and Development", and so forth. She was awarded as the 2nd Shanxi Science and Technology Progress Award in 2014. The research production of 2 new drugs has been transferred. 18 patent applications have been confirmed. She has published over 400 papers with 97 in SCI cited journals, and an academic monograph.

摘要/Abstract

Astragali Radix (AR) is the dried root of the *Astragalus membranaceus* (Fisch.) Bge. (mojia) and *Astragalus membranaceus* var. *mongholicus* (Bge.) Hsiao. (menggu). It has a variety of effects, including tonifying Qi and lifting yang, inducing diuresis to alleviate edema, myogenic and sore healing, and pus draining and toxin expelling. At present, the market mainstream goods are menggu ARs, which are divided into cultivated ARs and wild ARs. Among them, wild ARs in Shanxi are rich in flavor and sweet, and are considered to be of high quality by the industry. Moreover, the scientific connotation of the strong soybean smell and sweet taste of AR is explained, including material basis and relevance with quality. However, accurate and comprehensive evaluation of the quality of AR has been still a research hotspot. The indicator components based on the Pharmacopoeia (2015 edition) are one-sided. Though the fingerprints are more comprehensive in characterizing AR components, they are not strongly related to drug efficacy. In addition, the growth period of the upper and lower sections of wild AR is different due to the tip growth growth, which ultimately leads to inconsistent results of each index. Considering that the efficacy is the gold indicator of quality control, and AR is a multi-effect Chinese medicine, it is essential to establish a quality control standard for AR based on the efficacy of its different compatibility environments. Compared with traditional indicators, metabolomics plays a key role in the characterization of efficacy of traditional Chinese medicine (TCM) due to its sensitivity and systematicness, which is consistent with the integrity and complexity of TCM. A series of researches have been carried out for AR in our laboratory. The research results are intended to provide a basis for the oriented-evaluation of AR quality, provide guidance for the selection of AR and precise planting. It will also provide a method reference for quality evaluation of a ubiquitous multi-effect TCM.

报告/Topic

Integrated Systems Biology and Chemical Biology Approach to Exploring Mechanisms of Traditional Chinese Medicines

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Prof. Gang Bai is currently as the professor at College of Pharmacy of Nankai University, principle investigator of State Key Laboratory of Medicinal Chemical Biology; Managing director of professional Committee of Network Pharmacology and TCM Analysis, World Federation of Chinese Medicine Societies (WFCMS); Vice Chairman of product development and cultivation committee, China Association of TCM (CATCM); Chairman of special committee of TCM and natural product of Tianjin Pharmaceutical Societies. He has focused his research on systems biology and chemical biology of traditional Chinese medicine for more than 20 years and established an integrated research model for analysis of active ingredients of TCM, clarified its mechanism of action and tried to construct an intelligent quality control system for TCM.

摘要/Abstract

After thousands of years of development, traditional Chinese medicines (TCMs) have evolved into a complete scientific system characterized by multiple components, targets, and pathways, which mediates numerous pharmacological activities and efficacies. The development of "-omics" technology, including systems biology and network pharmacology, has enabled the illustration of TCMs from a more systematic view. Although the network adequately reflects the overall philosophy of TCMs, its complexity hinders the relevant research to a hover. In addition, the strategies involved appear to be in contrast to the original concise and efficacious disease therapy oriented focus on classic Chinese material medica (CMM). Based on the established holistic view and reductionism, in this topic, we discuss an integrated systems biology and chemical biology research approach that will facilitate and accelerate the understanding of the mechanisms of TCMs. Furthermore, we are optimistic that it will make clear the associated interactions between active natural products and their targets, and ultimately improve the strategies for complex disease therapies.

报告/Topic

Discovery of active natural products with new skeletons

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Professor Yonghui Zhang received his Ph.D. degree in 2004 from Huazhong University of Science and Technology (HUST), where he studied natural products chemistry. He joined the faculty of HUST as an associate professor (2005) and was then promoted to professor (2008). He was elected as an assistant dean (2010) and then the dean (2014) of School of Pharmacy. He has been elected as special-term profssor of "Changjiang scholar program" (2016, Ministry of Education) and "leading scientists, engineers and innovators" (2016, Ministry of Science and Technology; 2018, National Ten Thousand Talent Program). He is the winner of National natural Science Foundation for Distinguished Young Scholars. He is also the director of "Key laboratory of natural pharmaceutical chemistry and resource evaluation in Hubei province", and he has always devoted to investigations on natural products and innovative drugs. So far, he has found about 5 natural products or their derivatives that are potential for drug development.

摘要/Abstract

Fungi and plants are recognized as rich sources of structurally unique and biologically active natural products, which have attracted great interests from scientific community as challenging targets for discovering and developing new drugs. In the past few years, our investigations focus on the bioactive natural products from both fungi and plants, leading to the isolation and identification of more than 2000 compounds including more than 800 new ones, with cytochalasans/merocytochalasans, meroterpenoids/terpenoids, and polycyclic polyprenylated acylphloroglucinols (PPAPs) as representatives. These complex structures of merocytochalasans from *Aspergillus flavipes* and their proposed biosynthetic pathways make merocytochalasans to be a research hotspot both for biosynthesis and organic synthesis fields. Moreover, the study on the protein target of two 3,5-dimethylorsellinic acid-based meroterpenoids from *Aspergillus terreus* represents an good example for research on natural products with low yield via virtual screening. Meanwhile, the study on the fusicoccane diterpenoids from *Alternaria brassicicola* is a very nice piece of in-depth natural product structural revision that not only provides, scholarly structural revision for student learning, but important corrections to the literature and enticing new structures. Kinsenoside, a glycoside from *Anoectochilus roxburghii*, was found to be a potential immunosuppressive drug for autoimmune hepatitis. Based on the bioactive alkaloid NMHC isolated from *Zephyranthes candida*, a series of compounds were designed and synthesized, from which, ZYH005 was found to be potential in the treatment of acute promyelocytic leukemia (APL) and all trans retinoic acid (ATRA)-resistant APL.

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报告/Topic

中药挥发油的功效特点、品质特征与质量控制

Jiangxi University of Traditional Chinese Medicine
Ming Yang, Xiaofei Zhang, Xiaoli Liu

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长期致力于传统中药制药体系研究，特别在中药炮制、制剂、健康产品开发、制药装备等领域尤有特长，贯穿“辩证施治、随方炮制、以方制药”的原则，提出基于“证 -方-剂对应”的中药药剂学理论，创建了国家级中药炮制技术传承基地和中药制药装备研发基地。承担了国家项目 30 余项目，开发创新药物、健康产品、饮片新产品 30 多个，获部省级科技成果奖 10 余项，发表核心期刊论文 500 多篇。

摘要/Abstract

一、中药挥发油在临床中的作用特点具有“四快”：即起效快、走窜快、渗透快、消除快等特点，使得其具有独特的生理及药理学活性。

二、中药挥发油在品质特征表现为四个方面：易挥发、易乳化，易氧化、易聚合。使得其在提取、制备、储存、运输、使用过程中药效一致性差、质量不稳定，缺乏对其质量控制的手段，尤其是缺乏对的有效期及保质期的时限，严重影响了其质量及疗效的发挥。

三、主要研究内容 ：如何分析控制中药挥发油的质量是长期以来未能解决的大难题，如何对其建立一种以其“成分-性质-味道-理化参数”系统性、多维度的质量控制，是我们急需解决的问题。主要研究内容如下：

1. 本项目建立了一种多维度、双向性、系统性、人机互补相结合的“气-味-效”相结合的新的中药精油质量分析及控制方法。首先针对中药精油的挥发、氧化、聚合等方面，分别进行机理研究，对挥发、氧化及聚合过程中“时--量变化、时-效、时-成分、挥发动力学”等方面对其挥发稳定性进行系统性研究，在此基础上对其”成分-功效-毒性“三方面进行综合系统性评价，对其品质及质量进行评价，确定其最佳保质期及精油的陈化机理。

2. 建立对其不稳定性的客观评价方法，对质量过程控制充分考虑挥发与稳定的“双向性”，建立“挥发-稳定”的平衡点，探讨质量不稳定性与功效的变化规律。

报告/Topic

液相阀方案在中药分析的应用

Agilent Technology (China) Co., Ltd.

余彦海 工程师

摘要/Abstract

利用阀的灵活性提高中药分析方法开发效率，加快开发进度。

中药资源与生物技术研究会场

Chinese Medicinal Resource & Biotechnology

（桂冠一厅/Laurel Hall I）

2019-06-29，08:40-12:30

报告/Topic

Production of complicated flavonoids by microorganisms

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Prof. Jingwen Zhou received his Ph.D in Fermentation Engineering, at Jiangnan University in 2009, his M.S. in Microbiology at Huazhong Agricultural University in 2006 and a B.A. in Food Science and Technology at Huazhong Agricultural University in 2003. He is a Professor of Lab of Biosystems and Bioprocess Engineering in the School of Biotechnology at Jiangnan University. His research areas include: metabolic engineering of microorganisms for the efficient production of keto acids (pyruvic acid and α-ketoglutaric acid) and plant natural products (flavonoids and L-ascorbic acid), development of strategies related to carbon-nitrogen balance regulation, fine-tuning of metabolic pathway and high-throughput screening. He has over 80 peer reviewed publications and invited reviews, and awarded with National Award for Technological Invention 2nd Prize, WIPO-SIPO Award for Chinese Outstanding Patented Invention, and ACS membership award.

摘要/Abstract

Flavonoids are a group of important phytochemicals that have extensive applications. They could be regarded as the derivatives from naringeine or pinocembrin by a series of enzyme modifications. Production of flavonoids by microorganisms has been extensively investigated in last several decades. Almost all of the common derivative enzymes for flavonoids have been reported, and some of them were applied for the metabolic engineering of microorganisms for the production of complciated flavonoids. Besides, along with the development of metabolic engineering and synthetic biology tools, the titer and the yield of flavonids production by microorganisms are keeping increasing. Mining of more enzymes from plants and assembly of the more comlicated pathways in microorganisms faciliate the production of more flavonids with higher titer and yield. In order to achieve the efficient biosynthesis of more flavonoids in microorganisms, different modification enzymes from plants that could efficient accumulate corresponding flavonoids with spefici modifications have been either chemical synthesized according to transcriptomics data or PCR amplifed from cDNA of the plants. These modification enzymes include glycotransferase, hydroxylase, methyltransferase, prenyltransferase, isoflavonoid synthease, et al. By assembling these enzymes with suitable promoters and insered into the genome of *Saccharomyces cerevisiae* engineered for the enhanced supply of flavonoid precursors p-coumaric acid and malonyl-CoA, production of common flavonids with ideal titer could be achieved. Collection of more enzymes could finally achieve the customized production of flavonoids by microorganisms.

报告/Topic

The road to animal-free glycosaminoglycan production using metabolic engineering of recombinant microorganisms

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Prof. Mattheos Koffas is the Dorothy and Fred Chau '71 Endowed Professor in the department of Chemical and Biological Engineering at Rensselaer Polytechnic Institute and the Career Development Professor of the Biocatalysis Constellation at Rensselaer Polytechnic Institute since 2011. He received his PhD from MIT in 2001 under the supervision of Professor Gregory Stephanopoulos where he worked on amino acid production from *Corynebacterium glutamicum*. He was a Visiting Research Scientist at DuPont Central Research from 2001 to 2002 where he worked on methanotrophic bacteria, resulting in nine patents. He works in the field of metabolic engineering and systems biotechnology with particular emphasis on the biosynthesis of natural products. He is the Editor of Biotechnology Advances and Metabolic Engineering Communications. He currently serves on the editorial board of several Journals, including the Current Opinion in Biotechnology, Metabolic Engineering, Biotechnology Journal, Biochemical Engineering Journal and Biotechnology and Bioprocess Engineering. He has published 110 peer review papers and holds a number of patents some of which have been commercialized. He was recently elected a fellow of the American Institute of Medical and Biological Engineering society and was selected as the 2018 area 15c Keynote Speaker at the AIChE Annual Meeting.

摘要/Abstract

The field of metabolic engineering has demonstrated rapid growth with particular emphasis on engineering the biosynthesis of small molecules. Far less effort has been placed on the biosynthesis of large molecules, especially large natural products, which present some unique challenges. Some of these challenges include the tight coupling of product and biomass generation, the need to optimize simultaneously several different co-factors and precursors, engineering the transport and shedding of these molecules into the culture medium and engineering the functional expression of biosynthetic enzymes that usually come from mammalian species.

In this talk we will first present the development of a metabolic engineering process for the production of two heavily sulfated glycosaminoglycans (GAGs), namely the anti-coagulant drug heparin and the pharmaceutical/nutraceutical GAG chondroitin sulfate. We will first demonstrate the reconstruction of microbial biosynthetic pathways that allow the production of two unsulfated precursor polysaccharides termed heparosan and chondroitin. These pathways were identified in two pathogenic *E.coli* strains, K5 (for heparosan) and K4 (for chondroitin) and were reconstructed in non-pathogenic *E.coli* strains such as BL21 as well as other recombinant microorganisms (*Bacillus subtilis* and *Corynebacterium glutamicum*). Direct conversion of the unsulfated precursor polysaccharide chains requires the functional expression of multiple sulfotransferases, epimerases and de-acetylating enzymes that in the native mammalian host reside in the Golgi and require glycosylations as post-translational modifications. We will demonstrate the functional expression of such enzymes in simple prokaryotes, such as *E.coli* and *B. subtilis*, as well as unicellular eukaryotic species such as *Pichia pastoris*. Remarkably, only a very precise expression level, controlled by plasmid copy number and promoter strength, is necessary in order to achieve the full functional expression of the enzymes. Finally, we will demonstrate the engineering of *E.coli* strains for achieving high intracellular concentrations of the sulfur donor 3'-Phosphoadenosine-5'-phosphosulfate (PAPS).

The ability to synthesize heparin in the lab at milligram scale enables creative control over parameters that are not available to most labs working with heparin. Specifically, we will demonstrate for the first time the preparation of heavy heparin, or stable-isotope enriched perdeutero-heparin from microbially produced heavy heparosan. We anticipate that the availability of such heavy heparin will allow valuable structural information to be gained utilizing contrast variation small-angle neutron scattering (SANS) for large protein-heparin complex structures that are recalcitrant to crystallization. Furthermore, we demonstrate an application of heavy heparin by monitoring its clearance from rabbit plasma following IV administration, and we show that it exhibits the same *in vivo* half-life as unlabeled heparin.

报告/Topic

The research and development of resources industry chain in *Macleaya cordata*

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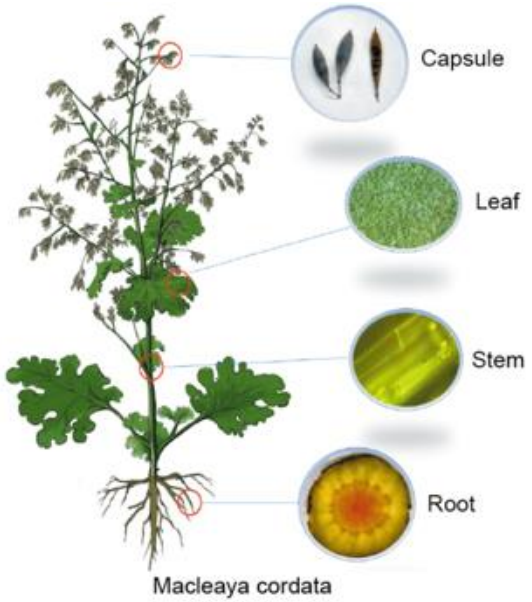
Prof. Jianguo Zeng is widely recognized as one of the forerunners of China's plant extract industry and a leading contributor to many of its technologies. In addition, he is also the lead author of the Whitepaper on the Plant Extract Industry in China. Dr. Zeng's academic and industrial research focuses on investigating the resource ecology, morphology, genetic improvement, cultivation, breeding innovation and metabolic engineering of *Macleaya cordata*, as well as the extraction, purification and pharmaceutical evaluation of its various active ingredients. Prof. Zeng's research lab has achieved the first successful whole-genome sequencing and assembly of *Mycleaya cordata*, and has also published the first reference gene catalog of the chicken gut microbiome. These scientific accomplishments have culminated in the development of two state-reconized class-II traditional Chinese veterinary drugs and proposed a new antibiotic replacement technology for regulating intestinal microbial, anti-inflammation and promoting growth. Prof. Zeng has presided over or participated in over 20 research projects at the national, provincial or ministerial level, and currently serves as the leader of the 13th National Five-Year Key R&D Program on Chinese Veterinary Medicine. He has published over 100 academic papers in Nature plants, Molecular plant, Microbiome and other international journals, and holds over 30 patents.

摘要/Abstract

Macleaya cordata (Willd.) R. Br. is a perennial herb that belongs to the Papaveraceae family and is typically prescribed as a traditional antibacterial medicine, and the sanguinarine is the most important active ingredient in *M. cordata*. This report describes the research of Prof. Zeng 's team for more than 20 years. Including the following content: successful development of two state-reconized class-II traditional Chinese veterinary drugs and two preparations; achieved the first successful whole-genome sequencing and assembly of *M. cordata*, and has also published the first reference gene catalog of the chicken gut microbiome， additionally, elucidation the mechanisms of sanguinarine and chlortetracycline on the regulation of intestinal microbial; proposed a new antibiotic replacement technology for regulating intestinal microbial, anti-inflammation and promoting growth. This topic also reports on the following research progress in *M.cordata*: morphology and ecology, breeding and cultivation, new ingredient discovery, extraction process, comprehensive utilization of resources，anti-inflammatory mechanism, etc.



Macleaya cordata

报告/Topic

Microbial production of medicinally important plant natural products

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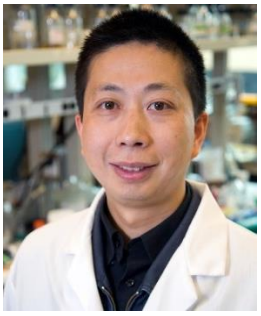
Jixun Zhan



Prof. Jixun Zhan received a Ph.D. in biochemical engineering from East China University of Science and Technology in 2003, and conducted postdoctoral training at the University of Arizona and the University of California, Los Angeles. He joined the Department of Biological Engineering at Utah State University as an assistant professor in 2008 and was promoted to full professor in 2017. Dr. Zhan leads a metabolic engineering laboratory at USU, and his research is focused on metabolic engineering and natural product biosynthesis. He is particularly interested in discovering new bioactive molecules, understanding the biosynthetic mechanisms, and rationally generating novel derivatives through engineered biosynthesis. His research has been published in a number of peer-reviewed journals such as *Nature Communications*, *Journal of the American Chemical Society*, *Metabolic Engineering*, and *Proceedings of the National Academy of Sciences of the United States of America*.

摘要/Abstract

Medicinal plants are a major source of bioactive molecules, such as resveratrol, curcumin and emodin. However, production of these health-benefiting natural products relies on large scale growth and extraction of the producing plants, which is often resource-intensive and time-consuming. Metabolic engineering and synthetic biology have become useful tools to enable efficient and sustainable production of plant natural products. This talk discusses how two different microbial hosts were engineered for the capability to produce desired molecules. In the first work, we used a “biosynthetic lego” approach to produce plant natural products in *Escherichia coli*. A library of biosynthetic legos was established using genes from different sources including bacteria, fungi and plants. Different combinations of these biosynthetic legos yielded four phenylpropanoid acids (cinnamic acid, *p*-coumaric acid, caffeic acid, and ferulic acid), three bioactive natural stilbenoids (resveratrol, piceatannol and pinosylvin), three natural curcuminoids (curcumin, bisdemethoxycurcumin and dicinnamoylmethane), as well as two "unnatural" natural products (dicafferolmethane and 2-chloro-resveratrol). Emodin is an active ingredient in many herbal medicines. In the second project, we identified an emodin biosynthetic gene cluster from *Shiraia sp*. and reconstitute the pathway in *Saccharomyces cerevisiae*. Several metabolic engineering approaches were used to enhance the production of emodin in the yeast.

报告/Topic

Pathway-specific Enzymes from the Leaves of Bamboo and Crops Biosynthesize the Antinociceptive Agent Isoorientin

*Yuwei Sun1, #, Jingya Yang3, #, Zhuo Chen1, 2, #, Ishmael Mutanda1, Qian Zhang1,2, Ying Zhang1,2, Shiyi Li3, Yong Wang1, **

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Prof. Wang Yong, professor / principal investigator of the CAS-Key Laboratory of Synthetic Biology, Institutes for Biological Sciences, Chinese Academy of Sciences. He obtained his Ph.D degree of biochemical engineering from East China University of Science & Technology, China in 2004 and was trained as a post-doctoral fellow at Department of Chemical and Biological Engineering in Tufts University, USA during Feb 2005 to Aug 2008. His research is centered on the design and assembly of recombinant microorganisms for the production of complex natural products. A particular focus is the elucidation of design principles for the production of unnatural natural compounds within the framework of the nascent field of synthetic biology. More than 70 papers have been published.

摘要/Abstract

The current crisis of opioid overdose has generated an urgent need for developing alternative analgesics from safer natural sources. Plant-derived *C*-glycosylated flavones (CGFs) are promising candidates as antinociceptive compounds with additional medical benefits. However, the effective exploitation of these compounds have been hindered by a poor understanding of the biosynthetic machinery in plants, as well as the inadequately defined pharmacokinetic mechanisms. The leaves of bamboo (*Bambuseae*) and related crops in the grass family are a largely unexploited bioresource with potential to produce a wide array of CGFs with medicinal value including pain alleviation. We report here novel *C*-glycosyltransferases (CGTs) and P450 hydroxylases from cereal crops and the bamboo species that accumulates high amounts of *C*-glycosylated flavones. Through comparative genomics and biochemical approaches, we revealed the evolutionary history of Gramineae-specific CGTs that confer chemical diversity to flavonoid *C*-glycosides. The characterized CGTs from multispecies are diverse enzymes transferring glucosyl or arabinosyl substitutes to the chalconoid substrates via stepwise or tandem glycosylation reactions. Mining and engineering of cytochrome P450s that decorate the flavonoid skeleton allowed the production of desired *CGFs* in an *Escherichia coli* cell factory. We explored the antinociceptive activity of major CGFs in mice models and identified isoorientin as the most potent, with comparable or better efficacy to commercial standards. Our discovery of the pain-alleviating flavonoids elicited from bamboo leaves establishes this previously unknown abundant source, and sheds light on the pathway and pharmacokinetic mechanisms of the compounds.

报告/Topic

Study on the preliminary process of medicinal plant materials

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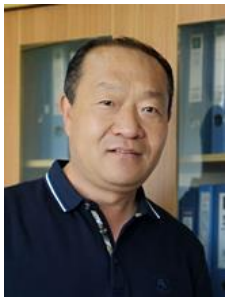

Professor Wen-yuan Gao is the Chair professor at department of TCM and natural products, Tianjin University. He is the secretary-general in the association of medicinal plant resources, World Federation of Traditional Chinese Medicine. He has foucused on his research on meoderna study of medicianl plant resources, including resource survey, medicinal plant tissue culture, process of TCM and developing functional food and new drugs from TCM. The industry culture of ginseng has established an company and one funcitonal food for relieving cough and asthma has gone to market. He has published more than 300 SCI papers and issued 5 books. By the way, he has also got 20 patents.

摘要/Abstract

The process of TCM is the key technology for its function formation, which is the weak point of the TCM study. The different process of TCM could produce different pharmaceutical functions with one medicinal plant material. During the past several years, we have carried out the process research on more than 50 kinds of medicinal plant materials, such as rheum officinale, Rhizoma Dioscoreae, papaya, Angelica sinensis, rhizoma gastrodiae, etc. The chemical constituent changes were determined before and after process by HPLC、GC、HPLC-MS、GS-MS, and also we conduct the pharmacokinetic and pharmacodynamic studies during the process of medicinal plant material. Based on the above study, we decide the Q-marker for the quality control of process of medicinal plant material. The traditional process methods of medicinal plant material have been c onducted for thousands of years, it should be improved by modern methods. However, some key technical links should be folowed with the modification by modern techniques.

Key words: Preliminary process, TCM, Q-marker.

经典名方会场
Classical Prescription

（桂冠二厅/Laurel Hall II）

2019-06-29，8:40-12:30

报告/Topic

中药经典名方研发的背景和要点

中国中医科学院

叶祖光，中国中医科学院首席研究员、博士生导师、国务院特殊津贴专家，973 中药项目首席科学家，中药安全评价中心(GLP)主任。中国中医科学院获中药药理学硕士学位，1986-1989 和 1992-1994 先后两次在美国西弗吉亚大学药理毒系访问学者。几十年来主要从事中药药理毒理学研究工作以及中药新药和保健品的研发工作。作为课题负责人承担了各种级别的国家研究课题 30 余项，其中获不同级别的成果奖 9 项。分别在国内学术期刊上发表论文百余篇，作为主编、副主编、编委编著学术著作 12 部。还担任：世界中医药联合会中药新型给药系统专业委员会主任、中药药理专业委员会副主任委员、中国中医药信息杂志主编以及中医药现代化杂志副主编等兼职工作。主要研究方向：中药药理毒理学以及中药新药和保健品的研发。

报告/Topic

经典名方共性问题的困惑与思考

中国中医科学院

张保献（1962.9～），男，河南省邓州人，中国中医科学院中药研究所研究员、博士生导师。中药雾化吸入制剂研究中心执行主任。1982 年河南中医学院中药系本科毕业，同年到河南省云阳中医药学校任教，1990 年获黑龙江中医药大学硕士学位，同年到中药研究所工作。长期以来致力于中药新剂型研究与新药开发。承担国家各级课题 30 多项。获得新药证书 12 个、授权发明专利证书 75 个。“常用中药饮片研究”获 1997 年度国家中医药局科技进步一等奖（主要参加者）；获中医研究院科技进步奖三等 2 项（主要参加者）。社会兼职：国家药典委员会制剂专业委员会副主任委员、2. 国家食品药品监督管理总局药品审评专家、国家食品药品监督管理总局保健食品审评专家、国家食品药品监督管理总局保健食品安全评估专家、国家食品药品监督管理局医疗器械审评专家、中国医药保健品进出口商会专家、世界中医药学会联合会新型给药系统专业委员会副主任委员、世界中医药学会联合会中药保健品专业委员会副主任委员、中国中药协会菌物专业委员会副主任委员、中国民族医药学会临床评价专业委员会副主任委员。

摘要/Abstract

基于历史文献出处，历代沿革和现代应用的考证分析，对经典名方的剂量，所用基原及药用部位的演变，炮制方法的沿革，煎煮方法确认与研究等方面，从不同的纬度进行了分析与思考，揭示了几种不同的结果可能性预测。同时又通过实验数据的分析和验证，对关键质量属性，量值传递以及标汤投料和煎药方法，物质基准的制定等问题，进行了探讨和思考，疑难问题进行了分析，为大家经典名方的研究提供多方位的参考。

报告/Topic

基于质量属性辩识与表征的中药经典名方制剂一致性研发策略

天津医药研究所

张铁军，男，1962 年 2 月出生。现任天津药物研究院中药部主任、研究员，天津医科大学、天津中医药大学硕士生导师，享受国务院特贴专家，天津市授衔专家。社会兼职：中国药学会中药与天然药物专业委员会委员；中华中医药学会中成药专业委员会常务委员；中国植物学会药用植物与中药专业委员会委员；世界中医药联合会中药给药系统专业委员会常务理事；天津药学会副秘书长，天津市植物学会秘书长；天津市中药现代化专家组专家；天津市新药审评专家；《医药科技与信息》特约编委，《中草药》、《中国药学年鉴》编委；天津大学化工学院兼职教授；天津中医学院硕士研究生导师，天津大学药学院联合博士生导师；享受国务院特殊津贴；天津市授衔专家。主持天津市攻关重大项目两项，天津市攻关培育项目一项，主持新药研究项目共 12 项；获 3 项国家发明专利授权，在国内外重要刊物上发表学术论文 20 余篇，出版学术专著 6 篇。专业领域：主要从事中药新药研究与中药资源研究。

摘要/Abstract

本文针对经典名方制剂一致性评价要求及其技术焦点问题，提出基于质量属性辨识与表征的一致性评价策略。首先从质量属性与有效性的“相关性”及其作为一致性评价的“可及性”角度，论述其作为一致性评价“抓手”可行性；进一步，结合研究实例剖析了质量属性的科学内涵，从中药质量的本草学属性、生物学内涵、化学实质以及生物效应表达方式等四个方面，论述了中药质量属性的科学内涵与表征方法；最后，从处方考辨、物质基准获取、质量属性辨析与表征、质量属性传递以及一致性评价与全程质量控制等五个方面论述了质量属性的应用。

报告/Topic

中药经典名方质量分离分析方法

中国科学院大连化学物理研究所

梁鑫淼，男，博士，中国科学院大连化学物理研究所研究员，博士生导师，国家杰出青年基金获得者，分离材料化学与组分中药研究组组长。1987 年大学毕业于杭州大学化学系，1987-1992 年博士就读于大连化物所分析化学专业，师从卢佩章院士和张玉奎院士。1994 年赴德国环境与健康研究中心从事合作研究。主要从事新型分离材料、多维分离方法与技术、天然药物、制备色谱技术及制药工艺应用等方面的研究。已发表 SCI 论文 370 余篇，申请中国发明专利 140 余项，申请 PCT 专利 4 项，获授权专利 63 项，参与编写专著 9 部，已培养研究生 90 余名，博士后出站 10 名。曾获辽宁省自然科学一等奖和二等奖（2001 年，2014 年）、获天津市自然科学一等奖（2006 年）、中科院“青年科学家奖”（1995 年）等。

报告/Topic

经典名方——中医药传承发展的突破口

中国医学科学院

杨洪军，男，1972 年 7 月生，医学博士学位，研究员，博士生导师。主要从事中药新药设计的理论与技术研究、中药防治血管性疾病的基础研究。学术兼职为中国中西医结合学会青年工作委员会副主任委员、全国中药标准化技术委员会副秘书长，北京生物医学工程学会中医工程委员会主任委员。根据中西药研发路径的不同，提出中药新药设计的基本框架，即以“组效关系”与“构效关系”相结合，包括：基于临床数据与文献信息的中药新药处方发现、基于计算与实验相结合的中药有效成分辨识、基于系统建模的中药新药组方优化。按照 “化学指纹-代谢指纹-网络药理学”的研究思路，对元胡止痛片进行了系统研究。提出含药肠吸收液的体外药理研究方法，并成功应用于脑心通胶囊对心肌细胞保护作用研究。近 5 年来，主持多项国家级课题，包括：国家科技基础条件平台项目，国家自然科学基金重点项目，国家科技支撑计划课题，国家重大新药创制专项课题等；获国家科技进步二等奖 2 项（排名第九、第十一），中国中西医结合学会科学技术二等奖 1 项（排名第一），获得中国中医科学院科技进步二、三等奖各 1 项（均排名第一）；近 5 年发表学术论文 40 余篇，其中 SCI 论文 12 篇，主编著作 2 部；主持开发中医传承辅助系统，获得软件著作权 3 项，获得发明专利和实用新型专利各 1 项。

中药标准导向的基础研究会场 II

Standard-oriented basic research of traditional Chinese medicine II

（桂冠三厅/Laurel Hall III）

2019-06-29，08:40-12:30

报告/Topic

Quality control and sustainable sourcing at the time of the blockchain technologies. What are the opportunities?

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Michael Heinrich is a Professor of Ethnopharmacology and Medicinal Plant Research (Pharmacognosy) and was until recently the head of the research cluster 'Biodiversity and Medicines' at the UCL School of Pharmacy. He currently serves as the joint chair of UCL's Research Ethics Committee (with Dr. L. Ang, Institute of Education).

The group's research is based on a transdisciplinary perspective integrating approaches from the biomedical and social sciences with an overall aim of tackling the fast changing global health needs. Key areas of interest include the prevention and early stage management of diabetes / metabolic syndrome and cancer chemoprevention based on the use of traditional medicines as well as value chains of (herbal) medicinal products. The research integrates methodological approaches from ethnopharmacology, natural product research, public health research, and anthropology.

He is Specialty Editor in Chief of Frontiers in Pharmacology (Ethnopharmacology) and Reviews Editor of the Journal of Ethnopharmacology as well as an associate editor of the Journal of Pharmacy and Pharmacology, among other roles.

摘要/Abstract

Ethnopharmacology started as a science engaging with traditional knowledge and today it is faced with an ever increasing global network of trade in goods. Knowledge about medicines, also has become a global 'good'. With 'traditional medicines and foods becoming world-wide commodities, numerous challenges have become even more into the centre of discussion, including the quality of the material sold, sustainable sourcing, equitable sharing of benefits and the need for a better understanding of health benefits and risks of such products. Blockchain systems are currently discussed in many areas of an ever more globalised economy. It is a fast emerging technology for a decentralised cryptographically-enhanced digital ledger recording transactions among stakeholders. This presentation looks at blockchain's potential uses in the context of high value and mostly low volume botanical material traded globally and used as medicines, health foods, in cosmetics and other applications.

The presentation gives a perspective on key areas in the supply of such products globally and how blockchain systems may help in overcoming the challenges listed above (Heinrich *et al* 2019). Both open and closed blockchain systems are possible options and based on the industrial demand it seems likely that, at least in the initial development, closed systems are the main ones to be utilized. The potential of Blockchain systems needs to be addressed within the context of ethnopharmacology and we need to understand what can and what cannot be achieved with this new technology.

报告/Topic

Andrographolide from the “King of Bitters”: strategies to overcome the blood–brain barrier

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Prof. Dr. Anna Rita Bilia is associate professor at the University of Florence. She is Director of the Post-graduate School of Hospital Pharmacy. In 1995 she got the national award "Claudio Redaelli" of the Italian Society of Phytochemistry and in 2002 she got the international "Egon Stahl Medal" of the Society for Medicinal plant and natural product Research, working in natural products. In 2018 she got the international “Qihuang Prize “ of the Academia of Chinese Medicine. She is leading the group of natural products analysis and pharmaceutical technology at the Department of Chemistry. She is expert of the European Pharmacopoeia and member of the TCM group. She is president of the International Society for Medicinal Plant and Natural Product Research (GA). She is the Italian delegate of the board of directors and member of the scientific committee of the European Scientific Cooperation on Phytotherapy (ESCOP) since 1997. She has been president of the scientific Italian Society of Phytochemistry and Sciences of Medicinal, Food and Fragrant Plants (SIF) from 2012 to 2018. Prof. Bilia’s list of publications shows more than 250 papers in the most reputed international journals of her field of research, she is authors of numerous invited book monographs and chapters.

摘要/Abstract

Andrographolide (AG) is the main and characteristic constituent of *Andrographis paniculata* (Burm.f.) Nees, of the *Acanthaceae* family. This plant is a well-known Asian medicinal plant that is widely used in India, China, and Thailand, generally denominated the ‘‘King of Bitters”: A monograph of Herba Andrographidis (Chuan Xin Lian) is included in the Pharmacopoeia of the People’s Republic of China, which reports that this decoction can ‘‘remove heat, counteract toxicity,

and reduce swellings.” The numerous potential activities of AG range from anti-inflammatory to antidiabetic action, from neuroprotection to antitumor activity, and from hepatoprotective to anti-obesity properties. However, AG has low bioavailability and poor water solubility, which can limit its distribution and accumulation in the body after administration. In addition, AG is not stable in gastrointestinal alkaline and acidic environments, and has been reported to have a very short half-life [1]. Among the diverse strategies that have been adopted to increase AG water solubility and permeability, the technological approach is the most useful way to develop appropriate delivery systems. In recent years, the possible significant role of this molecule in many diseases of the central nervous system has stimulated the development of blood–brain barrier (BBB)-targeting technologies, principally nanoparticles. These include polymeric nanoparticles (based on human serum albumin and poly buthylcyanoacrylate); solid-lipid nanoparticles, vesicles. Improved in vitro permeation properties through PAMPA systems and hCMEC/D3, brain-tissue distribution, and efficacy of AG loaded in the described drug delivery systems have been reported [2,3].

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报告/Topic

Liquids in discovery of natural products

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Prof. Krystyna Skalicka-Woźniak is the Head of The Medicinal Plant Unit, Medical University of Lublin. Her research interests include the discovery of bioactive compounds in plants, and the optimization of modern extraction and chromatographic techniques. The focus of her work for the past years was the application of counter-current chromatography (CCC) for the isolation of natural products, particularly coumarins and terpenoids, and their biological evaluation- mostly for antimicrobial, antiviral activities, as well as for Central Nervous System activity (epilepsy, anxiety and memory-related behavior in mice and zebrafish models). Her experience with CCC was acquired through a training period in a world-leading research center, the Brunel Institute of Bioengineering at Brunel University in London, and she is currently the leading practitioner of the applications of this technique in Poland. She is currently serving as a Subject Editor of the journal Phytochemistry Letters (Elsevier) and as General Secretary of Phytochemical Society of Europe and Advisory Board Member of Society for Medicinal Plant and Natural Product Research (GA).

摘要/Abstract

Separation of the natural products is extremely challenging, not only because the different polarities of molecules but also many bioactive compounds are very rare and easily lost during the preparation and separation. To address these issues, it is necessary to develop systematic separation methodology and to find highly efficient method for separation. The development of a purification protocol to pull an active, target molecule from the many hundreds that may be present in a mixture is an extremely challenging task. Countercurrent separation CCs, as a liquid-liquid technique, has a special place in the isolation of natural products and has been applied for the purification of chemical compounds in complex matrices due to its unique advantages. “Powerful liquids” let to build the platform between isolation and in vitro and in vivo screening of natural products. One of the very interesting “hyphenation” is that between CCs and the zebrafish in vivo model, which became increasingly used in key areas of neuroscience. The zebrafish share a homologous genome with vertebrate species and have numerous similar neural and physiological systems and share some key receptors that play an important role in the etiology of neurological disorders. The zebrafish epilepsy model with seizures induced by the GABAA antagonist pentylenetetrazole (PTZ) as well as light-dark transitions to monitor the isolation of anticonvulsant principles and those related to anxiety-like behavior will be presented during this lecture.

报告/Topic

Quality Control of Botanicals Using USP Monographs: HPLC and HPTLC Identify American Ginseng and Asian Ginseng, Distinguish Closely Related Species

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Dr. Cuiying (Macy) Ma is a Senior Scientific Liaison at U.S. Pharmacopeial Convention (USP) responsible for reviewing monograph submission and monograph development for botanical dietary supplements and traditional herbal medicines. Dr. Ma joined USP in 2006 as a Reference Standards Scientist until 2013 focused on botanical reference standards development and evaluation. Before joining USP, she performed research on bioassay guided isolation, structure elucidation of bioactive compounds from plants at Pharmacy College, University of Illinois at Chicago. She worked for eight years in the National Institute for the Control of Pharmaceutical and Biological Products (NICPBP, current name is NIFDC), Beijing, China as associate professor and assistant professor, focused on quality control methods development for Traditional Chinese Medicines (TCM). Dr. Ma holds a Ph.D. degree in natural products chemistry from the Hong Kong University of Science and Technology; a M.S. degree in analytical chemistry; and a B.S. degree in pharmacy (TCM) from Beijing University of Chinese Medicine and Pharmacology.

摘要/Abstract

The botanical monographs in *United States Pharmacopeia* and the *Herbal Medicines Compendium* define appropriate quality for botanical dietary supplements and herbal medicines, with science-based standards that include multiple interrelated tests. Selective chromatographic procedures, such as HPLC and HPTLC, are powerful methods to identify plant products and distinguish closely related species. USP monographs of American Ginseng, American Ginseng Extract, Asian Ginseng, and Asian Ginseng Extract are under revision to use a new UHPLC and a new HPTLC method. The chromatographic profiling of ginsenosides by both UHPLC and HPTLC can efficiently identify American ginseng and Asian ginseng, distinguish each other, and also distinguish from red ginseng and notoginseng. The acceptance criteria for HPLC involves content ratios and relative peak intensity of ginsenosides to differentiate different ginsengs and Asian ginseng from different plant parts in addition to peak location through comparison with the chromatograms of standard solutions and the reference chromatogram provided with USP botanical extract reference standard. Determination of the total content of ginsenosides provides a surrogate measurement for strength in both American ginseng and Asian ginseng.

报告/Topic

Discovering characteristic chemical markers for inspecting sulfur-fumigated herbs and relevant products

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Prof. Song-Lin Li is currently as the head of department of Pharmaceutical Analysis & Metabolomics, Jiangsu Province Academy of Traditional Chinese Medicine. He has kept his research interests on bioactive components and quality control of traditional Chinese medicine for more than 30 years. In the near decade, he focused on the establishment of a research system for the specific inspection of sulfur-fumigated herbs and their relevant products, which was successfully applied in "Specification for Chinese Medicinal Decoction Pieces in Jiangsu Province" for the herbal standards; and the newly-developed methods were also used by some herbal companies and medical institutions for the inspection of potential sulfur-fumigated raw materials and relevant products. Professor Li has published over 200 papers, among which over 100 in SCI cited journals.

摘要/Abstract

Sulfur-fumigation has been used for moth proofing and mold prevention of a few Chinese herbs for about one century. However, this processing method has been abused in the last decade during postharvest handling and storage of many herbs because of the lower cost, convenient in operation, and some illegal purposes such as bleaching herbs for higher profit. Recent studies demonstrated that sulfur-fumigation could result in not only residue of hazardous substances (sulfur dioxide (SO_2) and heavy metals), but also significant alteration of chemistry, pharmacokinetics and pharmacodynamics of herbs. So inspecting sulfur-fumigated herbs is critical in guaranteeing the quality, and thus the efficacy and safety of herbs. SO_2 residue is currently used as a marker to inspect the sulfur-fumigated herbs in Chinese Pharmacopoeia, United States Pharmacopoeia and Europe Pharmacopoeia. But accumulated studies found that SO_2 residue method may lead to false negative result. Furthermore, this method is non-specific when used for the inspection of complex products that prepared from one or more sulfur-fumigated raw materials. Therefore, it is necessary to find new markers that can be used specifically inspecting sulfur-fumigated herbs and their relevant products. In this study, I will present an LC-MS based metabolomics strategy for rapidly discover characteristic components of sulfur-fumigated herbs, and with the characteristic components as chemical markers, the method development and validation for the specific inspection of sulfur-fumigated herbs and their relevant products, as well as a monograph for the quality control of potential sulfur-fumigated herb, using six commonly used Chinese herbs and their relevant dispensing granule or complex products as examples.

报告/Topic

A strategy for identification and structural characterization of sesquiterpenoids from Tussilago farfara L.by multiple scan modes of mass spectrometry

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Prof. Yeong Shik Kim is currently as the professor of College of Pharmacy, Seoul National University and keeps the joint professorship of Natural Products Research Institute at the same university. His main interests are firstly focused on testing anti-inflammatory and antioxidant activities regarding herbal extracts and pure substances isolated from medicinal herbs. Second, he is working on target-based anticancer agents from natural products by the inhibition of transcriptional factors as well as blocking receptor binding. Third, he is developing the method for the preparative separation of natural products and studying the both in vitro mechanism and in vivo metabolism of these compounds, including anti-inflammatory, anticancer and neuroprotective activities. Overall, he is actively involved in discovery and development of new drugs from the resources of natural products. He has published over 350 papers in peer-reviewed journals.

摘要/Abstract

Tussilago farfara is a perennial medicinal plant that belongs to the Asteraceae family. Dried flower buds of *Tussilago farfara* (Farfarae Flos) are being used for treating severe cough, bronchitis, and asthmatic conditions. Farfarae Flos contains sesquiterpenoids composing of oplopane and bisabolane types substituted with diverse ester derivatives and about 30 sesquiterpene esters have been reported. Nevertheless, LC-MS-based analytical studies on the sesquiterpenoids and their fragmentation behavior have not been reported except for tussilagone, which is a chemical marker in Chinese Pharmacopoiea 2015. It is generally difficult to separate and characterize complex mixture of sesquiterpenoids because of their structural diversity. Therefore, we developed a reliable profiling strategy for the sesquiterpenoids from the enriched fraction. In our present study, an MS/MS dereplication strategy for the sesquiterpene esters was proposed and the sesquiterpenoid-enriched fraction from the Farfarae Flos was successfully profiled. Four diagnostic ions (*m/z* 215, 217 for oplopane and *m/z* 229, 231 for bisabolane) were selected and their fragmentation patterns were investigated to develop the dereplication method. The precursor ion scan mode of triple quadrupole (QqQ) mass spectrometry was applied to identify parent molecular ions of these diagnostic ions. Each fragmentation pattern of the selected precursor ions was investigated using the product ion scan mode of quadrupole time-of-flight (QTOF) mass spectrometry. Using the UHPLC-MS/MS workflow, 74 oplopane and bisabolane sesquiterpenoids of Farfarae Flos were identified and the fragmentation behaviors of the annotated compounds were analyzed. Furthermore, 11 sesquiterpenoids were separated from the STE fraction and structurally determined to validate the developed method. The suggested precursor ions and the corresponding diagnostic ions highlighted the presence of the sesquiterpene esters in the medicinal plant, and were applied to

sensitive quantification of these classes of compounds. Furthermore, the developed method could be used for screening and quantification of other sesquiterpene ester.

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报告/Topic

Highlighting Fractionation in Natural Products Analysis and Drug Discovery

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Dr. Xing-Cong Li received B.S. in Medicinal Chemistry from Shanghai Medical University M.S. in Phytochemistry from Kunming Institute of Botany, Chinese Academy of Sciences, and Ph.D. in Pharmaceutical Science from Hiroshima University, Japan. He is currently a Principal Scientist in the National Center for Natural Products Research at the University of Mississippi, USA. His contributions to science are reflected in more than 150 peer-reviewed publications (h-index 37) in the research areas of antimicrobial natural products discovery, development of natural product dereplication approaches, and determination of absolute configuration of natural products by computational chemistry. Dr. Li served scientific communities as Editor-in-Chief for Research and Reports in Medicinal Chemistry, Associate Editor for Current Organic Chemistry, an editorial board member for seven journals, and a reviewer for NIH Study Section, US Department of Defence Infectious Diseases Panel, and National Natural Science Foundation of China.

摘要/Abstract

Fractionation, including high throughput automated fractionation, is the basic chromatographic technique in natural products chemistry to generate fractions and eventually purified compounds from complex extracts of plants, marine organisms, and microbes. Coupled with biological activity testing, bioassay-guided fractionation approach has historically contributed to natural products analysis and drug discovery tremendously, as exemplified by the development of life-saving antimalarial drug artemisinin and anticancer drug taxol. In the current omics era, advanced analytical and chromatographic technologies have been utilized to complement the conventional bioassay-guided fractionation, creating unique platforms capable of performing comprehensive chemical and biological screening to discover novel chemical entities. It must be pointed out that for any natural products drug discovery platform, fractionation is the critical element that can be manipulated to improve discovery potential. In this presentation, the author describes several approaches of fractionation and how to best use these approaches, in conjunction with advanced spectroscopic techniques and databases, to address fundamental challenges of rediscovering known bioactive compounds. Examples for dereplication of known antimicrobial compounds and identification of new bioactive compounds are given. The fractionation approach that may be effectively used for the analysis of complex traditional Chinese medicine is also discussed.

报告/Topic

Innovation, Science and Research in a Contract Lab

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Dr. Aihua Liu currently is as Director of R&D at Dyad Labs in USA, and Director of Chromatography Department at Dyad Labs in USA. Prior to joining Dyad Labs, she was the Team Leader of the bioanalytical method development group at Covance, which was supporting pre-clinical and clinical trials testing. She holds a Ph.D. degree in Pharmacognosy, an M.S. in Pharmaceutical Chemistry, and a B.S. in Pharmacy. In the past 12 years, she has focused her research on developing and validating novel methods for bioanalytical analysis and dietary supplemental analysis using diverse state-of-the-art technologies (UPLC/HPLC, GC, MS, PDA, and FLD) under GLP and GMP regulations. She also has extensive experience in lab management, improving the efficiency and throughput of sample analysis. She has authored more than 30 peer-reviewed scientific articles and presented over 32 publications in different international scientific conferences.

摘要/Abstract

An ideal strategy to testing samples is to use an independent, accredited contract lab. One approach that a contract lab uses when developing a method is to use a compendia method, which is validated and has credibility within the industry. However, many compendia methods are time-consuming and labor-intensive, use old technology and are cost-prohibitive since it was developed years ago. Furthermore, many analytes and matrix are not included in the compendia method. In such situations, the contract lab has to perform further development to obtain a suitable method. In this talk, three case studies show how a contract lab develops new methods innovatively.

Case I is a quantitative method for analysis of Vitamin B_{12} by LC/MS/MS. The stability of B_{12} has been evaluated with different pH, temperature and light exposure. The stability data indicates that B_{12} is very sensitive to light and temperature. Sample extraction has to be conducted under yellow light and ice water to stabilize the standard and samples during sample process. Different columns and mobile phases have been screened to optimize the chromatography conditions. The DV% value of vitamin B12 is much lower compared to other vitamin B families and the serving size of different samples varies broadly. Two curves at high and low concentration were used to cover various types of sample. The method has been successfully validated and applied for sample analysis. **Case II** is a quantitative method for analysis of pesticides by GC/MS/MS and LC/MS/MS. Method development was started from USP and AOAC compendia methods. However, these extraction methods are not suitable for botanical and non-botanical dietary supplement samples. Method development focused on optimizing the extraction procedure. Analyte protectant solutions are used in sample extraction and injected to improve extraction recovery and chromatography. Back flush system on the column was applied on GC program to have a short run time of 20 min for all 112 pesticides. The method has been successfully validated in 12 different matrices. **Case III** is a qualitative method for protein identification by LC/MS/MS. Kjeldahl and Dumas methods have been extensively used to identify and quantify proteins. However, these methods measure N_2 amount and are not specific. In order to develop a specific method, trypsin has been used to digest proteins including whey, casein, rice, pea, and soy into

different peptides. Three relatively unique peptides from each protein source is monitored using LC/MS/MS to identify these proteins in samples. This method has been successfully validated and hundreds of samples have been analyzed. In 2018, this method has granted official first-action status from AOAC.

In order to develop fast/high throughput and robust method and cover new analytes/matrices, the contract lab has to develop and validate novel methods; such methods should be considered for submission to AOAC and USP to be new or more improved compendia methods.

报告/Topic

Antiosteoporotic investigation of traditional Chinese medicine for tonifying kidney, focusing on integrative mechanism

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Prof. Lu-ping Qin is currently the dean of the College of Pharmaceutical Sciences, Zhejiang Chinese Medical University. His researches are focused on: (1) Pharmacognostical, Phytochemical and Pharmacological researches on traditional Chinese medicines, especially with the activities of anti-osteoporosis and anti-rheumatoid arthritis. (2) Researches on endophytic fungi of medicinal plants, and their effects on the quality of traditional Chinese medicines. He has published 15 academic books and over 200 papers in SCI cited journals, been issued with 33 patents, and received several awards and prizes including National Science and Technology Progress Award.

摘要/Abstract

Osteoporosis, a chronic epidemic, is characterized by low bone mass and microarchitectural deterioration of bone tissues, leading to enhanced bone fragility and consequent increase in fracture risk. Traditional Chinese medicines (TCM) have a long history of use in the prevention and treatment of osteoporosis on the basis of theory "kidney dominating bone". The current progress of TCM for the prevention and treatment of osteoporosis were summarized and put forward the prospects in the future. Furthermore, our research in TCM anti-osteoporosis were introduced as example of Er-Xian Decoction, *Morinda officinalis* How, *Curculigo orchioides* Gaertn and *Rehmannia glutinosa* Libosch focusing on their integrative mechanism. Er-Xian Decoction, which is composed of six herbal medicines with *Epimedium* herbs being its major ingredient, has been found that the active constituents synergistically modulate the bone metabolism, and then decrease the bone loss. *Morinda officinalis* How has been used as a kidney tonic and for strengthening bones in TCM, the iridoid glycosides, polysaccharides, oligosaccharides and anthraquinones are characteristic chemical constituents and regulated bone metabolism through NF-κB, BMP and Wint/β-catenin pathway. *Curculigo orchioides* Gaertn has been found to reduce bone loss via anti-oxidation, and the phenolic glycosides protects against oxidation-induced bone loss by involving the regulation of FoxO1 pathway. *Rehmannia glutinosa* Libosch, which has been used in the treatment of *yin* deficiency syndrome in TCM, decreased bone loss through involving regulation of the steroid synthesis and IGF-1/PI3K/mTOR. These investigations maybe provide some insights for the elucidation of antiosteoporotic effects and mechanism of TCM for tonifying kidney.

Keywords: traditional Chinese medicine for tonifying kidney; osteoporosis; integrative mechanism

闭幕式大会报告

Standard-oriented basic research of traditional Chinese medicine II

（桂冠厅/Laurel Hall）

2019-06-29，14:00-16:45

报告/Topic

Toward a Traditional Medicine Category in the United States: Is the Time Right?

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Mr. Loren Israelsen is the founder and president of the United Natural Products Alliance (UNPA), a trade association of dietary supplement companies committed to safety, science and quality. He has been deeply involved in commercial, regulatory and political issues facing the global dietary supplement industry since 1980. He served as president of Nature's Way Products and has held industry positions including vice president/general counsel to the American Herbal Products Association, co-founder of the European American Phytomedicine Coalition (EAPC), industry liaison to FDA's Expert Advisory Committee on Ephedra, industry advisor to the Office of Dietary Supplements (ODS), expert panel member on IFT's Functional Food Report, and sat as an expert panel member to the Department of Defense/Rand study on dietary supplement use among military personnel. He was also an active participant in the introduction and passage of the Dietary Supplement Health and Education Act of 1994.

摘要/Abstract

2019 marks the 25th anniversary of the U.S. law, the Dietary Supplement Health and Education Act (DSHEA), which granted botanicals status as a food. Today's health consumers support natural and traditional medicines. Is this the time to open up the U.S. to traditional medicines?

报告/Topic

Seasonal Control of Flowering times

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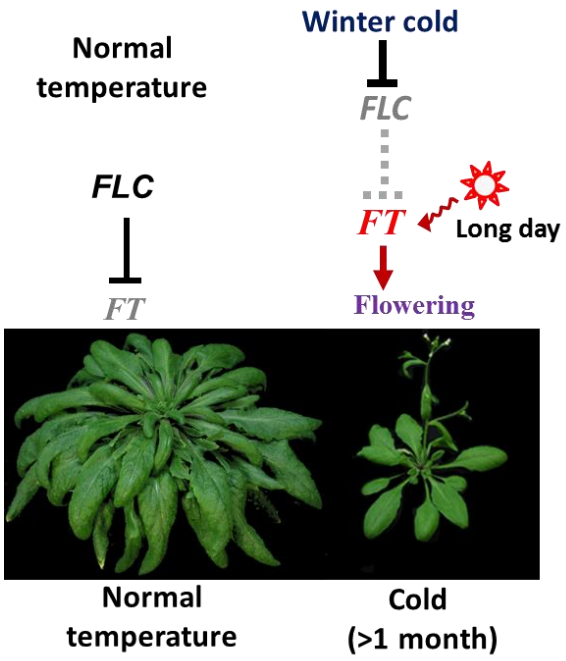
Prof. Yuehui He currently is a senior principal investigator and deputy director at the Shanghai Centre for Plant Stress Biology (PSC), Chinese Academy of Sciences (CAS). He earned his Ph.D. degree from the University of Kentucky (USA) in 2001, and was a tenured faculty member in the Department of Biological Sciences at the National University of Singapore (NUS) prior to his joining PSC in 2013. Prof. He's research has been focusing on plant environmental epigenetics with a goal to elucidate molecular epigenetic mechanisms underlying how plants flower at a 'right' season to maximize reproductive success. As a leading or correspondence author, he has published six research articles in top journals including *Science*, *nature*, *nature genetics*, and *nature biotechnology*. His research has advanced the understanding of how winter cold, through a process termed as vernalisation, enables plants to flower in spring and how day length changes, through the photoperiod pathway, induce flowering in plants.

摘要/Abstract

Plants must adapt to local environment and make adaptive adjustments in growth and development responding to environmental inputs, and in many plants flowering time or when to make a transition to flowering is signaled by temperature and/or day length changes. At high latitudes, naturally-growing Arabidopsis ecotypes (winter annual or biennial crucifers) overwinter before flowering. In early seedlings, a MADS-box transcription factor known as FLC, directly represses the expression of *FLOWERING LOCUS T* (*FT*, encoding a mobile florigen) to prevent floral induction by the photoperiod pathway. Winter cold or prolonged cold exposure leads to repressive histone modifications such as histone 3 lysine-27 trimethylation (H3K27me3) on *FLC* chromatin to silence *FLC* expression. When temperature rises in spring, the silenced *FLC* state is epigenetically maintained in subsequent growth and development. This enables *FT* induction and plants to flower and set seeds in response to increasing day lengths in late spring. Recently, we have found that a few of transcription factors function together with chromatin modifiers to mediate molecular epigenetic control of *FLC* expression and thus flowering time in Arabidopsis, in response to seasonal signals. These findings will be presented in this symposium.



报告/Topic

Agilent HRMS天然产物数据库助力中药研究

Dr. Song Yue is an engineer from Agilent Technology (China) Co., Ltd.

摘要/Abstract

介绍基于HRMS技术建立的天然产物质谱数据库用于中药研究的各个领域

报告/Topic

Rebuilding the Foundation of herbal medicine in the United States

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Roy Upton is the President and Editor of the American Herbal Pharmacopoeia (AHP). The primary focus of AHP is to revitalize knowledge of plant-based medicines in a country where the dominant western medical establishment has given focus to disease care but have forgotten concepts of health care. Herbal medicine traditions offer a tremendous amount in both disease care and the promotion of health. Roy Upton has been working professionally as an herbalist for almost 40 years and trained in Western, Chinese, and Ayurvedic herbal medicine. He is the author of numerous popular and scientific publications and lectures worldwide on the benefits of herbal medicine.

摘要/Abstract

The United States lost much of its herbal traditions in the twentieth century as advancements in chemistry and medicine focused more on the development of modern chemical drugs, partially as part of the natural evolution of the development of modern medicines and partially due to the discovery of novel compounds primarily for the development of profitable drugs. While focusing on the development and promotion of quality control standards for herbal medicines, the primary purpose of the American Herbal Pharmacopoeia (AHP) is to help to revitalize the herbal traditions that were lost in America and introduce Westerners to our own herbal tradition and those of others, most notably Ayurvedic and Traditional Chinese medicine. Each Monograph and Therapeutic Compendium is the result of a collaboration of medicinal plant experts worldwide and provides academicians, industry, and regulators with the most comprehensive review of the botanical in the English language. Presented will be an overview of AHP Monographs and Therapeutic Compendiums.

大会论文

Conference Paper

Phytochemical Investigation on the Fruits of Tujia Ethnomedicine “heilaohu”

Yanzhe Jia [1]***,Liang Cao*** [1]***,Yupei Yang*** [1]***,Pan Yi*** [1]***,Bin Liu*** [2]***,Nusrat Hussain*** [3]***,***

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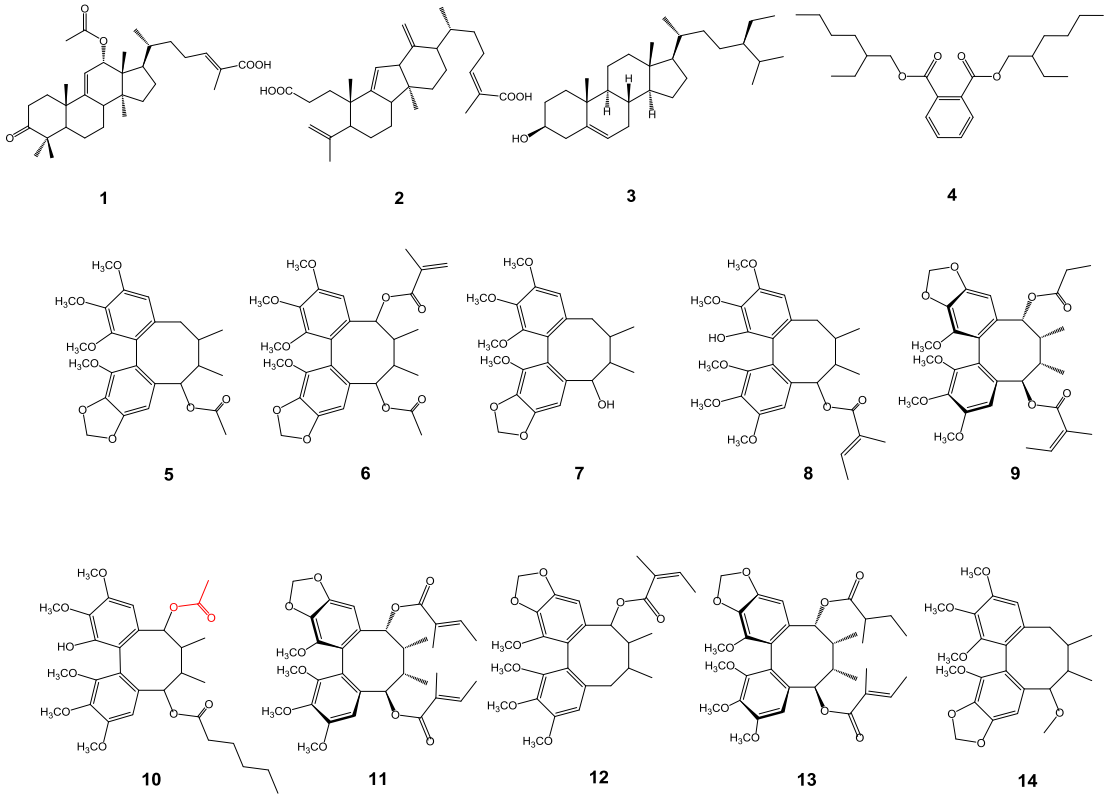
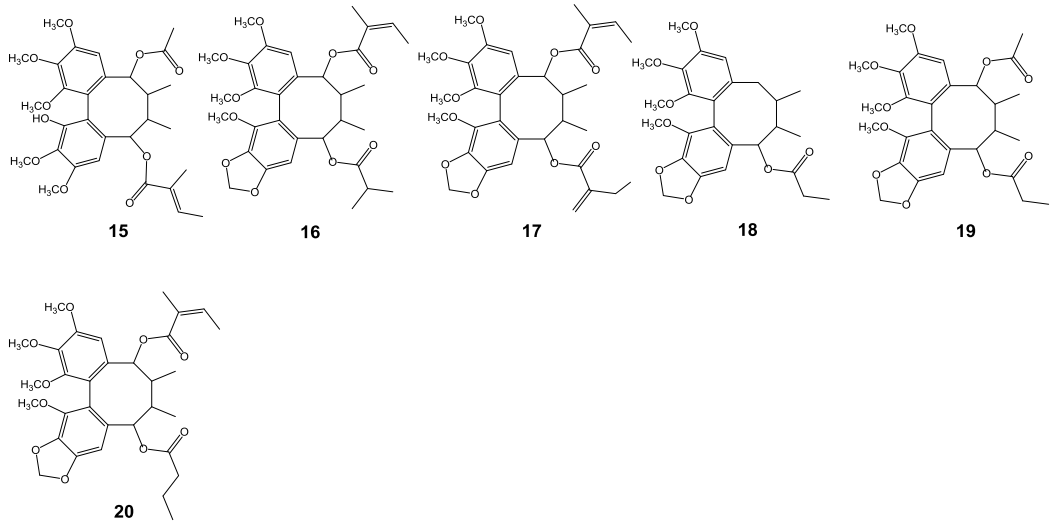
Abstract:

Kadsura coccinea (Lem.) A. C. Smith belongs to the medicinally important genus *Kadsura* from the Schisandraceae family, The roots, stems and fruits of *k. coccinea* are used by Chinese residents to treat stomach, duodenal ulcer, chronic gastritis, rheumatoid arthritis, bruises, dysmenorrhea and other diseases.in the study of the chemical composition of the *k.coccinea*'s fruit, The chemical investigation led to the isolation and two new and eighteen known compounds. Two new compounds(10 and 17) and fourteen know lignans(5-9,11-15 and 17-20) possessed dibenzocyclooctadiene skeletons. Similarly, three was triterpenoids(1-3) and one was other type of compound. Among the known compounds,1-2,4-9,11-15 and 17-20 were isolated from *K. coccinea* for the first time. The structures were established using IR,UV,MS,1D,and 2D-NMR spectroscopy.





Chemical structures of compounds 1-20 islolated from *k. coccinea* fruit

Keyword: *Kadsura coccinea*, Chemical structures, lignans ,triterpenoids

Integrated Metabolomic Profiling of the Antilipidemic Effects of *Polygonatum kingianum* Extract on Dyslipidemia in Rats

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Abstract:

Polygonatum kingianum (PK) has been used as a herb and nutritional food in China for centuries. Known pharmacological activities of PK include immune system stimulation, anti-aging effects and blood glucose regulation. To date, studies on the effects of PK on dyslipidemia and the mechanism for these effects have not been investigated. We aimed to identify the effects and mechanism of action of PK on dyslipidemia using an integrated untargeted metabolomic method. A rat model of dyslipidemia was induced with a high-fat diet (HFD) and rats were given PK (4 g/kg/day) intragastrically for 14 weeks. Changes in serum and hepatic lipid parameters were evaluated. Metabolites in serum, urine and liver samples were profiled using UHPLC/MS followed by multivariate statistical analysis to identify potential biomarkers and metabolic pathways. PK significantly inhibited the HFD-induced increase in total cholesterol and low density lipoprotein cholesterol in serum, and total cholesterol and triglyceride in the liver. PK also reduced hepatic high density lipoprotein cholesterol. PK significantly regulated metabolites in the analyzed samples to ward normal status. Nineteen, twenty-four and thirty-eight potential biomarkers were identified in serum, urine and liver samples, respectively. These biomarkers involve *Polygonatum kingianum* (PK) has been used as a herb and nutritional food in China for centuries. Known pharmacological activities of PK include immune system stimulation, anti-aging effects and blood glucose regulation. To date, studies on the effects of PK on dyslipidemia and the mechanism for these effects have not been investigated. We aimed to identify the effects and mechanism of action of PK on dyslipidemia using an integrated untargeted metabolomic method. A rat model of dyslipidemia was induced with a high-fat diet (HFD) and rats were given PK (4 g/kg/day) intragastrically for 14 weeks. Changes in serum and hepatic lipid parameters were evaluated. Metabolites in serum, urine and liver samples were profiled using UHPLC/MS followed by multivariate statistical analysis to identify potential biomarkers and metabolic pathways. PK significantly inhibited the HFD-induced increase in total cholesterol and low density lipoprotein cholesterol in serum, and total cholesterol and triglyceride in the liver. PK also reduced hepatic high density lipoprotein cholesterol. PK significantly regulated metabolites in the analyzed samples to ward normal status. Nineteen, twenty-four and thirty-eight potential biomarkers were identified in serum, urine and liver samples, respectively. These biomarkers involved biosynthesis of phenylalanine, tyrosine, tryptophan, valine, leucine and isoleucine, along with metabolism of tryptophan, tyrosine, phenylalanine, starch, sucrose, glycerophospholipid, arachidonic acid, linoleic acid, nicotinate, nicotinamide and sphingolipid. Thus, PK alleviated HFD-induced dyslipidemia by regulating many endogenous metabolites in serum, urine and liver samples. Collectively, this suggested that PK

may be a promising lipid-regulator to treat dyslipidemia and associated diseases.d biosynthesis of phenylalanine, tyrosine, tryptophan, valine, leucine and isoleucine, along with metabolism of tryptophan, tyrosine, phenylalanine, starch, sucrose, glycerophospholipid, arachidonic acid, linoleic acid, nicotinate, nicotinamide and sphingolipid. Thus, PK alleviated HFD-induced dyslipidemia by regulating many endogenous metabolites in serum, urine and liver samples. Collectively, this suggested that PK may be a promising lipid-regulator to treat dyslipidemia and associated diseases.

Development and optimization of Comprehensive 2D-LC method for Ganoderic acid in Ganoderma lucidum

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Abstract:

There are several ways to improve the peak capacity for complex samples such as TCM etc. : one is using long column with long gradient or using small particle size column (UHPLC), this will increase the analysis time and system pressure; another more powerful way is using 2D-LC, using two different column with different selectivity to get a very large peak capacity in short time while the system pressure was not so high, the more orthogonal the two columns are, the more peak capacity the method could get, but it would be more complex for the development and optimization of 2D-LC method.

In this article, we took the 2DLC method development and optimization process of ganoderic acid in Ganoderma lucidum as an example, discussed the setting and combination of different parameters and conditions such as selectivity of column, modulation and sampling, shift gradient in 2nd dimension and so on, these would significantly affect the peak capacity of the method.

An Agilent 1290 2D-LC system and two different columns were used, and an Agilent 6230 TOF MS was also used for qualitative analysis. This method could get more than 4700 effective peak capacity in 45min, and most of the ganoderic acid components co-eluted in the first dimension could get good separation in the second dimension.

Simultaneous determination of prostaglandin and hormones in excreta of *Trogopterus xanthipes*

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Abstract:

The excreta of *Trogopterus xanthipes* (Wulingzhi in Chinese, WLZ) was a well-known Chinese medicine with definite clinical effects on irregular menstruation. It has been firstly recorded in "Kaibao Bencao" in Song dynasty (in 973 A.D.). However, the chemical profiling and quantity of prostaglandin and hormones are ignored, which were involved in many reproductive events, such as ovulation and corpus luteum regression. In present study, qualitative and quantitative analyses were performed on UPLC-orbitrap-MS^n to highlight the advantages and connotation of endogenous components in WLZ. The 26 compounds were identified in urine of *Trogopterus xanthipes*, and an UPLC-MS/MS method was used for simultaneous quantitation four compounds in 20 batches of samples. The quantitative method showed a good linear correlation ($R > 0.995$) over a wide range for each compound. The method had a high sensitivity as established by LOD (0.5-1.0 ng/mL) and LOQ (1.0-2.5 ng/mL). The intra- and inter-day precisions were less than 9.17 (RSD%), and repeatability and stability were less than 6.14 (RSD%). The recovery assays were between 85.8% and 97.3%, which were evaluated with three different concentrations. The present integrated qualitative and quantitative assessment of WLZ provides an evaluation strategy to assess the constituent in traditional Chinese medicine.

Traditional Chinese Medicine Fingerprint and its Application

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Abstract:

The fingerprint of traditional Chinese medicine, refers to spectral diagram, including the spectrum and chromatogram, which can show chemical characteristics. In recent years, fingerprints have become more and more widely used in the direction of Chinese medicine, and can be applied to various aspects. The construction method of TCM fingerprint including HPLC, UPLC, GC, MS and their combination technique. This paper summarizes some applications of traditional Chinese medicine fingerprints, including in quality control of traditional Chinese medicine, in pharmacodynamics of traditional Chinese medicine, in traditional Chinese medicine compound and so on. Furthermore, it puts forward the prospects for the follow-up research of traditional Chinese medicine fingerprints.

Targeting liposomes: Recent advances in the stable entrapment and prolonged released of antitumor drugs

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Abstract:

Liposomes are currently in the stage of vigorous development. It has shown great application potential in many aspects, especially in the aspect of anti-tumor. In this paper, the theoretical and technical breakthroughs of liposomes in the research of anti-tumor targeting are summarized, and theoretical support and methodological guidance are provided for further development of liposomes. We have reviewed the literature of the past year and summarized the new achievements and breakthroughs in anti-tumor targeting of Liposome drug delivery system. Timosaponin-TAIII-loaded liposomes (LP) were prepared to improve TAIII solubility and extend its circulation time. The ip delivery of DFP-10825, TS shRNA conjugated with cationic liposome, shows a favorable antitumor activity without systemic adverse events via the stable localization of TS shRNA for a sufficient time and concentration in the peritoneal cavity of the peritoneally disseminated human ovarian cancer-bearing mice. Octreotide acts as a modified ligand for receptor-mediated targeting and the coated Fe3O4 nanoparticles offer the magnetic targeting property. SSTR2 overexpressed A549 cells and S180 cells were chosen to explore the targeting ability and antitumor effect of the oleanolic acid (OA)-loaded OMlips *in vitro* and *in vivo*. The COS grafted estrogen functionalized cationic liposomes, fortified with glutathione-responsiveness, showed great potential for specific intracellular drug delivery to estrogen receptor-expressing tumors such as osteosarcoma.PH-responsive liposomes consisting of hydrogenated soy phosphatidylcholine (HSPC) as a lipid, hyaluronic acid (HA) grafted with functional 3-diethylaminopropyl (DEAP) groups (hereafter denoted as HA-g-DEAP) as a pH-responsive polymer, and docetaxel (DTX) as an antitumor drug. In an *in vitro* tumor cell cytotoxicity test, the DTX-loaded liposomes caused a significant increase in HCT-116 tumor cell death, revealing their pharmaceutical potential in tumor therapy.

Research progress on pesticide residue analysis methods

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Abstract:

The residual organic pesticides in Chinese herbal medicines can cause nervous system damage. Some organic pesticides even have reproductive toxicity, which poses a certain threat to human health. Organic pesticides sprayed during the cultivation of Chinese herbal medicines are likely to cause pollution to Chinese herbal medicines. In addition, organic pesticides exposed to Chinese herbal medicines in storage and processing environments may also cause pollution of Chinese herbal medicines. Pesticide residues have many characteristics, such as many kinds, different properties, trace, which bring great difficulties to their routine analysis. At present, the analysis methods mainly focus on the pretreatment of samples and the selection of appropriate detection methods. The extraction, purification and detection methods of residual organic pesticides were reviewed in this paper. In addition, the current situation and existing problems of the analysis of pesticide residues in traditional Chinese medicine were introduced.

Determination of seven saponins components in Panacis Japonici Rhizoma with quantitative analysis of multi-components by single marker

***Shihan Tan*[1,2], *Hongnian Wu*[1,2], *Yating Lei* [1,2], *Ye Zhang*[2], *Yuanqing Wang* [3], *Ruilian Liu*[4], *Bo Jiang* [1,5], *Jianye Yan*[1,2*]**

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Abstract:

Objective To establish quantitative analysis of multi-components by single marker (QAMS) method for simultaneous determining the content of seven saponins in *Panacis japonici Rhizoma*, and evaluate the adaptation and application of QAMS method in the quality control of *Panacis japonici Rhizoma*.

Method The relative factor ($f_{s/i}$) of ginsenoside Rg_1, ginsenoside Re, ginsenoside Rb_1, pseudoginsenoside RT_1, chikusetsusaponin Ⅳ and chikusetsusaponin Ⅳa were established by HPLC method with chikusetsusaponin Ⅴ as internal standard, which were used to calculate the content of seven saponins in *Panacis japonici Rhizoma*. Meanwhile, external standard method（ESM）was used to calculate the content of seven saponins. The difference between QAMS and ESM were analyzed to evaluate the accuracy of QAMS.

Results The $f_{s/i}$ of ginsenoside Rg_1 , ginsenoside Re , ginsenoside Rb_1 ,chikusetsusaponin Ⅳ, chikusetsusaponin Ⅳa and pseudoginsenoside RT_1 were 1.2867, 1.4327, 0.9666, 0.9624, 1.2072, 0.9384,. There was no significant difference between the results determined by QAMS and ESM.

Conclusion The established QAMS method is accurate and can be used for quantitative analysis and quality evaluation the content of seven saponins in *Panacis japonici Rhizoma*.

Multi-Component Analysis of Aurantii Fructus Based on HPLC Fingerprints and Single Marker Quantification Method

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Abstract:

Aurantii fructus (AF) is a traditional Chinese medicine (TCM) used to treat many diseases for thousands of years. It's significant to establish a reasonable and feasible assessment method for the quality control of this herb. In this study, a quantitative analysis of multiple components with a single marker (QAMS) method was firstly established for simultaneous determination of 12 active components in AF by HPLC. Using naringin as the reference standard, the contents of the twelve components, including eriocitrin, neoeriocitrin, narirutin, naringin, hesperidin, neohesperidin, meranzin, poncirin, naringenin, nobiletin, tangeretin, and auraptene were determined, simultaneously. The results demonstrated that there was no significant difference between the QAMS method and the traditional external standard method (ESM). In addition, hierarchical clustering analysis (HCA), quality fluctuation analysis and similarity analysis (SA) were performed to differentiate and classify the samples based on the contents of 12 compounds. In conclusion, this study could be applied to the quality evaluation and control of AF, and giving references to promote the quality standards of TCM.

Chemical Constituents and Activity research Progress of *Kadsura Coccinea*

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Abstract:

Kadsura coccinea is widely distributed throughout southwest China. It have been used in Chinese folk medicine for the treatment of cancer, dermatosis and as an anodyne to relieve pain. In previous phytochemical investigations, lignans, triterpenoids, monoterpenoids, sesquiterpenoids, steroids, and amino acids were reported from this plant in which lignans and triterpenes are the main components. At present, the chemical constituents isolated from *Kadsura coccinea* include 129 triterpenoids and 96 Lignans. This paper reviews systematically summarizes the chemical constituents which have been reported and biological activities of *Kadsura coccinea*, provides basis for further research and development of *Kadsura coccinea.*

Keyword: *Kadsura coccinea*; Lignans; Triterpenes

Traditional Chinese Medicine Fingerprint and its Application

Guanghua Zhang[1, 2], Jinghui Wang[1, 2], Fu Long [4 *], Binbin Song[1], Wei Guo[1, 3], Zhongzhi Qian[1, 3*]

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Abstract:

Objective： Establish methods for determining 4 lipid- soluble tanshinone components (SFC-PDA) and 3 water-soluble salvianolic acid components in *Salvia miltiorrhiza* decoction pieces (UPLC). The 7 components are used to evaluate the quality of *Salvia miltiorrhiza* decoction pieces from difference sources. **Methods：** The UPCC-PDA analysis was performed on Viridis ® HSS SB C18100A（3.0 mm×100 mm，1.8μm）column. The mobile phase was Carbon dioxide- n-heptane-isopropanol（8:2，V/V）with isocratic elution mode at a flow rate of 1.5 mL min^{-1}. The column temperature was controlled at 45 ℃. ABPR pressure is 2000psi . The UPLC-PDA analysis was performed on BEH Shield RP (2.1 mm×100 mm，1.7μm）column. The mobile phase was consisted of acetonitrile - 0.1% phosphoric acid with gradient elution at a flow rate of 0.4 mL min^{-1}. The column temperature was controlled at 30 ℃. Results：7 main components *in Salvia miltiorrhiza* decoction pieces were well separated in UPCC and UPLC respectively. During the method validation, Linearity, repeatability, stability and recovery experiment results are meet the accept criteria of assay. The sensitivity of fat-soluble components and water-soluble components are comparable in HPLC and UPCC system. **Conclusion：** The UPCC method possesses the advantage of rapid, simple, accurate analysis, along with saving solvent and reducing environmental pollution. At the same time, the UPLC method is used to determine the water-soluble components. This two methods can be used for analysis the quality of *Salvia miltiorrhiza* decoction pieces, and greatly reduce the detection cost.

Analysis of alkaloids in the chewable products of *Areca catechu* using HPLC-UV

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Abstract:

Areca catechu commonly known as betel nut, which belongs to Arecaceae family, is widely distributed in China, India, Pakistan, and other Asian countries. The chewable husk products of *Areca catechu*, named "Binglang" including Qingguo and Yanguo widely was chewed by people in southern China. And the seeds of *Areca catechu* sliced into thin shard, along with tobacco, slacked lime and other flavors, were rolled into the leaves of the plant for chewing by Indian and Pakistanis. However, no quality control analytical method has yet been developed for chewable Binglang. In this study, A high performance liquid chromatography coupled with UV detector (HPLC-UV) method for quantitative analysis of four characteristic areca alkaloids and applied this method to the analysis of chewable Binglang from different countries and regions. Moreover, fingerprint similarity evaluation, and pattern recognition including principle component analysis (PCA) and random forest (RF) were applied to analyze the obtained spectrometric data. The results firstly revealed substantial variations in the levels of areca alkaloids among tested products, with arecaidine (0.014-2.422mg/g), arecoline (0.007-3.789mg/g), guvacine (0.028-1.231mg/g), guvacoline (0.004-1.105mg/g). This study presents the first important step toward providing a systematic method for comprehensive quality control of Binglang products.

Research Progress on Chemical Constituents of *Curculigo orchioides*

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Abstract:

Medicinal plants of *Curculigo orchioides* Gaertn, which are known for widely usages in traditional Chinese medicine (TCM), has been used for several thousand years in China. *Curculigo orchioides* Gaertn is the most famous Chinese medicine for nourishing and stengthening body. Thus far, 122 compounds have been isolated and identified in this plant, including biologically active compounds such as phenols and phenolic glycosides, lignans and lignan glycosides, triterpenes and triterpenoid glycosides, flavones, alkaloids, aliphatic compounds and other types of compounds. A range of biological activities have been reported from extracts of *Curculigo orchioides* Gaertn, including antioxidant, immunostimulatory effect, anti-osteoporotic, cardiovascular protection, estrogenic activity and the effects on sexual behavior, hepatoprotective and neuroprotective activity. This review systematically summarizes the chemical constituents and biological activities of the plant providing a theoretical basis for the isolation of active compounds and further research of *Curculigo orchioides* Gaertn. Medicinal plants of *Curculigo orchioides* Gaertn, which are known for widely usages in traditional Chinese medicine (TCM), has been used for several thousand years in China. *Curculigo orchioides* Gaertn is the most famous Chinese medicine for nourishing and stengthening body. Thus far, 122 compounds have been isolated and identified in this plant, including biologically active compounds such as phenols and phenolic glycosides, lignans and lignan glycosides, triterpenes and triterpenoid glycosides, flavones, alkaloids, aliphatic compounds and other types of compounds. A range of biological activities have been reported from extracts of *Curculigo orchioides* Gaertn, including antioxidant, immunostimulatory effect, anti-osteoporotic, cardiovascular protection, estrogenic activity and the effects on sexual behavior, hepatoprotective and neuroprotective activity. This review systematically summarizes the chemical constituents and biological activities of the plant providing a theoretical basis for the isolation of active compounds and further research of *Curculigo orchioides* Gaertn.

Keyword: *Curculigo orchioides* Gaertn; Chemical constituents; Pharmacological activities

Advances in Studies on the Chemical Constituents and Pharmacological Activities of the leaves of *Kadsura heteroclita*

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Abstract:

Kadsura heteroclita (Roxb.) Craib is a climbing woody liana belonging to the family Schisandraceae and is mainly distributed in southern mainland China. It is a well-known traditional Chinese medicine that has been used for a long time especially in the folk medicine of southern China. The original plant of folk medicine is FengQingJiXieTeng and DiXieXiang with the functions of dispelling wind and dampness, regulating the flow of qi to alleviate pain, and stimulating the circulation of blood and causing the muscles and joints to relax. At present, the chemical constituents isolated from *Kadsura heteroclita* include 70 lignans, 53 triterpenes, 7 sesquiterpenes, 2 steroids, 4 flavonoids, in which lignans and triterpenes are the main components and exhibit antitumor, antiviral, anti-oxidation and hepatoprotection activities.

In this paper, the chemical constituents of *K. heteroclita* and their pharmacological activities are reviewed, which would be helpful to provide a reference for further development and utilization of *K. heteroclita* resources.

Keyword: *Kadsura heteroclita*; lignans; triterpenes; antitumor; antiviral; Schisandraceae

Antibacterial stibenes from the tubers of *Bletilla striata*

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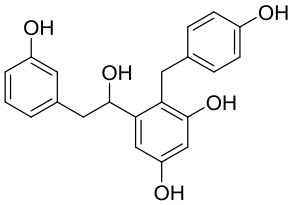
Abstract:

Two new bibenzyls, 2-(*p*-hydroxybenzyl)-1a,3,3',5-tetrahydroxybibenzyl (**1**) and 2-(*p*-hydroxybenzyl)-3,4',5-trihydroxybibenzyl (**2**), along with 18 known ones including phenanthrenes (**3**-**17**) and bibenzyls (**18**-**20**) were isolated from the tubers of *Bletilla striata*. The structures of new compounds were elucidated by the use of 1D/2D NMR spectroscopic data. Compounds **12**-**15** were isolated from the Orchidaceae for the first time. Most of the isolated compounds were evaluated for their antibacterial activities against 3 g-positive bacterial strains and 1 g-negative bacterial strain. Compounds **3**, **9**, **11**, **13**, **14**, **15** and **17** showed inhibitory activities, with MICs of (6–52 μg/mL) against *S. aureus* ATCC 6538.



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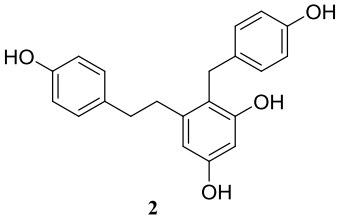

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Keyword: *Bletilla striata*; Stilbenoids; Bibenzyls, Phenanthrenes; Antibacterial activities

Rapid characterization of chemical components by UHPLC-QTOF/MS with full-composition database of traditional Chinese medicines

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Abstract:

The efficacy of traditional Chinese medicines (TCM) has been extensively validated. However, obtaining the overall chemical information of numerous TCM components remains a major challenge. Therefore, establishing a strategy for rapid and comprehensive identification of chemical ingredients in TCMs is critical. Database is a common method used in pharmaceutical research, more and more databases are used in traditional Chinese medicine research, such as Nature Products Information Database, Chinese Nature Products Database and so on. Although these databases contain most of the Chinese herbs and common TCM products, no mass spectrum database of full-composition of TCM has been established. Therefore, we propose a strategy to establish the mass spectrum database of full-composition of TCM for characterization by UHPLC-QTOF/MS. First, summarizing the information of TCM component, including the information on component names, structures and mass fragments based on the published reports. Then, after importing the acquisition data by UHPLC-QTOF/MS into the database, it could automatically detect and filter the data. The third step was to summarize and propose fragmentation patterns, such as characteristic fragment ions and neutral loss. Finally, through the fragmentation patterns, the components from TCM will be artificial confirmed. With this strategy, rapid characterization of the chemical components of pu-erh tea was successfully achieved. 66 major peaks in both negative and positive ion modes of pu-erh tea were identified, including 45 components in the ripened pu-erh tea, and 49 chemical components in the raw pu-erh tea. Meanwhile, through the multivariate statistical methods, including PCA and OPLS-DA, we carried out to find the different components during the pile-fermentation process of pu-erh tea, including *N*-ethyl-2-pyrrolidinone substituted flavan-3-ols (puerins), which are the characteristic components from the ripened pu-erh tea. According to the different components during the pile-fermentation process, we found that contents of catechins decreased, but puerins were derived. This strategy was also applied to analyze the component herbs of a hospital preparation with unknown ingredients, and there were 39 components identified by the full-composition database. According to the related information of Chinese herbs and their chemical components in the database, we inferred the component herbs of unknown preparation according to the identified components. These two applications illustrated that this strategy provided an efficient protocol for the rapid identification of chemical constituents in complex samples such as TCM by UHPLC-QTOF/MS with the mass spectrum database of full-composition of TCM.

Triterpenoids and Sesquiterpenoids from Tujia Ethnomedicine Heilaohu

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Huang-he Yu[†], *Qing-ling Xie*[†], *Bin Li*[†], *M. Iqbal Choudhary*[†], *Atta-ur-Rahman*[†], *and Wei Wang*[†]

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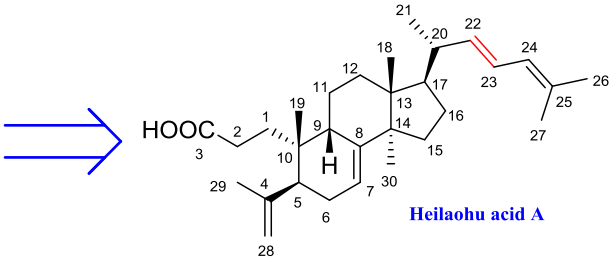
Abstract:

Kadsura coccinea, Heilaohu (Hlh), Tujia ethnomedicine is a common folk medicine to treat cancer and rheumatoid arthritis disorders. A detailed phytochemical investigation of an ethanolic extract of the roots of Hlh led to the isolation of seven new compounds (**1**-**7**), including five lanostane triterpenoids heilaohu acids A-E (**1**-**5**), one cuparane sesquiterpenes kadscoccinic acid (**6**) and one carotane sesquiterpenoids kadscoccinol (**7**), together with twenty-nine known analogues (**8**-**36**). The structures of isolated compounds were deduced mainly by analyzing their 1D and 2D NMR spectroscopic data along with HR-ESI-MS. In addition, all compounds (**1**-**36**) were screened for their *in vitro* cytotoxic activity against four different human cancer cell lines including HCT-116, BGC-823, HepG-2, and MCF-7, along with human rheumatoid arthritis fibroblast-like synoviocytes cell line (RA-FLS), by using the MTT bioassay. Compounds **1**, **13**, and **22**-**24** exhibited significant inhibitory activities against all four tumor cell lines with IC_{50} values ranging from 2.14 to 8.99 μM, compound **29** showed good anti-RA activity against RA-FLS cell line with IC50 value of 9.37 μM. Compounds **4**, **10**, **21**-**28**, and **31**-**36** were also evaluated for their antioxidant potential. The results showed significant activities of compounds **22** and **27** with IC_{50} values of 9.68 and 8.20 μM, respectively. The preliminary structure-activity relationship of tested compounds also discussed.

Kadsura coccinea



Heilaohu acid A

Cytotoxic against HCT-116 human cancer cell line with IC_{50} value of 7.94 μM

Preparation and application of novel transmembrane protein-liposome biological chromatography

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Abstract:

Transmembrane proteins belong to membrane proteins, which are embedded in lipid bilayers and exposed at both inner and outer surface of cell membranes. They play an important role in maintaining cell function. Transmembrane proteins are currently the most important drug targets, accounting for 70% of all known drug targets at this stage. Therefore, drug discovery based on transmembrane proteins is an important way to innovate drug research and has been a hotspot in the field of pharmacology worldwide. This research focuses on transmembrane proteins and establishes a new transmembrane protein-liposome biological chromatographic system, which is discussed from the following three aspects. The structure of transmembrane proteins is complex and they have one or more hydrophobic regions so the purification, recombination and preservation of transmembrane proteins are inseparable from detergents. However, with the presence of detergents, the structure and function of proteins are destroyed, and the interaction between drugs and transmembrane proteins is quite different from the actual situation *in vivo*. In order to solve the problem, a series of new models and analytical techniques have been developed. The most representative one is proteoliposome reconstruction technology. The principle of this technology is to use various liposome to reconstruct artificial membranes to simulate the environment of cell membranes. Then transmembrane proteins are embedded on them to simulate the natural environment to characterize their interaction with drugs. However, proteoliposomes are not rigid enough to be used as chromatographic stationary phase. So they can not be applied to rapid and convenient liquid chromatography-mass spectrometry (LC-MS) technology.

In order to solve this problem, referring to the technology of proteoliposome reconstruction and cell membrane chromatography, a new bacteriorhodopsin-liposome-silica gel stationary phase was constructed. The principle is to combine various liposomes into vesicles by membrane ultrasonic and hydration. Then bacteriorhodopsin was embedded on it. Next, the rhodopsin-liposome mixture was bond with silica gel by vacuum vortex. the physical parameters were investigated by particle size tester, scanning electron microscopy, and confocal microscopy. After the preparation of stationary phase, it was packed into the column by wet packing method. 9-cis-retinal and dexamethasone was used as positive and negative drug to evaluate the effectiveness of the column.9-cis-retinal was injected for 7 consecutive days to investigate the life of the column. A series of experiments proved that the method successfully combines protein, liposome and silica gel to prepare a new chromatographic stationary phase. The validity and lifetime of this complex substance are verified by LC-MS, which lays a foundation for further popularization and application of this method.

Next, a new two-dimensional transmembrane protein-liposome biochromatographic system has been developed on the basis of our previous studies on cell membrane chromatography and the new stationary phases in the

previous chapter. In this study, a two-dimensional FZD4-reverse C18 column/TOF-MS chromatographic system was established by frizzled family receptor 4 (FZD4). FZD4, a seven-time transmembrane protein, belongs to the frizzled protein family. Numerous studies have shown that FZD4 is a potential target for colorectal adenocarcinoma, bladder cancer and other cancers by affecting the WNT/beta-catenin pathway. This comprehensive 2D chromatographic system was constructed to screen potential anticancer components of FZD4 protein in *Radix Pueraria lobata* and *Scutellaria baicalensis Georgi*. By comparing the results of mass spectrometry with components database and excluding the false positive results on blank control chromatography, five potential active ingredients in *Radix Pueraria lobata* and seven potential active ingredients in *Scutellaria baicalensis Georgi* were found in the comprehensive 2D FZD4 chromatographic system in this chapter. To verify the anti-cancer activity of these components, human breast cancer cells (MCF7) were selected for a series of experiments. Firstly, the inhibition of cell proliferation experiment showed that oroxylin A, wogonin and puerarin had obvious killing effect on MCF7 cells. Secondly, Cell apoptotic experiments showed that oroxylin A, wogonin and puerarin kill cells through apoptotic pathway by flow cytometry. Then, western blotting results showed that wogonin and puerarin could significantly reduce the expression of FZD4 in MCF7 cells, while other compounds could not. Finally, the virtual docking of wogonin and puerarin with FZD4 protein was carried out by Discovery Studio 3.0 software. The results showed that wogonin and puerarin could be linked to the amino acid in binding site through hydrogen bond. Therefore, the established transmembrane protein-liposome biological chromatographic analytical system has the advantages of specificity and high-throughput for characterization of drug-target interaction, especially for screening of active components from complex samples.

Keyword: transmembrane protein, liposome, two-dimensional chromatography, traditional Chinese medicine, anti-cancer active components

Phytochemistry and pharmacological activities of Diterpenoid alkaloids from the genus *Aconitum*

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Abstract:

The genus *Aconitum* (*Ranunculaceae*) are widely distributed in the north temperate zones possessing important medicinal properties. The Aconitum have been characterized by the alkaloids and especially the study of diterpenoid alkaloids are always hot. Meanwhile substantial pharmacological researches have been focused on diterpenoid alkaloids from the genus *Aconitum* in the analgesia in cancer and anti-inflammation or used as insecticide. This review summarized the new diterpenoids alkaloids from *Aconitum* reported from 2015 to 2018 and a total of 86 new diterpenoids alkaloids were identified. In modern pharmacological studies, there are many reports about the analgesia, anti-inflammation, anti-tumor, anti-oxidation, anti-bacterial, cytotoxicity, antifeedant of diterpenoid alkaloids from the genus *Aconitum*. This review could provide further information for the development of *Aconitum* plants.

Absorbed components analysis of Bushen Huoxue prescription in rat serum by UPLC coupled with Q-Exactive quadrupole-orbitrap mass spectrometry

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Abstract:

Diabetic retinopathy (DR) is a common microvascular complication of diabetes and remains one of the leading causes of blindness worldwide. Bushen Huoxue Prescription (BP), consisting of Rehmanniae Radix, Salviae Miltiorrhizae Radix et Rhizoma, Ginseng Radix et Rhizoma, and Puerariae Lobatae Radix, showed an effect on preventing and treating DR, but the basis substances for its pharmacodynamics has not been thoroughly studied. In this study, the components in rat serum after oral administration of BP were explored. Firstly, the male SD rats were administered BP every 12 hours for 3 consecutive days with a dose at 11.67 g/kg. Secondly, the serum was collected and comprehensively profiled using ultra-performance liquid chromatography (UPLC) coupled with Q-Exactive quadrupole-orbitrap mass spectrometry in negative ion mode. Finally, according to the retention time, accurate molecular weight and molecular fragment peak provided by mass spectrometry, and comparing with the chemical reference standards and related references, a total of 25 components were identified in rat serum, of which rosmarinic acid, daidzein, salvianolic acid B, ginsenoside Rg_1, ginsenoside Re, puerarin and daidzin were verified by comparing with mass spectrometry information of the chemical reference standards. Besides, all the 25 components were prototype components, including 3 phenolic acids derived from *Salviae miltiorrhizae* Radix et Rhizomaa, 8 ginsenosides from Ginseng Radix et Rhizoma, and 14 isoflavones from Puerariae Lobatae Radix. The results implied that these 25 components may be the direct substances of BP working in vivo and this study may provide an evidence for further studying of the pharmacodynamic substances of BP.

Dissecting the metabolic phenotype of the antihypertensive effects of five *Uncaria* species on spontaneously hypertensive rats

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Abstract:

The sourcing of plants from multiple botanical origins is a common phenomenon in traditional Chinese medicines. *Uncaria* Stem with Hooks (UHs) is approved for using five botanical origins in the Chinese Pharmacopoeia (2015 Edition). All five UHs are commonly used for treating hypertension, even though the plants have different chromatographic fingerprints based on our previous study. However, their hypotensive effects and metabolic phenotypes have not been fully studied. In the present study, spontaneously hypertensive rats (SHRs) were orally administered five aqueous extracts (4 g crude drug/kg) prepared from the different UHs over a six-week period. Systolic blood pressure (SBP) was measured every week and urine was collected after SBP measurement. Untargeted metabonomics was performed using UPLC coupled with a LTQ-Orbitrap mass spectrometer. Bidirectional orthogonal projection to latent structures-discriminant analysis (O2PLS-DA), Student's *t* test, and correlation analysis were used for pattern recognition and the selection of significant metabolites. A similar and prolonged reduction of SBP was observed in each of the groups given the five different UHs, while the metabolic profiles were perturbed slightly compared with that of SHR. Further analysis has shown that only a few common, different components were observed within the five groups which showed the similar antihypertensive effect in spite of the distinct metabolic pathways due to their different alkaloid composition. These results help understanding the mechanisms of the phenomenon "different species, same effect" of UHs.

Research on the detoxification mechanisms of cinnabar against Semen Strychni-induced neurotoxicity in Shang-Ke-Jie-Gu Tablet

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Abstract:

As a widely used clinical traditional Chinese medicine in China for bone fracture, Shang-Ke-Jie-Gu Tablet (SKJGT) is composed by 12 kinds of Chinese herbs, including *Strychni Semen*, *Cinnabaris*, *Carthami Flos*, *Eupolyphaga Steleophaga*, *Myrrha*, *Notoginseng* Radix et Rhizoma, Starfish, Chicken bone, *Borneolum syntheticum*, *Calcined Pyritum*, *Olibanum* and Melo Semen. Considering cinnabar might induce chronic mercury intoxication after oral administration of SKJGT, which has received the most public concerns about its safety, the pharmacology and acute toxicity of Cinnabaris-free SKJGT were researched. Our previous studies showed cinnabar-free SKJGT (CFSKJGT) owned the more severe Semen Strychni-induced neurotoxicity compared with SKJGT, indicating that cinnabar was indispensable and cinnabar might reduce Semen Strychni-induced neurotoxicity in SKJGT. In this study, through study the effects of cinnabar on Semen Strychniinduced neurotoxicity in SKJGT, the effects of cinnabar on the dissolution, absorption, metabolism process, the dosage of cinnabar on the acute toxicity and analgesic and anti-inflammatory in SKJGT and the mercury accumulation *in vivo* after exposure to cinnabar in SKJGT. we explored that: The detoxification of cinnabar against Semen Strychni-induced neurotoxicity in SKJGT might be related to regulating amino acid and monoamine neurotransmitters, decreasing the damage in hippocampus and cerebellum, inhibiting absorptions of strychnine and brucine, and promoting their metabolisms in intestinal enzymes and gut microbiota, and increasing their plasma protein binding rate. In addition, there is no increase in risk of mercury poisoning caused by SKJGT and Semen Strychni might reduce cinnabar-induced toxicity when cinnabar against Semen Strychni-induced neurotoxicity in SKJGT.

Study on the Chemical Constituents of *Lonicera flos*

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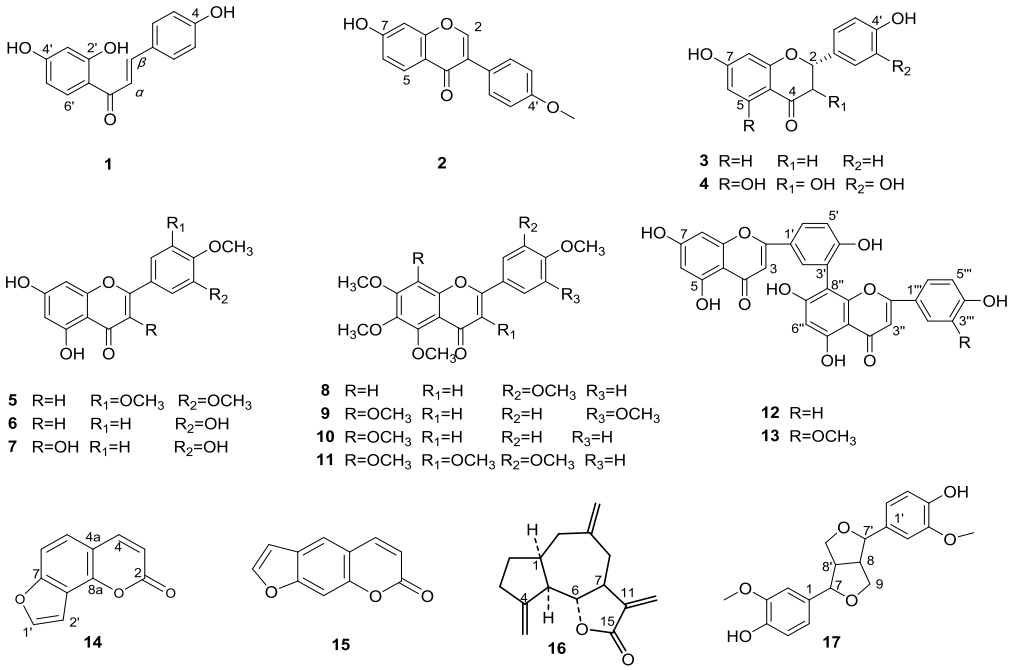
Abstract:

Aim: To investigate the chemical constituents in the flower buds of *Lonicera macranthoides* Hand.-Mazz. (*Lonicera flos*). **Methods**: Various column chromatography were used to isolate the constituents from the extracts of *L. macranthoides*. The chemical constituents of the plant were elucidated by spectroscopic methods, respectively. **Results**: 17 known compounds were isolated and identified which including 13 flavonoids named 4,2',4'-trihydroxychalcone (**1**), formononetin (**2**), liquiritigenin (**3**), taxifol (**4**), tricin (**5**), luteolin (**6**), quercetin (**7**), sinesetin (**8**), nobiletin (**9**), 5,6,7,8,4'-pentamethoxyflavone (**10**), 3,5,6,7,8,3',4'-heptamethoxyflavone (**11**), amentoflavon (**12**), 3'''-O-methylamentoflavon (**13**) and 4 other compounds named angelin (**14**), psoralen (**15**), dehydrocostus lactone (**16**), pinoresinol (**17**). **Conclusion**: Compounds **1-5**, **8-11** and **14-17** were obtained from this plant for the first time.



Chemical structures of compounds **1-17** isolated from *L. macranthoides*

Anti-depression effects of Xiaoyao pill increases hippocampal neurogenesis along the septo-tempora axis in chronic unpredicted mild stress rats

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Abstract:

Depression is a complex psychological illness characterized by loss of pleasure, mood disturbance and suicidal tendencies. Xiaoyao Pill (XYP) is a famous traditional Chinese medicinal prescription and has been widely used for the treatment of depression. The aim of this study is to explore the anti-depression mechanism of XYP in a chronic unpredicted mild stress (CUMS) depression rats. Firstly, Antidepressant-like effects of XYP were investigated through behavioral tests, and potential mechanism was assessed by neurotrophin and hippocampal neurogenesis. Antidepressant-like effects of XYP (0.67 and 0.17 g/kg/day) were estimated through Novelty suppressed feeding test, sucrose preference test, open-field test and Morris water maze test. Secondly, Effects of XYP on Cell proliferation and survival in the septo-temporal axis of the hippocampus were investigated by 5-bromo-2-deoxyuridine (BrdU), BrdU/ glial fibrillary acidic protein (BrdU/GFAP), BrdU/ hexaribonucleotide Binding Protein-3 (BrdU/ NeuN) and BrdU/doublecortin (BrdU/DCX). Thirdly, the expression of BDNF, NT-3, NGF in hippocampus was measured. Our results showed that XYP alleviated the CUMS-induced depressive symptoms displayed by enhanced sucrose consumption ($P<0.01$), decreased feeding latency ($P<0.05$), and increased locomotor activity ($P<0.01$), escape latency($P<0.05$), and distance of target quadrant($P<0.05$). Histology analysis revealed that XYP increased the number of new nerve cells labeled with BrdU, and Brdu+DCX, Brdu+GFAP, Brdu+NeuN positive cells in septo-temporal axis of S2 and T3($P<0.05$, $P<0.01$). Expression of BDNF, NT-3, and NGF increased significantly in the septo-temporal axis of S2 and T3($P<0.05$, $P<0.01$). These results provide direct evidence that XYP promote nerve regeneration across the septo-temporal axis of the hippocampus effectively, which may be related to its anti-depression effects.

Effects of UPLC-QTOF-MS parameters on the ionization and fragmentation behaviors of triterpenoid saponins from the root of *Ilex asprella*

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Abstract:

UPLC-QTOF-MS (LC-MS) method is widely used to qualitatively characterize the chemical profiles of herbal medicines, in which the generated adducts and fragments are crucial for confirming molecular ion (deprotonated/protonated ion) and deducing structure of detected components. However, if and how LC-MS parameters including mobile phase and MS parameters affect the quantity and intensity of adducts and fragments of detected components is scarcely concerned. In present study, three types of triterpene saponins in *Ilex asprella* (IA) were selected as a case study to investigate the effects of mobile phase and MS parameters on their ionization and fragmentation behaviors to obtain high intensity (high detection sensitivity) and quantity (rich information) of adducts and fragments, and then the optimum LC-MS parameters were applied to characterize the chemical profiles of IA. The results indicated that methanol as organic phase was benefit for generating more adducts with higher intensity compared to acetonitrile. Formic acid, as additive, suppressed the formation of $[M-2H]^{2-}$ and promoted the generation of other types of adducts at low concentration but inhibited the generation when the concentration exceeded 0.1%. MS parameters scarcely affect the quantity but mainly on intensity of adducts. Especially, cone voltage, source temperature and desolvation gas flow has relative higher impact compared with other MS parameters. Collision energy simultaneously affected the quantity and intensity of fragments. Moreover, MS parameters at the medium value largely increased the quantity and intensity of adducts and fragments, respectively. In addition, relationship between structure and ionization/fragmentation behaviors indicated that three-types of triterpene saponins (type A, B and C) presented structurally specific ionization and fragmentation behaviors due to their amounts of acidic substitutes. A total of 55 chemical components were detected and definitely or tentatively identified. Furthermore, 35 triterpene saonins were firstly discovered from IA. This study provided a new research strategy for qualitative analysis of herbal medicines which provided abundant MS information for the identification of unknown components.

2DLC-PDA/ELSD-QTOF-MS coupled with chemometric analysis to quantify and evaluate *Ginkgo biloba* leaves from different origins

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Abstract:

Ginkgo biloba L.(Ginkgoaceae) is the single extant species of the Ginkgophyta group, main surviving in China and some other parts of Asia. It thrived around 150 million years ago and was almost extinct later, during the ice age. Since the morphology of the Ginkgo tree has not changed and has remained intact for over 100 million years, it is often called a living fossil.

Various compounds have been isolated and identified in *Ginkgo biloba* L., including terpenoids, flavonol glycosides, biflavones, proanthocyanidins, alkylphenols, phenolic acids and polyprenols, etc. Terpene trilactones and flavonoids are considered the major bioactive compounds, and they are more intensively studied than the rest of the compounds. Since there are 24% flavonol glycosides and 6% terpene lactones in EGb 761, so the 70% compounds are rarely studied. The genuine flavonoid mix is highly complex and includes various flavonol glycosides and biflavones, etc. The content and distribution of this compounds are different in *Ginkgo biloba* leaves. Thus, the qualitative and quantitative analysis of genuine flavonol glycosides are important and attract the focused attention of many scholars.

To obtain an authentic and applicable analytical approach for quality evaluation of *Ginkgo biloba* leaves, a two-dimensional liquid chromatography coupled with photodiode array detector and time-of-flight mass spectrometry (2DLC-PDA-QTOF-MS) method was proposed and validated for analyzing and evaluating to use chromatographic fingerprinting followed by chemometric analysis with *Ginkgo biloba* leaves from different origins,. In this study, more than 150 kinds of compounds were identified from *Ginkgo biloba* leaves, and described the evaluation of *Ginkgo biloba* leaves using a fingerprint analysis. We quantified several characteristic components simultaneously, including six flavonol glycosides, five terpene trilactones and six carboxylic acids by 2DLC-PDA-ELSD. This optimized method was successfully applied to qualitative and quantitative analyze the explicit compositions in *Ginkgo biloba* leaves. Furthermore, the chemical component content of *Ginkgo biloba* leaves with different areas were analyzed using chemometric analysis. Correlation analysis indicated that the correlations between the flavonol glycosides, terpene trilactones and carboxylic acids contents vary with different *Ginkgo biloba* leaves from different origins. Among the three type of compounds existed different relationships. Contents of flavonol glycosides had positive linear corrtlation with terpene trilactones. The correlations among the contents of *Ginkgo biloba* leaves from different areas were different. In general, the contents of flavonol glycosides and terpene trilactones were relative high in south China, but the contents of carboxylic acids were on the contrary. Therefore, getting systematic knowledge of chemical constituents and contents in *Ginkgo biloba* leaves is significantly important for the development, safety and quality assurance of Ginkgo medicinal products.

Comprehensive different effects of safflower in rats acute myocardial infarction

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Abstract:

Acute myocardial infarction (AMI) is the major cause of death in the world wide. However, new drugs, which are studied follow by myocardial protecting mechanisms, have been reported less protective effect on myocardial ischemic injury. On the other hand, traditional Chinese medicine Hong-hua （*Carthamus tinctorius* L.）shows good effects on myocardial protection and myocardial ischemic damage. But preclinical study of Hong Hua is insufficient. Firstly, the rat AMI model was induced by ligating the left anterior descending coronary artery. Secondly, protective effect on myocardial ischemic injury were evaluated by survival and TTC staining. Thirdly, according to western blotting the changed protein were mainly involved the inflammation and apoptosis related pathways. Finally, Imaging Mass Spectrometry (IMS) were used to discriminate between non-infarction area and infarct area, The changed metabolites were mainly fatty acids. In our studies, safflower showed dual-direction regulation in cardioprotection. The hexane extraction from safflower. show protective effects in non-infarction zone, while increase infarct area. According to the transformation from metabolic profiling detection by Imaging Mass Spectrometry (IMS) and western blotting we try to explain the dual-direction regulation effects of safflower, and describe “yin” and “yang” change after treatment with safflower.

Network pharmacology-based prediction of active compounds and molecular targets in *Uncaria rhynchophylla* acting on hypertension and depression

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Abstract:

Uncaria rhynchophylla (Gou-Teng) is a traditional prescription for the treatment of hypertension and depression. It has been applied in clinics to treat the cardiovascular and central nervous system diseases according to Chinese Pharmacopoeia (2015 edition). However, a holistic network pharmacology approach to understanding the therapeutic mechanisms underlying hypertension and depression has not been pursued. **Aim of the study:** To understand active compounds and molecular targets in *Uncaria rhynchophylla* (UR) acting on hypertension and depression. **Materials and Methods:** In this study, total 129 *Uncaria* alkaloids was obtained from public databases like TCMAnalyzer, SymMap, TCMSP, ETCM, CMAUP and BATMAN-TCM, also from the literature review, and oral bioavailability and drug-likeness was screened using absorption, distribution, metabolism, and excretion (ADME) criteria by FAFDrugs4. Correlations between compounds and genes were linked using the TargetNet tools, and genes related to hypertension and depression were gathered using the DrugBank database. Common genes were identified and subjected to Metascape Express Analysis. **Results:** Total 50 genes related to 23 alkaloids in UR was obtained. Among them, 7 compounds (3-ethylamino-5-methoxy-1,2-benzoquinone, isocorynoxeine, corynoxeine, 3-diethylamino-5-methoxy-1,2-benzoquinone, harmane, 18,19-dehydrocorynxinic acid, 22-O-demethyl-22-O-β-D-glucopyranosyl isocorynoxeine) were linked to more than four genes, and are bioactive compounds and key chemicals. Core genes in this network were MAOA, CYP1A2, ADRA2B, while 4 genes (CES1, CYP1A2, MAOA, PTGS1) were linked to the most enriched terms R-HSA-211945 in hypertension, and 4 genes (CYP1A2, MAOA, MAOB, HTR2C) were linked to the most enriched terms Tryptophan metabolism in depression. **Conclusions:** The compound-target gene-disease network revealed close interactions between multiple components and multiple targets, and facilitates a better understanding of the potential therapeutic effects of UR on hypertension and depression.

Exploring ionization and imaging characteristics of different types of natural products with DESI imaging mass spectrometry

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Abstract:

Plant secondary metabolites are the efficacious material basis of traditional Chinese medicine (TCM), the distribution of which provides important reference for the reasonable exploitation, utilization and quality evaluation of TCM. Desorption electrospray ionization-mass spectrometry (DESI-MS) imaging allows visualization and localization of secondary metabolites without sample extraction or addition of any external label. This study is focused on DESI ionization characteristics of natural products with different types of structures, including flavonoids, alkaloids, iridoids, triterpenes, lactones, sterides, saponins, phenolic acids, etc, to lay a foundation for DESI imaging research of TCM. Experiments were carried out on a SYNAPT G2-S QTOF mass spectrometer, in negative and positive mode, over a mass range of m/z 50-1,200. DESI spray conditions were set at 3 μl/min, MeOH solvent, with a stage speed of 500 μm/sec and an image resolution of 500x500 μm. 88 reference compounds were dissolved to 1 mg/ml and 1 μL of each solution was spotted onto a filter paper. Imaging datasets were subsequently mined using MassLynx and High Definition Imaging (HDI) 1.4 software packages. As a summary, in positive mode, a majority of alkaloids had MS signal intensity an order of magnitude higher than other compounds, while the ones containing saccharide groups, like vincosamide and 3-dihydrocadambine, were only slightly ionized. Analogously, most of the saponins had relatively low signal intensity. This phenomenon was presumed to be attributed to the common glycosyl groups, which might through hydrogen bonds bind too strongly with the filter paper surface to be ionized. Besides, iridoids, triterpenes, lactones and sterides, with similar signal intensity to each other, could be observed well. In negative mode, the MS response signals of phenolic acids and most flavonoids were much better than that in the positive mode. The use of spray solvent additives such as formic acid and ammonium formate could alter adduct formation and thus improve the ionization efficiency of certain compounds, such as steroidal compound bufalin and triterpenoid compound 23-acetylalisol C. Noteworthily, isomers or structural analogues commonly found in TCM may produce the same fragment with different signal intensity while imaging. This could be due to the difference of ionization site and needs to be analyzed combining with MS^3 spectra. Furthermore, the DESI-MSI was employed for tissue imaging of fresh *Rehmanniae Radix*. The distinct localization of catalpol and rhmannioside D, as major efficacious components, was successfully observed.

"Commercial-homophyletic" comparison-induced robust biomarkers discovery for the authentication of herbal medicines, *Panax ginseng* as a case study

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Abstract:

A key segment in authentication of herbal medicines is the establishment of robust biomarkers that embody the intrinsic different independent of the growing environment or processing technics. We present a strategy by "commercial-homophyletic" comparison-induced biomarkers verification with new bioinformatic tools, to improve the efficiency and reliability in authentication of herbal medicines, and *Panax ginseng* was illustrated as a case study. First, an optimized ultra-performance liquid chromatography/quadrupole time-of-flight-MS^E approach was established for global metabolites profiling. Second, UNIFI™ combined with search of an in-house library was employed to automatically characterize the metabolites. Third, pattern recognition multivariate statistical analysis of the MS^E data of different parts of commercial and homophyletic samples were separately performed to explore potential biomarkers. Fourth, potential biomarkers deduced from commercial and homophyletic root and leaf samples were cross-compared to infer robust biomarkers. Fifth, discrimination models by artificial neutral network were established to identify mixture of leaf and root samples. Consequently, 164 compounds were characterized. The ANN models using the 13 robust biomarkers managed to exactly discriminate the different level of mixture of root and leaf samples. Conclusively, biomarkers verification using homophyletic samples conduces to the discovery of robust biomarkers. The integrated strategy facilitates authentication of herbal medicines in a more efficient and more intelligent manner.

Molecular regulation of artemisinin biosynthesis under cold condition

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Abstract:

Both of cold acclimation and stress promote the expression of artemisinin biosynthesis genes, leading to increase the artemisinin production in Artemisia annua. A 4℃-induced bHLH transcription factor (AabHLH112) positively regulated expression of artemisinin biosynthesis genes via AaERF1, revealing that molecular mechanism that cold acclimation regulated artemisinin biosynthesis. Genome-wide analysis indicated that another bHLH TF, namely AabHLH106, might be involved in regulating artemisinin biosynthesis under cold stress (0℃ condition). AabHLH106 was responsive to 0℃ and ABA treatment. It could indirectly up-regulate the expression of artemisinin biosynthesis. AabHLH106 interacted with AaMYC2 to form a transcriptional complex, in which AaMYC2 bound to the cis-elements in the promoters of artemisinin biosynthesis genes, and AabHLH106 transactivated the expression of artemisinin biosynthesis genes. Furthermore, a SnRK2-type kinase AaAPK1 interacted with AabHLH106 to enhance the transactivating function of AabHLH106 on artemisinin biosynthesis, suggesting that AaAPK1-mediated phosphorylation of AabHLH106 played a key role in regulating artemisinin biosynthesis under cold stress. Besides regulating artemisinin biosynthesis, either AabHLH112 or AabHLH106 regulated cold tolerance through binding to the AaCBF1 promoter. Overexpression of AabHLH112 or AabHLH106 significantly promoted artemisinin biosynthesis and enhanced cold tolerance in Artemisia annua plants.

Cardioprotective effects of DQTM on acute myocardial infarction is associated with the arachidonic acid metabolome-mediated inflammatory response

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Abstract:

Danqi Tongmai tablet (DQTT), an innovative TCM formula under clinical trials, is composed of salvianolic acids (SA) and panax notoginsenosides (PNE) for the treatment of coronary heart disease and angina pectoris. Previous studies demonstrated that DQTT had cardio-protective effects in rat with acute myocardial infarction (AMI). However, the mechanisms by which DQTT prevent AMI heart failure are still unclear. In this study, we explored the arachidonic acid metabolome-mediated inflammatory response in AMI rat after orally DQTT. An animal model of AMI was conducted by ligation of left anterior descending (LAD) coronary artery in rat. *In vivo* results showed that DQTT administration could improve cardiac functions and alter pathological changes in model of AMI. This study presents a metabolomic method to assess a broad spectrum of regulatory lipid mediators in plasma from AMI rats. A broad range of both pro-inflammatory and anti-inflammatory lipid mediators was detected, including PGE2, PGF2, PGD2, PGJ2, PGI2, PGE1, 6-Keto-PGF1, TXB2, LTB4, 6-trans-LTB4, 20-COO-LTB4, 5-HETE, 5-OxOETE, LXA4, 20-HETE, 18-HETE, 17-HETE,16-HETE, 15-HETE, 15-OxOETE, 11-HETE, 12-HETE, 12-OxOETE, 8-HETE, 8-HPETE, 9-HETE, and EpETrEs. DQTT regulated key molecules, cyclooxygenases (COXs) and lipoxygenases (LOXs), in arachidonic acid metabolism pathway. DQTT attenuated inflammation induced by arachidonic acid LOX and COX pathway. This study provides insights into anti-inflammatory therapeutics in managing heart failure after AMI.

Keyword: notoginseng total saponins (NS); safflower total flavonoids (SF); bile excretion; synergistic action; LC-MS

Comparative study on excretion of main components in herb pair notoginseng-safflower and single herbs by LC–MS/MS in rat bile

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Abstract:

Traditional Chinese medicines herbal pairs (TCM-HP), which consist of two standard single herbs in traditional Chinese prescriptions, exert better therapeutic outcomes and fewer side-effect via synergistic actions. The combination of notoginseng total saponins (NS) and safflower total flavonoids (SF), namely CNS, presents a synergistic effect on the myocardial ischemia rats. Notoginsenoide R1 (NGR1), Ginsenosides Rg1 (GRg1), Rb1 (GRb1), Re (GRe), Rd (GRd), and hydroxysafflor yellow A (HSYA) are the effective ingredients of CNS. To our knowledge, pharmacokinetic profiles before and after the compatibility play an important role towards in explaining TCM-HPs integrative mechanisms, and biliary excretion is the primary factor influencing systemic exposure to most ginsenosides. The aim of this study was to find the clues for CNS synergistic actions by comparing the biliary excretion profiles after oral administration of CNS and its individual extracts. Rats were received NS (60 mg/kg), SF (50 mg/kg), and CNS (NS 60 mg/kg + SF 50 mg/kg). Bile samples were collected at 0–2, 2–4, 4–6, 6–8, 8-10, 10–12, 12–24, 24–36 h and extracted with dichloromethane and n-butanol in a ratio of 1:2 (v/v) three times for analysis. The primary circulating and biological components HSYA, GRg1, GRe, GRd, and NGR1 were chosen to compare the bile excretion between SF, NS, and CNS groups. An ultra-performance liquid chromatography coupled with hybrid triple quadrupole-linear ion trap mass spectrometer (UPLC–QTRAP–MS/MS) method for the qualification study of four compounds was conducted, and well satisfied the requirements from the guidelines of FDA (specificity, calibration curve, sensitivity, precision, accuracy, matrix effect, recovery, and stability), and was applied to the rat bile excretion study. The UPLC–QTRAP–MS/MS method was proved to be linear ($r \geq 0.9941$) at the tested concentration ranges. The accumulative excreted ratios of HSYA were 0.26% and 0.24% within 36 h after oral administration of SF and CNS to rats. Comparing with the SF group, the cumulative excretion ratio of HSYA in the CNS group was decreased by 0.92 times. In the NS group, the cumulative excretion ratios of NGR1, GRe, GRd, and GRg1 were 2.89%, 3.03%, 1.10%, and 0.76% within 36 h, which were decreased by 0.96, 0.84, 0.57 ($p < 0.05$), and 0.92 times compared with the CNS group. The cumulative excretion ratios of the five compounds in NS or SF group were all lower than that in CNS group. The 20(S)-protopanaxadiol type (ppd-type) GRd presents a more gently accumulative excreted curve, and the cumulative excretion ratio of GRd significantly decreased after the compatibility. The results indicated that the CNS could reduce the bile excretions of the bioactive constituents and promote their absorptions. To the best of our knowledge, this is the first report on the biliary excretion of TCM-HP notoginseng-safflower and its single

herbs in rat bile. A UPLC–QTRAP–MS/MS method was validated and applied for depicting the bile excretion profiles of main bioactive compounds, including HSYA, GRg1, GRe, GRd, and NGR1. In this study, we found CNS could decreased the excretion ratios of bioactive compounds in CNS, which may be one of the reasons for CNS′s synergistic actions.

Occurrence and analysis of mycotoxins in domestic Chinese herbal medicines

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Abstract:

Chinese herbal medicines (CHM) have been widely used in China for disease treatment or health care from immemorial time. However, in recent years, many studies have shown that mycotoxins could be produced by fungi during unfavourable pre- or post-harvest stage of herbal materials, which leads to major concern for consumer safety. At present, more attentions have been paid for the development of mycotoxins detection method in CHM, at the same time, numerous researches have been performed to aim to demonstrate which kinds of raw herbal martials are more susceptible to mycotoxin contamination. It is worth noting that some kinds of medicinal materials were found to be with high contamination rate and level, and multiple mycotoxins contamination occurred in some matrixes. In addition to AFs, so far, regulations and limit standards for other mycotoxins in CHM have not yet been widely established. Therefore, it is necessary to conduct the in-depth research to indicate which CHM are easily contaminated and establish the limit standards for important mycotoxins in herbal medicines.

Now there has been a tendency towards the development of rapid analytical method for mycotoxin detection in Chinese herbal matrix. During recent years, biological analysis methods have been tried to apply to the detection of mycotoxins in CHM including Enzyme-linked Immunosorbent Assay and Gold Immunochromatographic Assay. However, some novel technologies such as immune biosensors with ultra-sensitivity which have been reported for mycotoxin detection in food and feed should be more emphasized, especially for mycotoxin detection in the CHM samples with complicated matrixes.

In recent years, researches on the presence of mycotoxin in CHM mainly focus on analysis of mycotoxin varieties, contamination level and detection method, while few researches on toxigenic mechanisms, detoxification techniques and prevention and control measures. In addition to the herbal medicine itself, the factors of mycotoxin contamination in the medicinal materials are intimately related to the place of origin, processing methods and storage conditions. Therefore, in the future research, it should be emphasized to carry out the investigation on the mechanism of the mycotoxin occurrence in CHM under various matrixes or storage conditions, and then establish the efficient prevention strategy for reducing the possibility of fungi and mycotoxins contamination in CHM.

Flavonoid and triterpenoid *O*-glycosyltransferases from *Glycyrrhiza uralensis*

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Abstract:

Licorice (*G. uralensis*) is a popular herbal medicine containing diverse *O*-glycosides, including at least 70 flavonoid and triterpenoid glycosides. However, the reason of such diversity has rarely been elucidated at the genetic and biochemical level. A homology-based method was used to mine the licorice transcriptome data and 43 candidate *O*-glycosyltransferases (*O*-GT) genes were discovered. Functions of 17 heterologously expressed proteins were analyzed by enzymatic catalytic reactions using eight native substrates. The glycosylated products were separated and confirmed by NMR characterization or comparing with reference standards, to identify the catalytic sites of GTs. We identified 11 *O*-GTs which could catalyze the formation of licorice secondary metabolites. They include GuGT6, an isoflavone 7-*O*-GT; GuGT1 / 26 / 39, flavonol 3-*O*-GTs; GuGT10 and GuGT14, promiscuous GTs that catalyze multiple flavones, chalcones and triterpenes. Several important glucosides in licorice, including liquiritin, isoliquiritin, ononin, and 3-*O*-*β*-D-glucuronopyranosyl glycyrrhetinic acid, could be synthesized by these eleven new *O*-glycosyltransferases, indicating their contribution to flavonoid and triterpenoid diversity. These enzymes were also used to effectively catalyze the glycosylation of other natural products, and it was meaningful for the synthetic of natural or unnatural glycosides. The discovery of licorice GT genes improved the understanding of *O*-glycosides diversity in licorice, and provided new biocatalytic tools for the synthesis of licorice compounds and other plant natural products.

Cellular lipidomics-based protective exploration of Safflower Injection for ischemic stroke

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Abstract:

Ischemic stroke, the most common form of stroke (approximately 80%–90%), is one of the leading cause of death and long-term disability worldwide. Promising results from clinical trials have fueled a growing acceptance of Safflower Injection (SI) for the treatment of ischemic stroke. In this study, the cerebroprotection of SI were firstly confirmed on permanent middle cerebral artery occlusion (MCAO) in rat. Then, the protective effects and potential mechanisms of SI were explored through an untargeted lipidomics strategy based on microglia (BV2). The oxygen-glucose deprivation and reperfusion (OGD/R)-induced BV2 injury model were developed, and a UPLC-QTOF MS method was carried out to profile the lipids of different cellular groups. The results showed that SI exhibited remarkable neuroprotection on OGD/R exposed BV2, which was evidenced by reduction of the cellular damage and diminishment of excessive accumulation of intracellular reactive oxygen species. Meanwhile, 82 lipid biomarkers of injury induced by OGD/R have been identified, perturbations of which could be partly (39 out of 82) reversed by SI intervention. The cellular lipidomics provides that the protection of SI against OGD/R-induced injury were closely related to the glycerophospholipid metabolism, sphingolipid metabolism and retrograde endocannabinoid signaling metabolism.

Meta-analysis of Chinese herbal medicine in alleviating anemia caused by 5-fluorouracil based chemotherapeutic drugs

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Abstract:

Objective: To study the literature of Chinese herbal medicine in alleviating anemia caused by 5-fluorouracil chemotherapeutics, and to screen the effective drug regimens for preventing chemotherapy-related anemia. Methods: By using meta-analysis method, we have systematically and comprehensively searched the relevant literatures on the treatment or prevention of chemotherapeutic anemia in patients with colorectal cancer in CNKI, VIP Database, Wanfang Database and SinoMed databases. By formulating inclusion and exclusion criteria, we screened the relevant literatures and extracted them. RevMan 5.3 software was used for meta-analysis of important literature information. Results: A total of 50 articles were included in this review. A meta-analysis was conducted on the studies of the same Chinese herbal prescriptions or preparations. A total of 10 articles including 4 prescriptions or preparations were selected. The four prescriptions or preparations and their preventive effects were Aidi injection (OR: 0.26, 95% CI: 0.13-0.52, P = 0.0001), Sijunzi Decoction (OR: 0.30, 95% CI: 0.10-0.90, P = 0.03), which could effectively prevent anemia caused by fluorouracil chemotherapeutic drugs. The data of Junzi Fuzheng Decoction (OR: 0.87, 95% CI: 0.42 - 1.81, P = 0.71), Shengxue Decoction (OR: 0.57, 95% CI: 0.27 - 1.20, P = 0.14) between the treatment group and the control group had no statistical difference, which could not indicate that they could effectively prevent anemia caused by 5-fluorouracil based chemotherapy. Conclusion: The use of Aidi injection and Sijunzi decoction can effectively reduce the incidence of anemia in the treatment of colorectal cancer with 5-fluorouracil chemotherapy.

Keyword : Chinese herbal medicine; colorectal cancer chemotherapy; capecitabine; anemia; Chinese medicine prescription; Chinese medicine preparation; meta-analysis

Integration of molecular network virtual screening with affinity mass spectrometry screening for the efficient discovery of ligands from natural herbs

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Abstract:

Achieving the rich source of compounds from nature herbs in the pharmaceutical industry suffers from low efficiency and prohibitive cost via the conventional bioassay-based screening platforms. Here we developed a new strategy that constructing TCM molecular network to guide affinity mass spectrometry and virtual screening for efficient discovery of herb-derived ligands towards specific protein targets. Simultaneously, Our screening approach based on Scaffold Hunter and MS-DIAL metabonomic analysis integration with a molecular networking workflow enables the creation of a flexible visual analytics framework from several fields and the high-throughput interrogation of hundreds of natural herb constituents in a rapid process. In a benchmark study, several compounds from traditional Chinese herbs identified by this approach were confirmed to interact with the small G-protein of Ras and proved to be effective in cancer cell bioactivity profiles. Our modified screening approach dramatically improves the systematicness and throughput sensitivity of ligand screening from herbal extracts.

Insight into the new challenge for quality control of *Ganoderma lucidum*

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Abstract:

Ganoderma lucidum is always cultivated in a similar conditions, while its quality is still fluctuated. This is a common problem for quality control of traditional Chinese medicines containing high similarity. In this study, we focus on the geographical discrimination, intraspecific differentiation, and rapid analysis of *G. lucidum* to develop the quality control system. Firstly, 161 batches of samples were systematically profiled by UPLC-QTOF/MS, and 551 triterpenoids were characterized based on the home-built compound database and commercial compound characterization softwares. Moreover, their producing areas were successfully discriminated by their small molecule compounds and a new bilinear support vector machine method based on parameter L2. Comparison to the classical chemometrics approaches (principal component analysis and partial least squares discriminant analysis), our developed method showed higher accuracy among 10 sampling origins with reaching to the 95%. As for the active polysaccharides, our study indicated their acidic hydrolysates, the total polysaccharides and the anticancer compound mannose, were the good quality markers for intraspecific differentiation using HILIC-ELSD/ESI-TOF-MS and OPLS-DA analysis. In particular, the highest polysaccharides content was 1.77 ± 0.61%, and the mannose was 0.07 ± 0.02 mg/g. Finally, a rapid analysis method based on NIR technology along with random forest algorithm was developed to determine the quality marker in *G. lucidum*. The accuracy was 96.87% in self-training set and was 93.33% in independent test set. The contents of total polysaccharides were 2.27% ~ 3.97%, 2.27% ~ 3.90%, 2.72% ~ 3.99%, and 3.01% ~ 3.99% in Shaanxi, Sichuan, Hubei, and Zhejiang, respectively. The results indicated the samples from Zhejiang Province showed best quality. In brief, our developed quality control system is good for overcoming the new challenge for quality variation of *G. lucidum*.

Keyword : *Ganoderma lucidum*; geographical discrimination; intraspecific differentiation; rapid analysis; quality control; UPLC-QTOF/MS.

Comparative study on excretion of main components in herb pair notoginseng-safflower and single herbs by LC–MS/MS in rat bile

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Foundation: National Natural Science Foundation of China (No. 81530097).

Abstract:

BACKGROUNDS & AIMS: Traditional Chinese medicines herbal pairs (TCM-HP), which consist of two standard single herbs in traditional Chinese prescriptions, exert better therapeutic outcomes and fewer side-effect via synergistic actions . The combination of notoginseng total saponins (NS) and safflower total flavonoids (SF), namely CNS, presents a synergistic effect on the myocardial ischemia rats . Notoginsenoide R1 (NGR1), Ginsenosides Rg1 (GRg1), Rb1 (GRb1), Re (GRe), Rd (GRd), and hydroxysafflor yellow A (HSYA) are the effective ingredients of CNS . To our knowledge, pharmacokinetic profiles before and after the compatibility play an important role towards in explaining TCM-HPs integrative mechanisms, and biliary excretion is the primary factor influencing systemic exposure to most ginsenosides . The aim of this study was to find the clues for CNS synergistic actions by comparing the biliary excretion profiles after oral administration of CNS and its individual extracts. **METHODS:** Rats were received NS (60 mg/kg), SF (50 mg/kg), and CNS (NS 60 mg/kg + SF 50 mg/kg). Bile samples were collected at 0–2, 2–4, 4–6, 6–8, 8-10, 10–12, 12–24, 24–36 h and extracted with dichloromethane and n-butanol in a ratio of 1:2 (v/v) three times for analysis. The primary circulating and biological components HSYA, GRg1, GRe, GRd, and NGR1 were chosen to compare the bile excretion between SF, NS, and CNS groups. An ultra-performance liquid chromatography coupled with hybrid triple quadrupole-linear ion trap mass spectrometer (UPLC–QTRAP–MS/MS) method for the qualification study of four compounds was conducted, and well satisfied the requirements from the guidelines of FDA (specificity, calibration curve, sensitivity, precision, accuracy, matrix effect, recovery, and stability), and was applied to the rat bile excretion study . **RESULTS:** The UPLC–QTRAP–MS/MS method was proved to be linear ($r \geq 0.9941$) at the tested concentration ranges. The accumulative excreted ratios of HSYA were 0.26% and 0.24% within 36 h after oral administration of SF and CNS to rats. Comparing with the SF group, the cumulative excretion ratio of HSYA in the CNS group was decreased by 0.92 times. In the NS group, the cumulative excretion ratios of NGR1, GRe, GRd, and GRg1 were 2.89%, 3.03%, 1.10%, and 0.76% within 36 h, which were decreased by 0.96, 0.84, 0.57 ($p < 0.05$), and 0.92 times compared with the CNS group. The cumulative excretion ratios of the five compounds in NS or SF group were all lower than that in CNS group. The 20(S)-protopanaxadiol type (ppd-type) GRd presents a more gently accumulative excreted curve, and the cumulative excretion ratio of GRd significantly

decreased after the compatibility. The results indicated that the CNS could reduce the bile excretions of the bioactive constituents and promote their absorptions.

CONCLUSION: To the best of our knowledge, this is the first report on the biliary excretion of TCM-HP notoginseng-safflower and its single herbs in rat bile. A UPLC–QTRAP–MS/MS method was validated and applied for depicting the bile excretion profiles of main bioactive compounds, including HSYA, GRg1, GRe, GRd, and NGR1. In this study, we found CNS could decreased the excretion ratios of bioactive compounds in CNS, which may be one of the reasons for CNS's synergistic actions.

Keyword : notoginseng total saponins (NS); safflower total flavonoids (SF); bile excretion; synergistic action; LC-MS

Four new *ent*-Kaurane diterpene glycosides from *Isodon henryi*

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Abstract:

Diterpenoids from Isodon plants possessing potent cytotoxic activities, are potential candidates for the treatment of cancer. As known, a few diterpenoid glycosides have been reported occurring in the herbs from Isodon plants. Accordingly, we wonder the structure-cytotoxicity relationship of diterpene glycoside. In order to obtain the diterpene glycosides and clarify the effect of the introduction of sugar on the cytotoxicity of diterpenoids. In this study, the above-ground water extracts of Isodon henryi were used to separate and prepared by locking diterpenoid glycosides. Seven compounds were isolated including six ent-kaurane diterpene glycosides (1-6), and four new compounds, ent-7,20 -epo -xy-kaur-16-en-1α,6β,7β,15β-tetrahydroxyl-11-O-β-D-glucopyranoside (1), ent-7,20-epoxy- kaur-16-en-6β,7β,14α,15β-tetrahydroxyl-1-O-β-D-glucopyranoside (2), ent-7,20-epoxy-kaur -16-en-6β,7β,15β-trihydroxyl-1-O-β-D-glucopyranoside(3),ent-7,20-epoxy-kaur-16-en-7β,11β,14α,15β-tetrahydroxyl-6-O-β-D-glucopyranoside (4), two known compounds (5-6). And one diterpene aglycon (7) of compounds 2 and 6 from Isodon henryi. Their structures were elucidated on the basis of spectroscopic methods and electronic circular dichroism analyses. Furthermore, the cytotoxicity for 7 compounds were evaluated to study the effect of glycosylation on cytotoxicity of diterpene compounds. The results indicate that introduction of glycosyl group has no significant effect on cytotoxic activity. And the cytotoxic activity was significantly reduced without α,β-unsaturated pentones and exocyclic methylene groups in the structure of 7,20 epoxy ent-kaurane diterpenoids.

Rapid characterization of saponins in fresh and steamed Panax notoginseng root slices by liquid extraction surface analysis-mass spectrometry

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Abstract:

Notoginseng Radix et Rhizoma (Sanqi), is the underground part of Panax notoginseng (Burk.) F. H. Chen (Araliaceae), and one of the most valuable TCMs. It is widely used in China with a long history for treatment of haemorrhage, swelling and cardiovascular disease. In the past 20 years, steamed P. notoginseng has been considered to have strong pharmaceutical activity in the treatment of tumor, angiocardiopathy, etc. Particularly, triterpenoid saponins are the principal chemical and pharmacological ingredients in P. notoginseng. It is of great importance to determine the difference of between fresh and steamed P. notoginseng and the components of saponins. In this study, we applied the direct and rapid extraction on the surface of sanqi slices by a liquid extraction surface analysis combined with mass spectrometry (LESA-MS). Chip-based multi-channel nano-spray ion source (TriVersa Nanomate) coupled with linear ion trap mass spectrometer with negative full-scan mode was performed. About 2.0 μL solvent comprising 80:20 acetonitrile to water with 0.1% formic acid was used to rapidly extract the saponins in the xylem, phloem and cambium of root slices of fresh and steamed P. notoginseng. The results showed that the saponin compounds and their contents in fresh and steamed P. notoginseng root slices were different. In fresh root slices, ginsenoside Rg1, Rb1, Re, Rd, notoginsenoside R1 and malonyl group components were more abundant. In steamed slices, ginsenoside Rg5, Rk1 and other minor polar components could be detected, while the relative content of large polar components was lower. In addition, in fresh root slices, the relative content of saponins in xylem was the highest. However, the phloem saponins content was the highest in the steamed root slices. The proposed method is rapid, stable and high sensitive, and the whole process does not need traditional cumbersome pretreatment such as crushing, extraction and separation. It can conduct a non-destructive preliminary study on the difference of saponins between fresh and steamed P. notoginseng root slices.

Keyword : Liquid extraction surface analysis-mass spectrometry; LESA-MS; Panax notoginseng; Saponins

Discrimination of Panax ginseng from different geographical origins using LESA-MS

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Abstract:

Panax ginseng has been widely used in the treatment of cardiovascular, kidney, reproductive disease in China. Various bioactive constituents in P. ginseng including ginsenoside (protopanaxadiol, protopanxatiol, ocotillol and oleanolic acid types), polysaccharides, alkaloids, glucosides, phenolic acid have been investigated in the previous study. The distributions usually locate in the East Asia, especially northeast of China, Korea and Japan. The source from different regions might lead to the differential bioactive constituents. To comprehensively distinguish P. ginseng of five places of northeast of China, Jilin province. A quick qualitative analysis using LESA-MS was established for the discrimination of P. ginseng from Changbai, Jingyu, Dunhua, Yanji. For phloem, cambium and xylem of fresh and dried root, some markers were screened by MS and MS/MS using LTQ XL mass spectrometer. The results showed that: (1) The solution of acetonitrile: water = 8:2 had the better performance than that of methanol: water = 8:2 for LESA-MS of P. ginseng; (2) In the root of fresh P. ginseng, the fragment ion of m/z 387 and m/z 728 were identified tentatively as monoacylglycerol and ginsenoside Rh1, respectively. Three ions m/z 377 (β-monolinolein), 811 (ginsenoside Rg1) and 885 (malonylginsenoside Rg1) could distinguish root of dried P. ginseng from others. In addition, phloem, cambium and xylem of fresh and dried ginseng had similar chemical constituents, while the intensity of compounds varied for different parts; (3) By using the PLS-DA analysis, the value of R2Y (0.65) indicated that the variance of the model had the good performance. Q2 (0.55) was more than 0.5 suggested that it had a good predictive ability of model; (4) Two-dimension score plot of PLS-DA suggested that five regions of Jilin province could be discriminated well by LESA-MS. Especially, the spots of Jingyu, Dunhua and Yanji closed to each other. It indicated that the samples of those regions had the similar chemical profiling. It is expected that the proposed method could be used for identification of herbal medicals in the further study with more tested samples.

Keyword : Discrimination; P. ginseng; Geographical origins; LESA-MS

Using Liquid Extraction Surface Analysis Mass Spectrometry (LESA-MS) for Steroid Hormones Determination In vitro

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Abstract:

Benign prostatic hyperplasia (BPH) is a common male urinary system disease. With the aging of world population trends in the intensification, this problem is getting worse. Studies have shown that steroid hormones and 5α-reductase is closely related to BPH. 5α-reductase converts testosterone to dihydrotestosterone, and excess dihydrotestosterone will cause androgen-related diseases such as androgenetic alopecia, benign prostatic hyperplasia. However, the drugs finasteride and dutasteride have side effects that cannot be ignored. Therefore, it is necessary to find an effective and fewer side effects 5α-reductase inhibitor. This study innovatively uses the LESA-MS direct injection analysis method for drug screening, which simplifies sample pretreatment and improves experimental efficiency. Cells were seeded in 96-well plates and divided into four groups: Blank control group (BK), Dutasteride group (DD), Finasteride group (FD) Curcumin group (CC). After extracting with ethyl acetate, transfer solvent to new 96-well plate and then directly inject for LESA-MS detection. The drug screening results of LESA-MS are consistent with the results of HPLC-MS, which suggests that LESA-MS is an effective drug screening method. This is the first time that LESA-MS has been used to reveal changes of steroid hormones in cells and applied to the 5α-reductase inhibitor screening experiment.

Keyword : 5α-reductase inhibitor, Benign prostatic hyperplasia, LESA-MS, Dihydrotestosterone

Rapid quantitative profiling of bile acids in bear bile powder using UHPLC-CAD/MS technique

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Abstract:

Bear bile powder (BBP) is a precious Traditional Chinese Medicine (TCM) with good clinical efficacy. Due to scarcity of the resource, bile powders of other animal origins are frequently found in the market. Routine methods used for quality control of BBP show disadvantages of insufficient chemical information and time-consuming. Therefore, a rapid and sensitive quantitation method targeting the bioactive bile acids (BAs) is critical for the quality control of BBP and the assurance of clinical efficacy. In this study, a novel method employing ultra high-pressure liquid chromatography tandem charged aerosol detector (UHPLC-CAD) was developed to profile the BAs in BBP, and mass spectrometry served to supply the structure information. Ten batches of BBP from different sources were collected and analyzed. As a result, eight BAs could be quantitated in only 15 minutes. Developed method was validated in terms of linearity, precision, accuracy, sensitivity, and repeatability. Further, the superiority of CAD over traditionally used evaporative light scattering detector (ELSD) was also verified in this study. In conclusion, the newly developed UHPLC-CAD/MS method could be utilized to evaluate the quality of BBP in a fast and sensitive manner. This study also provided reference for quality control of other herbal drugs which mainly contain components without strong ultraviolet absorption.

Keyword : bear bile powder; bile acid; UHPLC; charged aerosol detector; mass spectrometry

Metabolic profiles and pharmacokinetics of *R,S*-goitrin in rats through liquid chromatography combined with electrospray ionization–tandem mass spectrometry

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Abstract:

Several chemical and biological studies have revealed *R,S*-goitrin as the main bioactive constituent of *Isatis indigotica* Fort. responsible for antiviral and antiendotoxin activities. However, few pharmacokinetic studies of *R,S*-goitrin have been conducted. To comprehend the kinetics of *R,S*-goitrin and promote its curative application, a rapid and sensitive UHPLC–MS/MS method was developed. The selected reaction monitoring transitions were m/z 130.0 → 70.0 for R,S-goitrin and m/z 181.1 → 124.0 for the internal standard in a positive-ion mode. The established UHPLC–MS/MS method achieved good linearity for *R,S*-goitrin at 10–2000 ng/mL. The intraday and interday accuracy levels were within ± 9.7%, whereas the intraday and interday precision levels were <11.3%. The extraction recovery, stability, and matrix effect were within acceptable limits. The validated method was successfully applied for the pharmacokinetic analysis of *R,S*-goitrin in rats after oral administration. Moreover, a total of six metabolites were structurally identified through UHPLC-Q/TOF-MS. The proposed metabolic pathways of *R,S*-goitrin in rats were demethylation, acetylation, glutathionylation, and oxygenation.

Keyword : *R,S*-goitrin, LC-Q/TOF-MS, pharmacokinetics, drug metabolism

Quality assessment and classification of Goji berry by an HPLC-based analytical platform coupled with multivariate statistical analysis

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Abstract:

HPLC fingerprint analysis, principle component analysis (PCA), hierarchical cluster analysis (HCA), and orthogonal partial least squares discriminant analysis (OPLS-DA) were introduced for quality assessment of Goji berry. The fingerprint of Goji berry was developed by analyzing 67 samples of Goji berry from different species and growth years. The correlation coefficients of similarity in chromatograms were higher than 0.900 for the same species and growth years while varieties from 0.726 to 0.986 for different species and growth years. PCA and HCA results showed that the samples could be clustered reasonably into different groups corresponding to different species and growth years. OPLS-DA model identified ten marker compounds for identifying different species and nine marker compounds for identifying different species. Some compounds have been identified by mass spectrometry. The content of the marker compounds was varied among samples. The contents were significantly high in samples of two-years and fifteen-years, showing a large difference in the dynamic accumulation of nine marker components. The quality of "Ningqi" No.7 and "Ningqi" No.9 were better than other three varietie, because of the high contents of ten marker compounds. This work distinguished Goji berries from different species and growth years and assessed the quality of Goji berries, combining HPLC fingerprint with chemometric methods which is a very flexible and reliable method.

Keyword : HPLC Fingerprint; PCA; OPLS-DA; Marker Compounds; Quality

Rapid screening anti-osteoporosis ingredients from Chinese medicine prescriptions by osteoblast membrane chromatography/ high performance liquid chromatography-time of flight mass spectrometry

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Abstract:

Objective: Cell membrane chromatography is a promising technique for screening active components from complex matrices. In this study, an osteoblast membrane chromatography coupled with liquid chromatography time-of-flight mass spectrometry method was developed for recognizing and identifying the specific active components from two Chinese medicine prescriptions (Erxian Decoction and Liuwei Dihuang Decotion).

Methods: The method used MC3T3-E1 osteoblasts (5×107) was used as the cell membrane source. Osteoblast cell membrane chromatographic column (2 mm×10 mm) was prepared by coating silica gel (0.05 g) with cell membrane. The active ingredient in Liuwei Dihuang Decotion aqueous extract and Erxian Decoction (90 mg/mL) were firstly screened by cell membrane chromatography. The mobile phase was water and the flow rate was 0.20 mL/min. Then, the cell membrane chromatographic retention components were qualitatively analyzed by UPLC-QTOF/MS method. The mobile phase was acetonitrile-water at a flow rate of 0.40 mL/min. The column was WATERS ACQUITY UPLC BEH C18 (10mm×2mm id). Then, the osteoblast model and prednisolone-induced zebrafish model was used to verify the pharmacological effects of the main active ingredients.

Results: Osteoblast membrane chromatography/HPLC-QTOF-MS analysis system could efficiently screen out 22 potential active ingredients in EXD, including 2 potential active ingredientsfrom Curculiginis rhizoma, 5 potential active ingredientsfrom Epimedii folium, 2 potential active ingredients from Angelicae scinensis radix, 8 potential active ingredients from Phellodendri chinese cortex, 3 potential active ingredients from Morindae officinalis radix, 2 potential active ingredients from Anemarrhenae rhizome. The method also quickly and selectively identified 21 potential anti-osteoporotic active ingredients from Liuwei Dihuang Decotion. The efficacy test showed that the above 6 ingredients significantly promoted the cell proliferation, increased alkaline phosphatase activity of osteoblasts, and improved head skeleton mineral area of zebrafish.

Conclusion: In this study, we used osteoblast membrane chromatography and network pharmacology to screen the main anti-osteoporosis active ingredients of two Chinese medicine prescriptions. Osteoblast CMC/UPLC-QTOF/MS screening method can quickly obtain anti-osteoporosis active ingredients in complex traditional Chinese medicine prescriptions, and has the advantages of simple operation, rapid, high efficiency and sensitivity.

High-selectivity selective monitoring of in-source fragmentation sapogenin ions as a novel characteristic chromatogram for the simultaneous identification of seven *Panax*-derived herbal medicines as raw materials or from the formulae

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Abstract:

In-source CID of ginsenosides in positive mode (pIS-CID-G) has been reported frequently even using different mass spectrometers (e.g. LCQ Advantage 3D IT and MAT TSQ 7000 from Finnigan, AB Sciex QTrap 3200, Agilent 6210 TOF and 6520 Q-TOF, and Waters Xevo Q-TOF), which gives very weak precursors or even thoroughly fragmented, generating very little useful information for the structural elucidation of ginsenosides. We presume that the occurrence of pIS-CID-G may be attributed to the design of ion source on modern mass spectrometers (such as higher source temperature and desolvation temperature) in pursuit of sensitivity enhancement. Unfortunately, very few reports are available that aim to clarify the underlying mechanism of pIS-CID-G and explore its potential significance with regard to the quality control of Ginseng.

In the current work, we aim to clarify the genesic mechanism of pIS-CID-G and explore its potential role in precise identification and differentiation of seven Panax-derived herbal medicines (e.g. P. ginseng, P. quinquefolius, P. notoginseng, Red ginseng, leaf of P. ginseng, P. japonicus, and P. japonicus var. major) which are currently recorded in Chinese Pharmacopoeia (2015 edition). A primary universality test could justify the occurrence of pIS-CID-G on six high-resolution mass spectrometers from Agilent (6520 QTOF and 6545 QTOF), Waters (Xevo G2-S QTOF and Vion™ IMS-QTOF), and Thermo Fisher Scientific (Q Exactive Q-Orbitrap and LTQ-Orbitrap Velos Pro). Further comparison studies, on a Vion IMS-QTOF instrument, indicated the in-source sapogenin ion clusters were the results of successive H2O eliminations from the sapogenin moiety and highly specific for the classification of ginsenosides: m/z 443.39/425.38/407.37 for protopanaxadiol (PPD) type, 441.37/423.36/405.35 for protopanaxatriol (PPT) type, 439.36 for oleanolic acid (OA) type; and 493.39/475.38/457.37/439.36/421.35 for octillol (OT) type. pIS-CID-G was favored by the addition of acid

additive in mobile phase but was less affected by in-source CID energies. A novel characteristic chromatogram was established by selective ion monitoring (SIM) of four specific pIS-CID-G product ions (m/z 407.37, 423.36, 439.36, and 457.37), which surprisingly enabled the untargeted profiling of major ginsenosides from both the raw herbal materials and TCM formulae despite their complex chemical matrix. Simultaneously metabolomic analysis of seven Ginseng species (60 batches in total) eventually disclosed 15 marker ginsenosides. More importantly, the presence of P. ginseng, P. quinquefolius, P. notoginseng, and Red ginseng), from 20 different TCM formulae could be easily discerned. Conclusively, SIM of pIS-CID-G product ions renders a novel characteristic chromatogram enabling the untargeted profiling of ginsenosides no matter how complex the chemical matrix is.

Keyword : HPLC Fingerprint; PCA; OPLS-DA; Marker Compounds; Quality

Integration of in-depth multicomponent characterization, untargeted metabolomics and mass spectrometry imaging to unveil the holistic chemical transformations of Ligustri Lucidi induced by wine processing

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Abstract:

Being one principle feature of the fundamental traditional Chinese medicine (TCM) theory, processing of the raw materials is performed prior to clinic use (by stir-frying, roasting, carbonizing, calcining, steaming, boiling, and stewing, etc), aiming to enhance the effect and(or) reduce the toxicity. Changes in efficacy or toxicity must be correlated to the chemical variations. Ligustri Lucidi Fructus (LLF; Nu-Zhen-Zi in Chinese) is derived from the mature fruit of Ligustrum lucidum Ait. (Oleaceae) and currently serves as both herbal medicine and food material with significant tonifying effects after Ministry of Health announced that LLF can be used for health products in 2002. Multiple classes of bioactive natural ingredients have been isolated (including triterpenoids, iridoids, flavonoids, phenylethanoid glycosides, and others) and a variety of pharmacological effects (e.g. anti-tumor, hepatoprotective, immune regulating, antioxidative, anti-ageing, anti-inflammation, and reducing hypercholesterolaemia) are reported. Despite a collection of documents have been available regarding the chemical variations of LLF after processing, they focused on very few (typically less than five) or a single subclass of marker compounds (such as the triterpenoids oleanolic acid, and ursolic acid; the iridoids specnuezhenide, oleuropein, G13, ligustroside, neonuezhenide, oleoside-11-methyl ester, and neuzhenidic acid; and the phenylethanols echinacoside, acteoside, salidroside, tyrosol, and hydroxytyrosol). Considering that, processing of LLF could result in the variations of multicomponents, to reveal the underlying chemical basis for the processing mechanism, more powerful approaches that can support the holistic evaluation are in great need.

In the current work, we present a strategy, by integrating comprehensive multicomponent characterization, untargeted metabolomics, and mass spectrometry imaging (MSI), to reveal and locate the markers closely associated with processing of LLF processed by wine steaming. UHPLC/Q-Orbitrap-MS-based rapid polarity-switching precursor ions list-(PIL) included Full Mass/dd-MS2 was developed for the systematic multicomponent characterization. By including PIL and enabling the IIPO function (*If idle-pick others*), more sensitive characterization of the target components and simultaneously acquiring the MS2 information of those unknown

were achieved, thus facilitating the simultaneously targeted and untargeted characterization. As a result, 158 compounds (involving 20 phenylethanols, 97 iridoids, 20 triterpenoids, 16 flavonoids, and 5 others) were identified or tentatively characterized from a QC sample via one injection analysis. Holistic, continuous variation trajectory was visualized in PCA score plot from the raw samples to processed products at different time-points (0–12 h, n=6). Pattern recognition OPLS-DA between the raw and 12 h-processed samples unveiled 29 potential processing markers for LLF. Moreover, the peak area ratio of thirteen markers thereof to oleuropein aglycone (used as a stable internal standard) surprisingly could enable the differentiation of commercial raw and processed LLF samples. MSI examination by iMScope TRIO could primarily verify and visualize the spatial distribution of some of the discovered chemical markers. In conclusion, this integral strategy unveiled processing-induced holistic chemical transformations of LLF, which is of vital significance for elucidating the underlying processing mechanism of TCM.

Dimension-enhanced comprehensive characterization of ginsenosides from white ginseng and red ginseng by two-dimensional liquid chromatography coupled to ion mobility-quadrupole time-of-flight mass spectrometry

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Abstract:

A “bottleneck” issue that hinders the modernization of traditional Chinese medicine (TCM) lies in the dimness of chemical substances they contain, which definitely restricts the pharmacological and efficacy investigations as well as their quality control. The inherent complexity in the chemical substances of TCM, which is featured by the co-existing of primary and secondary metabolites, wide spans of polarity, molecular weight, and content, and pervasive isomerism, renders the chemical analysis being a head-scratching work involved in natural product research. To deconvolute the chemical complexity of TCM, more and more insufficiencies are exposed or reported when applying one-dimensional LC-MS: i) failing to acquire the MSn information of some minor or those trace ingredients due to co-elution as a result of the singular separation mechanism; ii) the limited coverage of components because of the application of impotent MS scan methods; iii) irreproducible results due to high dependence on professional skills in analyzing the obtained MSn data; and iv) difficult to discriminate isomers on account of the limited dimension of structure information.

Integrating chemomics, metabolomics and gut microbiota genomics to investigate correlation between quality and efficacy of herbal medicine: Ginseng, a pilot study

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Abstract:

Herbal medicines are popularly used to prevent and treat disease for thousands of years. Herbal medicinal materials are derived from various extrinsic/intrinsic conditions which greatly affect the quality and efficacy of herbal medicines. Herbal medicines are featured by "multiple components against multiple targets". Thus, holism-based approaches should be employed to characterize the quality and efficacy of herbal medicines as well as their correlations. In this study, ginseng materials harvested by 4-6 years were selected as a pilot study. An integrated strategy by chemomics, metabolomics and gut microbiota genomics coupled with biochemical parameters determination was employed to comprehensively characterize the quality and anti-fatigue activity of ginseng in 4-6 growth years (G4, G5 and G6), and then the obtained multi-omics data were processed by multivariate statistical analysis to investigate the correlation between the quality and efficacy. The results showed that G4, G5 and G6 possessed different quality and also exerted different anti-fatigue activity in improving biochemical parameters, metabolic disorder and gut microbiota dysbiosis. Furthermore, the quality significantly correlated

with the anti-fatigue activity, as indicated by the specific correlation networks between ginsenosides/carbohydrates and gut bacteria/endogenous metabolites. The potential mechanisms involved in the correlations included the structural specificity-based interaction between ginsenosides/carbohydrates and gut microbiota and then the gut microbiota-driven impacts on endogenous bile acid, amino acid, fatty acid and lipid metabolism. The case study provides a promising strategy to comprehensively investigate the correlation between the quality and efficacy of herbal medicine, and guide the clinical application in terms of different disease phenotypes.

Keyword : Ginseng; Chemomics; Metabolomics; Gut microbiota genomics; Quality-efficacy correlation

Characterization and comparison of the metabolomes among three parts (root, stem leaf, and flower bud) of Panax quinquefolius by UHPLC/Q-Orbitrap-MS-based improved data-dependent MS2 acquisition and metabolomics

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Abstract:

Despite Panax quinquefolius L. serves as a crucial source for food additives, healthcare products, and herbal medicine extensively consumed worldwide, unawareness of the metabolome difference among the root (PQR), stem leaf (PQL), and flower bud (PQF), seriously restricts its quality control.

In the current work, a powerful platform, ultra-high performance liquid chromatography/quadrupole-Orbitrap mass spectrometry (UHPLC/Q-Orbitrap-MS), was fully utilized to comprehensively identify the metabolome compositions and to discover the chemical markers enabling parts differentiation for P. quinquefolius. First, in-depth metabolites profiling and characterization were performed by coupling reversed-phase UHPLC and improved untargeted data-dependent MS2 acquisition (dd-MS2) the in negative mode using precursor ions list (PIL)-included Full Mass/dd-MS2 with "If idle-pick others" enabled. A novel fixed-range, discrete mass defect filtering (MDF) vehicle was established allowing a fixed tolerance of 10 mDa based on the m/z features of the precursors of 499 ginsenosides that had been isolated from the whole Panax genus. It could achieve rigid screening of target ginsenosides from a complex herbal extract by orthogonal integer mass and mass defect filtering. We could screen 71 (from 3453 ions), 89 (from 6842), and 84 (from 7369) target precursor masses for PQR, PQL, and PQF, respectively. This PIL-including improved DDA approach could achieve more sensitive characterization of the target masses, and simultaneously to dissociate untargeted ones if idle. It exhibited large improvement in characterizing targeted components (demonstrated using a PQL sample) and comparable performance in identifying the unknown compared with conventional DDA. As a result, 347 saponins were identified or tentatively characterized, and 52 were confirmed by the aid of reference compounds. Notably, 157 compounds characterized have not ever-isolated from the whole genus, which unsurprisingly contain 93 previously unreported masses. Then untargeted metabolomics was utilized by analyzing the negative-mode full-scan data of 45 batches of P. quinquefolius samples. In processing of the metabolomics data, in particular, we

achieved efficient peak extraction and fine ion fusion by in-house editing precursor adducts using the Progenesis QI software. Pattern recognition chemometrics by PCA and OPLS-DA were applied to classify the multi-batch samples and to probe into potential markers. Consequently, 347 ions showed VIP > 1.0, and 29 thereof with VIP > 5.0. These 29 ions were ascribed to 24 marker compounds. In contrast, 1) the root contains abundant m-Rb1, Rb1, Ro, and m-Rb1 isomer but rare m-Rb2 and p-F11; 2) both the stem leaf and flower bud involve rich p-F11 and m-Rb2, but relatively low intensity of m-Rb1 and Rb1; 3) the saponin compositions of the stem leaf and flower bud are similar; the relative intensity of Rc and m-Rb1 may be the marker for their differentiation. The methods established and the results obtained in this work would be an example in quality control of TCM useful for the elaboration of QC monograph.

Keyword : Ginseng; Chemomics; Metabolomics; Gut microbiota genomics; Quality-efficacy correlation

“Force iteration molecular designing-precursor ion list” (FIMD-PIL) strategy for systematic characterization of A. orientale and A. plantago-aquatica.

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Abstract:

A new “force iteration molecular designing” strategy, based on UHPLC-HRMS platforms, was presented for the first time for the systematic characterization and comparison of protostane triterpenoids in A. orientale and A. plantago-aquatica.The strategy was realized by following three steps: 1) In the positive mode, the MSn fragmentation behaviors of 41 PT standards were systematically approached using UHPLC/LTQ-Orbitrap MS. Then fragmentation rules of different subtype PTs were summarized. On this basis, fragmentation behaviors of four representative PTs were compared in different dissociation modes, and a method for fragment acquisition named MS2/CID-MS2/HCD was proposed. 2) A software “force iteration molecular designing precursor ion list” (FIMD-PIL) was designed according to “force iteration” theory and QI database. Using this software, a precursor ion list (PIL) was obtained and applied to selectively trigger MSn on LTQ-Orbitrap for systematic characterization and identification of PTs. 3） Systematic comparion of PTs in A. orientale and A. plantago-aquatica was conducted from various aspects, such as carbonylation and nor-carbonylation deribatives, four-ring and five-ring deribatives and the subtype classification of PTs.

“New protostane-type triterpenoids from Alisma. plantago-aquatica.with lipid-lowering activities

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Abstract:

In order to explore the material basis of AR and obtain adequate representative compounds for LC-HRMS, and to discover novel terpenoids with bioactive properties, an UHPLC-Orbitrap-QDa strategy was proposed. As a result, 20 compounds, including 6 new ones, were isolated. Although lots of researches had been conducted on the efficacy and mechanism from many aspects, however, they just focued on extracts and main compounds. Many biological activities of pure compounds still need to be further investigated to uncover the therapeutic basis. On the basis of traditional uses at “lipid-lowering”,the pure compounds were evaluated on LDL-Uptake andPCSK9 protein level in HepG2 cells. As a result, PTs showed remarkable activites in all test modes and significant structure-activity relationship.

Nontargeted metabonomics - support vector machine model strategy for distinguishing two species of Alisma Rhizoma

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Abstract:

To ensure batch consistency of the quality for individual herb and Chinese patent medicine, and to solve the problem of confusion of different species in the market, the differences of material basis between A. plantago-aquatica and A. orientale were interpereted in this thesis, which provided the technical support and scientific basis in solving the confusion problem in AR. In this study, nontargeted metabonomics based on herbal samples identified by DNA barcoding system, “multi-duplicated samples” and “traceability samples” verification methods were utilized in combination to achieve the chemical differentiation between two sources. In addition, a support vector machine model with above chemical differentiation compounds as variables was developed and applied to distinguish two species and botanical origins based on the validation of accuracy, system suitability and prediction zone.

Ginkgol Biloba Extract as an adjunctive treatment for ischemic stroke: A systematic review and meta-analysis of randomized clinical trials with trial sequential analysis of recurrence rate

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Abstract:

Objective: The existing eligible randomized controlled trials (RCTs) were critically appraised for the effectiveness and safety of Ginkgol Biloba extract（GBE） for ischemic stroke.

Design: Systematic review and meta-analysis (CRD42018110211, http://www.crd.york.ac.uk/PROSPERO).

Methods: Seven electronic databases were searched from inception to August 2018. Risk ratio (RR) and mean difference (MD) with a 95% confidence interval (CI) were used as effect estimates using RevMan 5.3. Meta-analysis with trial sequential analysis (TSA) was performed to evaluate recurrence rate of long term use GBE as adjunctive treatment for convalescence stage of ischemic stroke was performed where data were available.

Results: We identified 15 RCTs involving 1829 participants. Majority of the included trials were of high risk of bias in methodological quality. For acute ischemic stroke, adding GBE to conventional therapy achieved higher Barthel Index scores (MD 6.48, 95% CI: 3.81 to 9.15) and lower neurological function deficit scores (MD −1.39, 95% CI: −2.15 to −0.62). For patients in their convalescence (or sequelae) stage of ischemic stroke, GBE was superior in improving dependence (MD 7.17, 95% CI: 5.96 to 8.38) compared to placebo or conventional therapy，but no difference recurrence rate (RR 0.70, 95% CI: 0.48 to 1.03, TSA inconclusive) and cardiovascular events (RR 0.83, 95% CI 0.39 to 1.77). Five trials reported adverse drug reactions/events.

Conclusion: GBE appears to improve neurological function and quality of life based on conventional therapy for ischemic stroke, it seems generally safe for clinical application. However, the result of benefit especially for recurrence rate are inconclusive due to generally weak evidence, and further large, rigorous trials are still warranted.

Keyword : Ginkgol Biloba Extract Ischemic stroke Meta-analysis

Extension-mass defect filter combined with multidimensional data acquiring and metabolic network prediction for comprehensive characterization of metabolic profiles of bufadienolides in rats plasma

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Abstract:

Comprehensive characterization and identification of metabolites in plasma are very significant to evaluate the efficacy and safety of traditional Chinese medicine (TCM) in vivo. However, it is usually hindered by the insufficient characteristic fragments of metabolites, ubiquitous matrix interference, complicated screening and identification of metabolites. In the study, an effective strategy was established to systemataciallly characterize the metabolites of bufadienolides from Venenum Bufonis and deduce the metabolic pathways in rats plasma. There were four steps in the strategy. Firstly, the blank plasma and samples were injected into UHPLC/LTQ-Orbitrap-MS in full scan model with continuous five times to screen the valid matrix compounds and metabolites by MZmine software. Secondly, the extension-mass defect filter model was established to obtain the precursor ions lists of metabolites of bufadienolides. Thirdly, the acquisition mode which has been optimized was applied to trigger more MS/MS fragmentations of metabolites to present the characteristic fragments on the basis of the precursor ions lists. Fourthly, the acquired data were imported into Compound Discoverer software for identification of metabolites with metabolic network prediction. Finally, the main metabolic pathways of bufadienolides in vivo were deduced and summarized. The results showed that a total of 148 metabolites were characterized, and the 7 main original bufadienolides were detected in rats plasma. The biotransformations of bufadienolides mainly were hydroxylation, dihydroxylation and isomerization. This strategy could be widely used to characterize the metabolic profiles of TCM or prescription and provide the essential data for the rational drug use.

Label-free quantitative proteomics of earthworm from two geographic origins

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Abstract:

Dilong (named earthworm) is a traditional medicine and has been used to treat blood clots and asthma in China for a long time. In our study, we collected 2 of 4 species of earthworms, which were collected in Chinese Pharmacopoeia. At present, there is no proteomics research of Dilong and no study about difference between in Guangdilong(GD) and Hudilong(HD), which are collected from Guangdong Province and Shanghai Municipality, respectively. To discover the proteome of Dilong, we used RNA-seq method along with label-free quantitative analysis. In three biological replicates of two species (GD and HD), we identified 4 314 protein groups totally and 692 differentially expressed proteins (DEPs). Our research demonstrated that lumbrokinase, which was the key protein related to blood clots activity of Dilong, was identified in both GDs and HDs and discovered 3 proteins which may have potenital blood clots activity.

Keyword : earthworm, RNA-seq, proteomics, label-free, lumbrokinase

Light-induced artemisinin biosynthesis is regulated by the bZIP transcription factor AaHY5 in Artemisia annua

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Abstract:

Artemisinin, the frontline drug against malaria, is a sesquiterpenoid extracted from Artemisia annua. Light has been proposed to play an important role in the activation of artemisinin biosynthesis. Here, we report the basic leucine zipper transcription factor AaHY5 as a key regulator of light-induced biosynthesis of artemisinin. We show that AaHY5 transcription overlaps with that of artemisinin biosynthesis genes in response to light and in *A. annua* tissues. Analysis of AaHY5 over-expression and RNAi-suppression lines suggests that AaHY5 is a positive regulator of the expression of artemisinin biosynthesis genes and accumulation of artemisinin. We show that AaHY5 complements the hy5 mutant in Arabidopsis thaliana. Our data further suggests that AaHY5 interacts with AaCOP1, the ubiquitin E3 ligase CONSTITUTIVE PHOTOMORPHOGENIC1 in *A. annua*. In yeast one hybrid and transient expression assays, we demonstrate that AaHY5 acts via the transcription factor *GLANDULAR TRICHOME-SPECIFIC WRKY 1 (AaGSW1)* in artemisinin regulation. In summary, we present a novel regulator of artemisinin gene expression and propose a model in which AaHY5 indirectly controls artemisinin production in response to changing light conditions.

Keyword : HY5, *Artemisia annua*, Artemisinin biosynthesis, Light signal, Secondary metabolism, Transcriptional regulation

A highly efficient strategy of "exclusion list MS data acquisition – molecular networking classification" to characterize the total components of Naodesheng Tablets comprehensively

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Abstract:

A highly sensitive and efficient strategy of "exclusion list MS data acquisition – molecular networking classification" combining the techniques of exclusion list and MS molecular networkings was proposed to comprehensively characterize the components in Naodesheng Tablets. The parent ions triggering MS2 fragmentations were excluded with the exclusion list, and after 10 times of data acquisition, the MS2 fragmentations of all components were sensitively triggered. According to the similarities of MS2 fragmentations, the components were obtained and identified as isoflavonoid C-glycosides, pentacyclic triterpenoid saponins, tetracyclic triterpenoid saponins, isoflavonoid O-glycosides and flavonoid O-glycosides. Finally, 341 compounds were identified from five compound clusters. This study illuminated the chemical composition of Naodesheng Tablets and established the foundation for the construction of quality control system of it. After combining MS molecular networkings, the identified compounds quantity were added up to 3.94 times. Hence, the combining strategy of this study is highly sensitive, efficient, intelligent and automatic in data processing, also widely applied to the comprehensive characterization of the complex system of Chinese patent medicines (CPMs).

Cardioprotective mechanism study of salvianic acid A sodium in rats with myocardial infarction using a proteome microarray approach combined with multi-omics analysis

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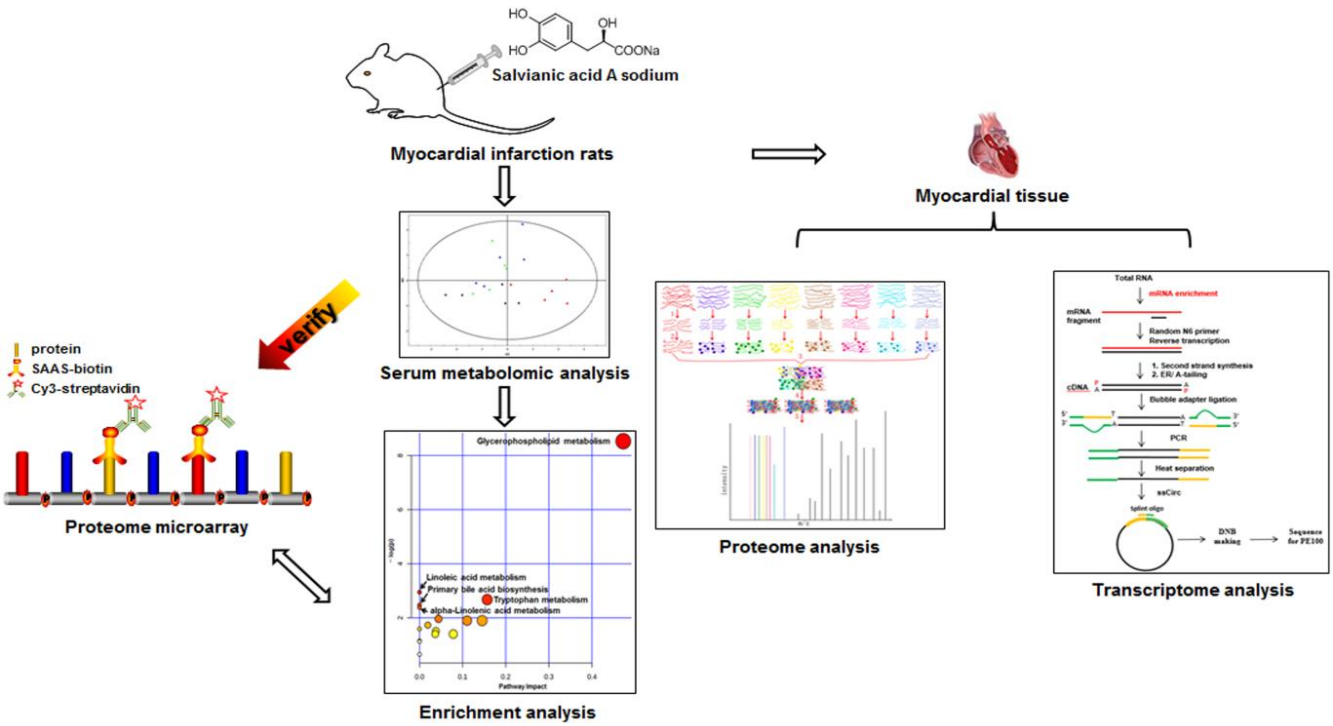
Abstract:

Salvianic acid A (SAA) is an active compound derived from the well-known herbal medicine Danshen, which has been widely used for clinical treatment of cardiovascular diseases in China. Injectable salvianic acid A sodium (SAAS) is a new drug developed by our group that has been entered into phase I clinical trials for treatment of coronary heart disease and stable angina pectoris conducted by the China Food and Drug Administration (CFDA). However, the direct binding protein(s) of SAAS is still unknown and the underlying cardioprotective mechanism remains to be further elucidated. In this study, Sprague-Dawley rats were subjected to left anterior descending artery ligation to investigate the cardioprotective effect of SAAS against myocardial infarction (MI). A human proteome microarray was used to identify the direct binding proteins of SAAS, which was further verified by metabolomic profiling of rat serum after MI using an ultra-performance liquid chromatography/quadrupole time-of-flight mass spectrometry (UPLC-QTOF-MS) based approach. Moreover, proteome and transcriptome profiling of myocardial tissue was performed to investigate the underlying molecular mechanisms. Results showed that SAAS effectively protected against myocardial injury and improved cardiac function. Totally, 370 proteins were identified to specifically bind SAAS and strikingly enriched in metabolic pathways. Rat serum metabolomic profiling identified 26 potential biomarkers and metabolic pathway analysis indicated SAAS remarkably reversed the metabolic changes induced by MI injury. Functional enrichment analysis of the differentially expressed proteins and genes indicated that SAAS participated in the regulation of actin cytoskeleton, phagosome, focal adhesion, tight junction, apoptosis, MAPK signaling and Wnt signaling pathways, which are closely related to cardiovascular diseases. Taken together, SAAS may exert its cardioprotective effects by targeting multiple pathways at the proteome, transcriptome, and particularly metabolome levels. This study has provided not only new insights into the pathogenesis of myocardial infarction but also a roadmap of the cardioprotective molecular mechanisms of SAAS, which may provide pharmacological evidence to aid in its clinical application.


Salvianic acid A sodium
Myocardial infarction rats
Myocardial tissue
Serum metabolomic analysis
verify
protein
SAAS-biotin
Cy3-streptavidin
Proteome microarray
Glycerophospholipid metabolism
Linoleic acid metabolism
Primary bile acid biosynthesis
Tryptophan metabolism
alpha-Linolenic acid metabolism
Enrichment analysis
Proteome analysis
Total RNA
mRNA enrichment
Random N6 primer
Reverse transcription
Bubble adapter ligation
PCR
Heat separation
Transcriptome analysis

Exploring for alternative resource of Bear Bile Powder——Directed biotransformation of tauroursodeoxycholic acid through engineering *Escherichia coli* cell factory

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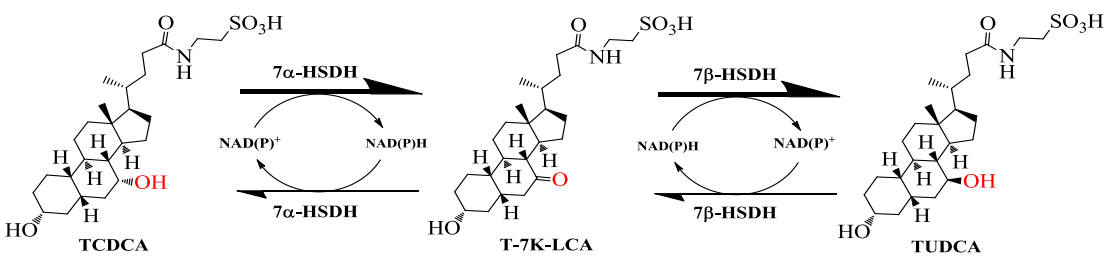
Abstract:

Bear bile powder is a valuable medicinal material characterized by high content of tauroursodeoxycholic acid (TUDCA) at a ratio of 1.0-1.5 to taurochenodeoxycholic acid (TCDCA). Here, we reported the large-scale directional biotransformation of tauroursodeoxycholic acid (TUDCA) through Escherichia coli engineered with a two-step mimic biosynthetic pathway of TUDCA from taurochenodeoxycholic acid (TCDCA) using bidirectional oxidative and reductive enzymes 7α-hydroxysteroid dehydrogenase (7α-HSDH) and 7β-hydroxysteroid dehydrogenase (7β-HSDH) genes (named as α1, α2, β1, and β2) with ePathBrick. The large-scale production of TUDCA containing products by balancing the bidirectional reactions through optimizing fermentation process of the engineered E. coli in fermenters. The fermentation medium was firstly optimized based on M9 medium using response surface methodology, leading to a glycerol and yeast extract modified M9-GY medium benefits for both cell growth and product conversion efficiency. Then isopropylthio-β-galactoside induction and fed-stock stage was successively optimized. Finally, a special deep-tank static process was developed to promote the conversion from TCDCA to TUDCA. Applying the optimal condition, fermentation was performed by separately supplementing 30 g refined chicken bile powder and 35 g crude chicken bile powder as substrates, resulting in 29.35 ± 2.83 g and 30.78 ± 3.04 g powder products containing 35.85 ± 3.85 % and 27.14 ± 4.23 % of TUDCA at a ratio of 1.49 ± 0.14 and 1.55 ± 0.19 to TCDCA, respectively, after purification and evaporation of the fermentation broth. The recovery yield was 92.84 ± 4.21 % and 91.83 ± 2.56 %, respectively. This study provided a practical and environment friendly industrialized process for producing artificial substitute of bear bile powder from cheap and readily available chicken bile powder using engineered E. coli microbial cell factory. It also put forward an interesting deep-tank static process to promote the enzyme-catalyzing reactions toward target compounds in synthetic biology-based fermentation.

Keyword : TUDCA, Fermentation, Biotransformation, Escherichia coli, Process optimization, Deep-tank static process



New integrated technology for separation and preparation of active ingredients of traditional Chinese medicine

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Abstract:

The separation and analysis of traditional Chinese medicine complex systems has always been the difficult and hot issue of quality control for traditional Chinese medicine for decades. However, the efficiency of extraction and separation of traditional Chinese herbal medicines is low and remains unresolved. This study was aimed at developing rapid separation and preparation methods for 6 kinds of traditional Chinese medicine monomers, providing novel experimental ideas and analytical methods for research and innovative drug pharmacokinetic studies. A new standardized and integrated technology for the online separation of pharmacodynamic substances of Chinese medicine was established, which provided candidate compounds, reference materials and an effective platform for the separation and preparation of traditional Chinese medicine active monomers. In addition, rapid separation and preparation methods for 6 kinds of traditional Chinese medicine monomers from 7 Chinese traditional medicine namely *Gardeniae Fructus*, *Hypericum Perforatum*, hawthorn leaf, Biond Magnolia Flower, radix angelicae, Blackberrglily Rhizome, and Fructus Aurantii Immaturus were successfully established, including two-dimensional liquid chromatography column switching system and high speed countercurrent online purity monitoring system, which overcome the limitations of traditional separation technology in terms of time consumption, cumbersome and pollution easily caused by off-line transfer.

Studies on chemical components and HPLC profile analysis of Cordyceps militaris

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Abstract:

Cordyceps mushroom belonging to the family of Clavicipitaceae is a group of entomopathogenic fungus with numerous pharmacological and therapeutic implications that are mainly distributed in Asia, Europe North and America. There are currently more than 680 documented species of Cordyceps, which have similar life cysles and have developed mechanisms to invade insects and grow on them, the major difference being the locality where they grow and the host infect they infect. Among them, Cordyceps militaris (L. ex. Fr.) Link is the type and representative species that has been already described in the 17th and early 18th century literature, which has been known and widely used as a folk medicine and tonic food in China, Korea and other Asian countries for a long time. Different compounds or extracts prepared from this fungus have been reported to exert various activities including immunomodulatory, anti-inflammatory, antimicrobial, anti-influenza, anti-allergy, anti-oxidation, against reproductive damage and antitumor activities. The fruiting body of C. millitaris has been cultured artificially on a large-scale production in China and Korea during the past decades and considered as a potential substitute of natural C. sinensis, a valued and official species of Cordyceps used in traditional Asian medical practice, for their similar chemical composition and biological activities. Previous chemical investigation revealed that nucleosides (eg. cordycepin), cordycepic acid, sterols (eg. ergosterol) and polysaccharides are the main components of C. millitaris, and these constituents have been demonstrated to exert multiple pharmacological activities.

In this study, a new nucleoside (1), a new natural product nucleoside (2), two new pyrrole alkaloids derivatives (3–4), as well as eight known compounds (5–12) were isolated from the fruiting body of C. millitaris. The structures of the new compounds were elucidated through extensive analysis of spectroscopic data including 1D and 2D NMR, HRESIMS, IR and UV. All the isolated compounds were detected for their bioactivities against LPS-induced NO production in RAW 264.7 cells. A HPLC method was developed for simultaneous determination of six nucleosides with gradient elution of methanol and water as mobile phase. Taking three nucleosides as control, a TLC method was established by using ethyl acetate-acetone-ammonia volume fraction of (2.5:6:1.5) as a developing solvent on high performance silica gel precoated plate (HSGF254) and to identify

them under UV 254 nm. The results showed that the contents of six nucleosides, including uridine, inosine, guanosine, a-denosine, cordycepin and N6-(2-hydroxyethyl)-adenosine, in *C. militaris* from different sources differed significantly with the average contents were 0.043%, 0.097%, 0.022%, 0.082%, 0.986% and 0.175%, respectlively. The uridine, a-denosine and cordycepin are obviously characteristic with good separating in TLC which could be used to identify C. militaris. The qualitative and quantitative analyses established by taking six characteristic nucleosides as the markers are rapid, simple, reproducible, and which can be used to control the quality of *C. militaris*.

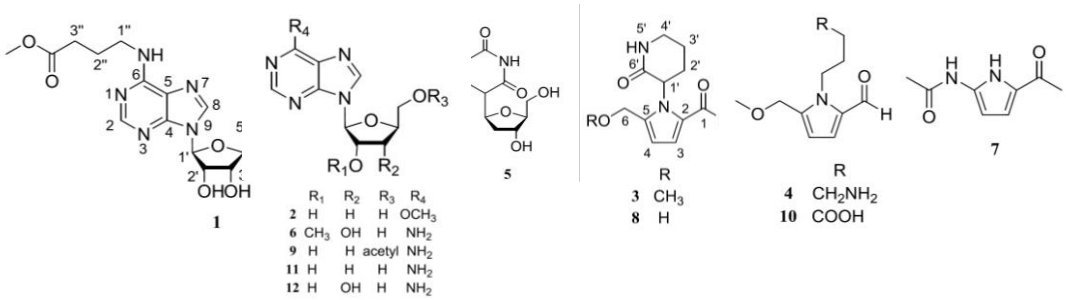
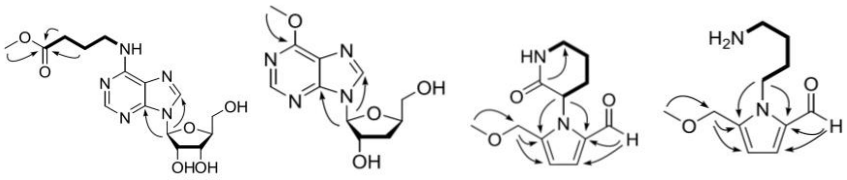


Figure 1. Chemical structures of compounds **1**–**12** isolated from *Cordyceps militaris*.



1 **2** **3** **4**

Figure 2. Selected ^{1}H-^{1}H COSY and HMBC correlations of **1**–**4**.

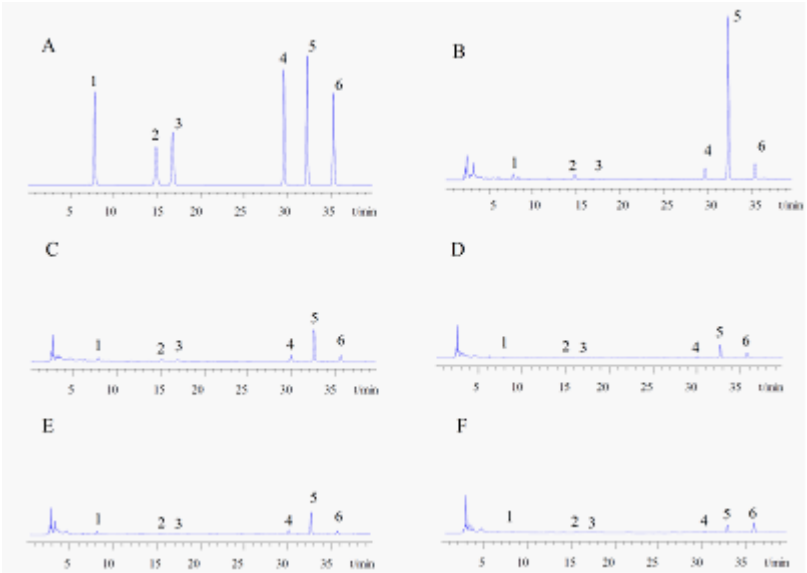


Figure 3 The typical HPLC-DAD chromatograms of six nucleoside reference standards and the fruiting body of *Cordyceps millitaris*. A. reference standards B-F. fruiting body of *Cordyceps millitaris* from different suppliers; 1. uridine 2. inosine 3. guanosine, 4. a-denosine 5. cordycepin 6. N6-(2-hydroxyethyl)-adenosine

Keyword : Cordyceps militaris; chemical constituent; chemical profiling; HPLC; TLC

Discovery of a UDP-Glycosyltransferase involved in the biosynthesis of the anti-viral plant metabolites lignan glycosides

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Abstract:

Lignan glycosides serve as anti-viral compounds in Isatis indigotica. UDP-glycosyltransferases generate the complexity and diversity of these compounds, but the catalytic mechanism of lignan glycosylation in I. *indigotica* has not been reported. Here, we presented the precise location of diverse lignans in different organs and tissues, and discussed the mechanism underlying their glycosylation. Applying ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometer (UPLC-Q-TOF/MS) profiling, twelve lignans were identified and most of them were mainly accumulated in roots. Subsequently, atmospheric pressure matrix-assisted laser desorption/ionization imaging (MALDI) visualized seven putative lignans in root tissues at cellular level, resolving metabolic information of these metabolites with morphological details at the microscopic level. Mining of the I. indigotica genome identified a novel IiUGT71B2 that catalyzed mono-glycosylation at 4-O or 4-O′ position of lariciresinol and matairesinol in vitro with the supply of UDP-glucose. In silico molecular docking and site direct mutagenesis proposed Ala356 and Tyr395 as critical catalytic bases, with the furan ring of lignan ligands being essential structure for substrate specificities of IiUGT71B2. Co-expression of I. indigotica pinoresinol/lariciresinol reductase (IiPLR1) and IiUGT71B2 in wild tobacco (*Nicotiana benthamiana*) resulted in the formation of lariciresinol mono-glycosides validating the potential for metabolic engineering of active lignans in a heterologous plant system. Our study firstly found that the key enzyme involved in the glycosylation of lignans in I. *indigotica*, which led to a more complete understanding of the biosynthetic pathway of the anti-viral metabolites lignan glycosides, and thus may serves to improve the quality of crude drug.

AaMYB2 negatively regulates Artemisia annua trichome initiation by interacting with the HD-ZIP transcription factor AaWOX1

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Abstract:

Artemisinin is an important drug for curing malaria. It is synthesized and stored in glandular trichomes of leaves or buds in Artemisia *annua* L (A. *annua*). However, the factors affecting trichome development are not clear in A. *annua*. To understand the development of trichomes, a new gene AaMYB2 was cloned from A. *annua*. It contained an open reading frame (ORF) of 546 bp and encoded 182-amino acid protein with a predicted molecular mass of 43.28 kDa, with a calculated isoelectric point of 5.27. Transgenic Arabidopsis plants over-expressing AaMYB2 showed a sharp decline of trichome number, indicating its negative regulation on trichome formation. The expression of AaMYB2 in A. *annua* is high in mature leaves and low in young leaves. In addition, yeast two-hybrid and pull-down analysis demonstrated that AaMYB2 could interact with AtGL3, suggesting that AaMYB2 regulates trichome formation depending on the complex MYB-bHLH-TTG1 in Arabidopsis. In addition, AaMYB2 negative regulates anthocyanin biosynthesis. Moreover, using plants overexpressing the AaMYB2, we found that AaMYB2 negative modulates trichome density and artemisinin content in A. *annua*. We demonstrate that overexpression of AaMYB2, the trichome density decreased to 44.7% 64.0%, and artemisinin content decreased to 11.5% 49.4%, while in the AaMYB-RNAi plants, the trichome density increased to 33% 93.3%, and artemisinin content increased to 32.2 84.0%. Transcriptome and metabolome analysis indicates negative regulated anthocyanin biosynthetic pathway genes by AaMYB2. Finally, we found that AaMYB2 interacts with AaWOX1, which displays a negative role in trichome density. These findings revealed AaMYB2 and AaWOX1 regulate trichome density, mediated by an AaMYB2-AaWOX1 complex.

Qualitative and quantitative analysis on chemical constituents of Anoectochilus roxburghii by HPLC-DAD-MS/MS and UV-vis

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Abstract:

Objective A rapid and efficient method using high performance liquid chromatography coupled with diode array detection and tandem mass spectrometry (HPLC-DAD-MS/MS) was developed for identification of 14 major flavonoids and quantitative of Rutin, Isoquercitrin, Kaempferol-3-O-rutinoside, Narcissoside, Astragalin, Quercetin, Kaempferol, Isorhamnetin in Anoectochilus roxburghii (Wall.) Lindl. **Methods** The identification of flavonoids were combination of DAD, MS and MS/MS spectra. In order to precision determination of total flavonoids in Anoectochilus roxburghii (Wall.) Lindl, three classify developer method including NaNO2-Al(NO3)3-NaOH, AlCl3-KAc and Triethylamine were used. **Results** Then triethylamine developer was chosen by comparing three UV specific visualisation methods of the identified flavonoids. With narcissoside as the standard，triethylamine as the developer，UV-Vis method was applied to determination of total flavonoids at 410 nm. The HPLC-DAD was established to quantify the content of 8 kinds of flavonoids. The total flavonoid content determined by UV-Vis method has a strong correlation with the total flavonoid content determined by HPLC (r=0.94), and the classical NaNO2-Al(NO3)3-NaOH chromogenic reaction method has a low correlation with the HPLC (r = 0.13). **Conclusion** The results indicate that the new approach conbining HPLC-DAD-MS/MS and UV-Vis is applicable in qualitative and quantitative quality control of medicinal from Anoectochilus roxburghii.

Keyword : High performance liquid chromatography coupled with diode array detection and tandem mass spectrometry (HPLC-DAD-MS/MS); Ultraviolet and visible spectrophotometry(UV-Vis); Rutin; Isoquercitrin; Kaempferol-3-O-rutinoside; Narcissoside; Astragalin; Quercetin; Kaempferol; Isorhamnetin; Total flavonoid; Triethylam

GC-TOF-MS-Based Metabolomics to Reveal the Protective Effect of Gua-Lou-Gui-Zhi decoction against Ischemic Stroke in Rat

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Abstract:

Objective In this study, the protective effect of Gua-Lou-Gui-Zhi decoction (GLGZD) on ischemic stroke in a middle cerebral artery occlusion (MCAO) rat model was investigated by the GC-MS-based metabolomics approach. **Methods** The rat model of ischemia reperfusion injury induced by introduction of transient middle cerebral artery occlusion (MCAO) followed by reperfusion. Longa score method was used to test the neurobehavior of rats. TTC staining method was used to detect the cerebral infarction in rats. To investigate the changes of endogenous metabolites in rat serum via gas chromatography-time of flight mass spectrometry (GC-TOF-MS) and combined with multivariate statistical analysis. **Results** 2,3,5-triphenyltetrazolium chloride (TTC) staining of brain tissues showed that GLGZD significantly reduced the infarct area after MCAO surgery. Metabolomic profiling showed a series of metabolic perturbation occurs in ischemic stroke compared with sham group. Thirteen differential metabolites such as indole acetic, malonic acid, ethanolamine, mycolic acid, ornithine etc. GLGZD can reverse the MCAO-induced serum metabolic deviations by regulating multiple metabolic pathways including interconversion of sugar and glucuronide, tryptophan metabolism, pyrimidine metabolism and glycerophospholipid metabolism. **Conclusion** The current study provided a useful approach for understanding the mechanism of MCAO-induced ischemic stroke and a reliable basis for evaluating the efficacy of GLGZD in the treatment of ischemic stroke. GLGZD can increase energy metabolism, lipid metabolism, amino acid metabolism pathway and reduce nerve cell-reperfusion injury in rats.

Keyword : Gua-Lou-Gui-Zhi decoction; Metabolism; GC-TOF-MS; rat

Determination of five flavonoids in cultivated *Anoectochilus roburghii* by QAMS method

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Abstract:

Objective: An ultra high performance liquid chromatography (UPLC) method was established and verified to simultaneous determination of five flavonoids, including rutin, narcissoside, quercetin, kaempferol and isorhamnetin. **Methods:** The UPLC separation was achieved on an Uitimate UHPLC AQ C18 column (2.1 mm×100mm, 1.8 μm) with a gradient elution using acetonitrile (containing 0.1% formic acid, A) and 0.3% formic acid water (B), and the column temperature was set at 38 ℃. The flow rate was 0.3 mL•min-1 and the detected wavelength was set at 368 nm. The injection volume was 5 μL. Narcissoside was used as the internal standard to determine the correction factors (RCFs) of the other four flavonoids (rutin,qu-ercetin , kaempferol and isorhamnetin). Then the method was used to calculate the five compounds in 36 batches of Anoectochilus roburghii (Wall.) Lindl samples. The content of five constituents in A. roburghii was also calculated by the external standard method (ESM) at the same time. Compared with the content results determined by the ESM and QAMS method, the feasibility and accuracy of QAMS method were verified. **Results:** Within the linear range, the RCFs of rutin, narcissoside, kaempferol and isorhamnetin were 1.016、0.4650、0.4228 and 0.4539, with a good repeatability. There was no significant difference between the content of 36 batches of A. roburghii samples by QAMS and ESM, but there were differences in the content among the four different cultivars. **Conclusion:** The QAMS method is accuracy, stably, could be used as a new technique for quality control of A. roburghii.

Keyword: Anoectochilus roburghii; quantitative analysis of multi-components by single-marker (QAMS); quercetin; rutin; narcissoside; kaempferol; isorhamnetin; relative correction factor (RCFs); ultra performance liquid chromatography (UPLC);

Rapid and sensitive method for simultaneous determination of first-line anti-tuberculosis drugs in human plasma by HPLC-MS/MS: Application to therapeutic drug monitoring

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Abstract:

First-line anti-tuberculosis drugs are playing vital roles for curbing rapid spread of tuberculosis. mutidrug therapies are commonly applied in clinical to achieve better treatment outcomes. However, drug resistance and adverse reactions came along with this therapies and therapeutic drug monitoring is a feasible way to precaution side effects. For this reasons, a simple and sensitive method based on LC-MS/MS and single protein precipitation was developed and validated for simultaneously quantifying of pyrazinamide, isoniazid, ethambutol, streptomycin and rifampicin in human plasma. Optimized chromatographic separation was achieved on a ZORBAX SB-C18 column with heptafluorobutyric acid, an ion-pair reagent, in the mobile phase at a flow rate of 0.3mL/min. The mass detection was achieved using electrospray ionization in the positive ion mode with a multiple reaction monitoring scan: m/z 124.1→79.1 for pyrazinamide, m/z 138.1→120.9 for isoniazid, m/z 205.3→116.2 for ethambutol, m/z 582.3→262.6 for streptomycin, m/z 823.4→791.2 for rifampicin and m/z 180.1→110.1 for phenacetin(Internal standard, IS). The LLOQ of pyrazinamide, isoniazid, ethambutol, streptomycin and rifampicin was 200, 80, 0.2, 2000, 200ng/mL, respectively. The Intra-day and inter-day accuracy and precision were within 15.0%. The method had been successfully applied to simultaneous determination of four first-line Anti-tuberculosis drugs in plasma from tuberculosis patients.

Keyword : LC-MS/MS; Anti-tuberculosis drugs; Human plasma; Tuberculosis patients

Light-induced artemisinin biosynthesis is regulated by the bZIP transcription factor AaHY5 in Artemisia annua

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Abstract:

Artemisinin, the frontline drug against malaria, is a sesquiterpenoid extracted from Artemisia annua. Light has been proposed to play an important role in the activation of artemisinin biosynthesis. Here, we report the basic leucine zipper transcription factor AaHY5 as a key regulator of light-induced biosynthesis of artemisinin. We show that AaHY5 transcription overlaps with that of artemisinin biosynthesis genes in response to light and in A. *annua* tissues. Analysis of AaHY5 over-expression and RNAi-suppression lines suggests that AaHY5 is a positive regulator of the expression of artemisinin biosynthesis genes and accumulation of artemisinin. We show that AaHY5 complements the hy5 mutant in Arabidopsis thaliana. Our data further suggests that AaHY5 interacts with AaCOP1, the ubiquitin E3 ligase CONSTITUTIVE PHOTOMORPHOGENIC1 in A. *annua*. In yeast one hybrid and transient expression assays, we demonstrate that AaHY5 acts via the transcription factor GLANDULAR TRICHOME-SPECIFIC WRKY 1 (AaGSW1) in artemisinin regulation. In summary, we present a novel regulator of artemisinin gene expression and propose a model in which AaHY5 indirectly controls artemisinin production in response to changing light conditions.

Keyword : HY5, *Artemisia annua*, Artemisinin biosynthesis, Light signal, Secondary metabolism, Transcriptional regulation

*Ii*WRKY34 plays a major role in the polyploidy vigor of *Isatis indigotica*

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Abstract:

The autotetraploid Isatis indigotica have better yield, enhanced lignan accumulation and stress tolerance compared with its diploid progenitor. However, the understanding of genetic mechanisms for these trait differences is still limited. In this study, IiWRKY34, with higher expression levels in tetraploid than diploid I. indigotica, was screened as one of the most important contributors to the control of these quantitative traits. Over-expression and RNAi analysis in transgenic I. indigotica hairy roots indicated that IiWRKY34 significantly improves root biomass, boosts lignan biosynthesis, and enhances salt and drought tolerance. Integrated analysis of transcriptome and metabolome profiling demonstrated IiWRKY34 expression had far-reaching consequences on both primary and secondary metabolism, reprograming carbon flux towards phenylpropanoids such as lignans and flavonoids. Transcript-metabolite correlation analysis was applied to construct the regulatory network of IiWRKY34 for lignan biosynthesis. One candidate target Ii4CL3, a key rate-limiting enzyme of lignan biosynthesis as indicated in our previous study, has been demonstrated to indeed interact with IiWRKY34. Collectively, the results suggested the differently expressed IiWRKY34 might have contributed to the polyploidy vigor of I. indigotica, and manipulation of this gene will facilitate improvements in yield, lignan production and stress tolerance in I. indigotica and other crops.

Keyword : polyploidy vigor, WRKY transcription factor, biomass production, lignan biosynthesis, stress tolerance.

One-step solid extraction for simultaneous determination of eleven commonly used anticancer drugs and one active metabolite in human plasma by HPLC–MS/MS

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Abstract:

Therapeutic drug monitoring for anticancer drugs could timely reflect in vivo drug exposure and it was a powerful tool for adjusting and maintaining drug concentration into a reasonable range, so that an enhanced efficacy and declined adverse reactions could be achieved. A liquid chromatography-tandem mass spectrometry method had been developed and fully validated for simultaneous determination of paclitaxel, docetaxel, vinblastine, vinorelbine, pemetrexed disodium, carboplatin, etoposide, cyclophosphamide, ifosfamide, gemcitabine, irinotecan and SN-38 (active metabolite of irinotecan) in human plasma from cancer patients after intravenous drip of chemotherapy drugs. One-step solid phase extraction was successfully applied using Ostro sample preparation 96-well plate for plasma samples pretreatment with acetonitrile containing 0.1% formic acid. Chromatographic separation was achieved on an Atlantis T3-C18 column (2.1 × 100 mm, 3.0 μm) with gradient elution using a mobile phase consisting of acetonitrile and 10 mM ammonium acetate plus 0.1% formic acid in water, and the flow rate was 0.25 mL/min. The Agilent G6410A triple quadrupole liquid chromatography-mass spectrometry system was operated under the multiple reaction monitoring mode with an electrospray ionization in positive mode. Linear range was 25.0-2500.0 ng for Paclitaxel, 10.0-1000.0 ng for Docetaxel and SN-38, 100.0-10000.0 ng for Vinorelbine and Pemetrexed, 10.0-10000.0 ng for Vinblastine and Irinotecan, 1.0-1000.0 ng for Cyclophosphamide and Ifosfamide, 50.0-5000.0 ng for Carboplatin, Etoposide and Gemcitabine. Linearity coefficients of correlation were > 0.99 for all analytes. The intra-day and inter-day accuracy and precision of the method were within ±15.0% and less than 15%. The mean recovery and matrix effect as well as stability of all the analytes ranged from 56.2% to 98.9% and 85.2% to101.3% as well as within ±15.0%. This robust and efficient method was successfully applied to implement therapeutic drug monitoring for cancer patients in clinical.

Keyword : Anticancer drugs, LC-MS/MS, Human plasma, one-step solid phase extraction

Engineering the chloroplast genome of *Datura innoxia* mill. for hyperproduction of scopolamine

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Abstract:

The particularity of the chloroplast structure makes it a potential green factory. It is ideal for engineering because it offers a number of attractive advantages, including high-level foreign protein expression, feasibility of expressing multiple genes or pathways in a single transformation event, absence of epigenetic effects, and gene containment due to lack of transgene transmission through pollen. However, broad application of chloroplast engineering has been largely hampered by both the lack of chloroplast genomes and the lack of chloroplast transformation systems. Here we describe the development of a chloroplast transformation system for Datura innoxia mill., a widely used poisonous plant with great medicinal and economic value. This is the first report on the chloroplast engineering for hyperproduction of bioactive compounds in medicinal plants. Hyoscyamine and scopolamine are main components of Datura plants. However, the demand of scopolamine is greater than hyoscyamine. In this study, hyoscyamine 6β-hydroxylase (h6h), which can catalyze hyoscyamine to form scopolamine through two steps, was over expressed in the chloroplasts of D. innoxia by a reconstructed vector (Fig. 1) through particle bombardment. After spectinomycin resistance screening, regenerated plants were harvested. The alkaloids in leaves of this plant were tested and found out that, the ratio of scopolamine to hyoscyamine in h6h transferred plants was significantly higher than that of the control ones (Fig. 2). This result confirmed that the chloroplast transformation of h6h gene can improve the accumulation of scopolamine in leaves of D. innoxia. This study paves the way to efficient production of scopolamine in D. innoxia, and makes the leaves of D. innoxia to be new resources for extraction of scopolamine.

Chemical profiling and quantitation of bioactive compounds in *Eucommia ulmodies* by UPLC-Q-TOF-MS/MS and HPLC-DAD

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Abstract:

Eucommia ulmodies Oliver.(*Eucommia ulmodies*),is a famous traditional chinese medicinal plant. *Eucommiae cortex* (Duzhong) is the dried bark of *Eucommia ulmoides* Oliv. and widely used for strengthening tendons, bones and muscle, benefitting liver and kidney, preventing miscarriage and so on. *Eucommiae* folium is the dried leaf of *Eucommia ulmoides* Oliv.Modern studies have shown that the chemical constituents and pharmacological effects of *Eucommiae* cortex and *Eucommiae* folium are similar. To get a better understanding of the chemical constituents in *Eucommia ulmodies*, ultra-high performance liquid chromatography coupled with electrospray ionization quadrupole time-of-flight tandem mass spectrometry (UPLC-Q-TOF-MS/MS) was employed for chemical profiling of *Eucommia ulmodies*. A total of 33 compounds including lignans, iridoid, phenylpropanoids as well as flavonoids were unambiguously or reasonably identified. To compare the contents of bioactive compounds between old leaves and young leaves of *Eucommia ulmodies*. Chemical variation of 10 batches of old leaves of *Eucommia ulmodies* and 10 batches of young leaves of *Eucommia ulmodies* was subsequently investigated by quantitation of 9 major compounds. The results determined by HPLC coupled with diode array detection (HPLC-DAD).The results shows that the main chemical components in old leaves and young leaves of *Eucommia ulmodies* were basically similar but the difference of the relative content of main chemical composition between young and old leaves of *Eucommia ulmoides* was great. The content of aucubin,geniposidic acid, asperuloside and chlorogenic acid(which are the major bioactive compounds in leaves of *Eucommia ulmoides*) in younger leaves of *Eucommia ulmodies* was significantly higher than that old leaves. The established method could be used to better identify the chemical components in the leaves of *Eucommia ulmodies*, and distinguish the old leaves and young leaves, providing a reference for its quality control based on leaves of *Eucommia ulmoides*.

Keyword : *Eucommia ulmoides* Oliv., Chemical profiling, Quantitation,Quality control

Transcriptome analysis reveals novel enzymes for apo-carotenoid biosynthesis in saffron and enables heterologous production of crocetin in yeast

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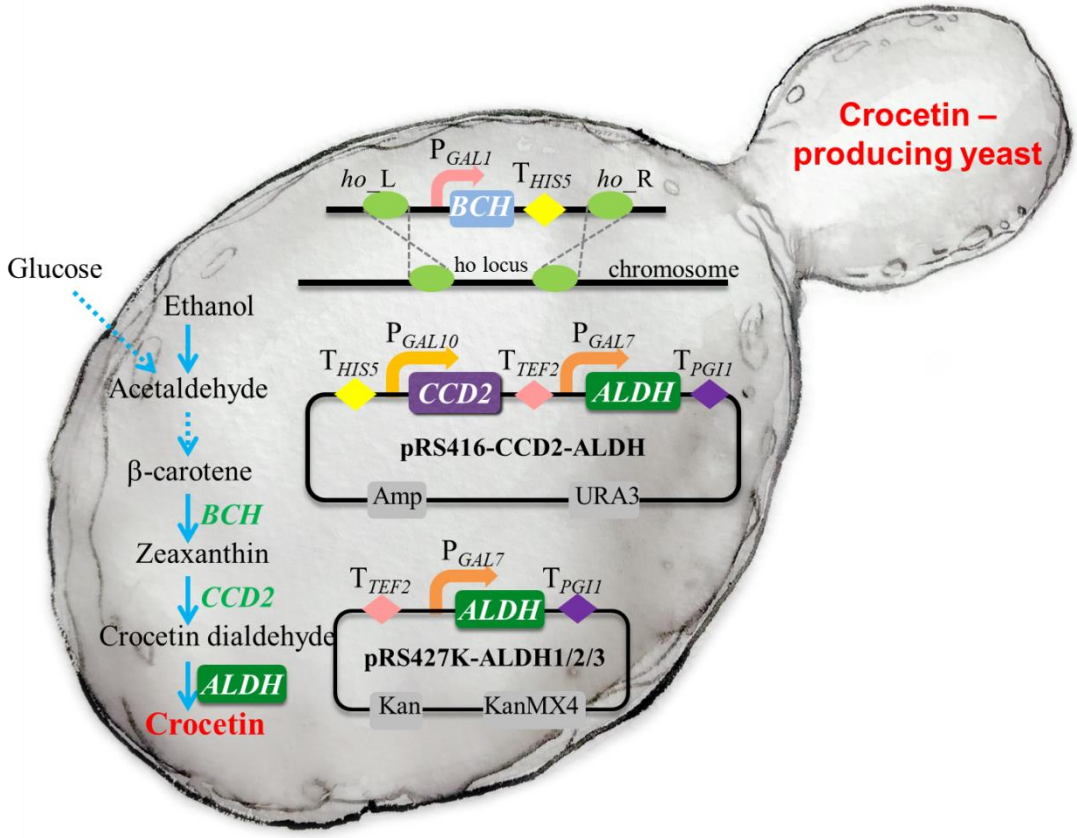

Abstract:

Crocus sativus is generally considered the source of saffron spice and rich in apo-carotenoid compounds such as crocins, crocetin, picrocrocin and safranal, which possess effective pharmacological activities. However, little is known about the exact genes involved in apo-carotenoids biosynthesis in saffron and the potential mechanism of specific accumulation in the stigma. In this study, we integrated different developmental stigmas to perform in-depth transcriptome and dynamic metabolomic analyses to discover the potential key catalytic steps involved in apo-carotenoid biosynthesis in saffron. A total of 61202 unigenes were obtained, and twenty-eight regulators and thirty-two putative carotenogenic genes were captured after the co-expression network analysis. Moreover, 15 candidate genes were predicted to be closely related to safranal and crocin production, in which one aldehyde dehydrogenase (CsALDH3) was validated to oxidize crocetin dialdehyde into crocetin and a crocetin-producing yeast strain was created. In addition, a new branch pathway that catalyses the conversion GGPP to copalol and ent-kaurene by class II diterpene synthases CsCPS1 and three class I diterpene synthases CsEKL1/2/3 were investigated for the first time. Such gene-to-apo-carotenoid landscapes illuminate the synthetic charactersistics and regulators of apo-carotenoid biosynthesis, laying the foundation for deeply understanding the biosynthesis mechanism and metabolic engineering of apo-carotenoids in plant or microbe.

Keyword : *Crocus sativus* L., saffron, apo-carotenoids, transcriptomic profiling, metabolomic profiling, co-expression network, diterpene synthases, aldehyde dehydrogenase

Structural insight into the elucidation on enhanced catalytic activity of glycosidase KfGH01 for the production of vina-ginsenoside R7

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Abstract:

As the principal compounds in the genus Panax, ginsenosides are a class of triterpene saponins with various pharmacological activities and provide numerous health benefits. In particular, vina-ginsenoside R7 (VG-R7) that holds promise for treating neuroinflammation is rarely found in associated plants. Enzymatic transformation is an effective tool that has been increasingly applied in the production of desired compounds, due to advantages such as specificity, less byproduct, and increased yield. Notoginsenoside Fc (NG-Fc), as an appropriate substrate, is a structurally similar compound that is easily isolated from the leaves and stems of Panax notoginseng. However, there are no enzymes for preparing VG-R7 from NG-Fc yet. Therefore, in the present study, we first screened some candidate protein sequences belonging to glycoside hydrolases family 1, 3 and 43. KfGH01 was found that can specifically hydrolyze the linkage of β-D-xylopyranosyl-(1→6)-β-D-glucopyranoside at the C-20 position of NG-Fc, but the production of VG-R7 was limited by its catalytic activity. Hence, we utilized strategies of directed evolution and semi-rational design to enhance the catalytic activity of KfGH01. This approach yielded a variant with two amino acid residues mutation (I248F/Y410R), which presented about a 270-fold enhanced kcat/KM value in comparison to KfGH01. Furthermore, we propose an enzymatic mechanism to explain the increased catalytic efficiency of the mutation in KfGH01 through X-ray crystallography, molecular docking, and molecular dynamics simulations.

Keyword : Glycosidase, Vina-ginsenoside R7, Enzymatic transformation, Directed evolution, Molecular dynamics simulation

A sensitive and efficient method for determination of capecitabine and its five metabolites in human plasma based on one-step liquid-liquid extraction

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Abstract:

Colorectal cancer is the most common critical disease both in developed and developing countries. Capecitabine, which has served in clinical practice at least for ten years, is a first-line anti-digestive tract cancer drug for its better efficacy, patient compliance and lower side effects. An ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) method has been developed and completely validated for simultaneous determination of capecitabine and its five metabolites in human plasma from colorectal cancer patients after administration of capecitabine tablet. One-step liquid-liquid extraction was successfully applied using ethyl acetate and isopropanol (19:1, V:V) for sample pretreatment. Chromatographic separation was achieved within 5 min based on an Atlantis T3-C18 column (3.0 μm, 2.1 × 100 mm) with gradient elution using mobile phases consisting of 0.0075% formic acid in water (pH 4) and in acetonitrile, and the flow rate was 0.3 mL/min. Linear range was approximately 20.0-5000.0 ng/mL for all analytes. Linear correlation coefficients were > 0.99 for all regression curves. The intra-day and inter-day accuracy and precision of the method were within ±15.0% and less than 15.0%, respectively. The mean recovery and matrix effect as well as stability of all the analytes ranged from 59.27% to 90.15% and from 74.84% to 114.48% as well as within ±15.0%. This simple, rapid and sensitive method was successfully applied in 42 sparse clinical samples to verify its practicability.

Keyword : Capecitabine and its metabolites; UHPLC-MS/MS; Human plasma; One-step liquid-liquid extraction

A direct, sensitive and efficient method for determination of Alpha-fluoro-beta-alanine excretion in urine: exploration of the influence from magnesium isoglycyrrhizinate in rat

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Abstract:

Alpha-fluoro-beta-alanine (FBAL), the final metabolite of capecitabine, is a toxic compound excreting with urine. Magnesium isoglycyrrhizinate injection is a traditional Chinese medicine prescribed with capecitabine as a hepatoprotective agent. The purpose of this study is to develop a ultra-high performance liquid chromatography coupled to tandem mass spectrometry method for direct, efficient and sensitive determination of FBAL in urine and explore the influence of magnesium isoglycyrrhizinate on the excretion of FBAL. The method development and validation was completed according to Chinese pharmacopeia. The run time was 3 min based on an HILIC column and linear range was 20-10000 ng/mL. Analyte extraction was achieved by direct dilution using 50% acetonitrile aqueous solution with the matrix effect range 48.98%~52.10% and the recovery range 78.68% ~ 83.28%. The stability, intra- and inter-day precision and accuracy, specificity, carry-over, dilution effect and linearity all conformed to the criterions. This new developed method was applied investigate the influence of magnesium isoglycyrrhizinate on the excretion of FBAL, and the results proved that the magnesium isoglycyrrhizinate has no influence on the excretion of FBAL in rats.

Keyword : UHPLC-MS/MS; Alpha-fluoro-beta-alanine; magnesium isoglycyrrhizinate; rat urine; excretion suppression

比较基因组揭示黄芩属植物黄酮化合物生物合成进化机制

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Abstract:

黄芩属植物约300余中，富含黄酮类化合物，该属植物多入药，具有清热解毒等功效。黄芩和半枝莲收载于《中国药典》，黄芩为大宗常用中药材，其遗传背景解析及优良品种选育具有重要意义。此外，黄芩素、汉黄芩素、黄芩苷、汉黄芩苷等黄酮类化合物的生物合成及合成生物学研究在国际上备受关注。本研究联合二三代测序技术，破译黄芩属黄芩和半枝莲的结构基因组，基于全基因组比较分析揭示黄芩属黄酮类化合物生物合成途径的平行进化。i）根据二三代测序数据特点，整合开发本草基因组结构解析的生物信息学流程，组装黄芩和半枝莲高质量基因组，Contig N50分别为2.1 Mb和2.5 Mb；ii）通过Hi-C染色体构象捕获技术，构建黄芩和半枝莲染色体水平基因组，基因组完整性为91.5%和93.0%，共线性揭示两者基因组的大片段重排，半枝莲染色体数量扩张，推测与物种分化后半枝莲LTR转座子插入相关；iii）黄芩、半枝莲物种分化发生在14百万年（MYA），黄芩、半枝莲物种分化后未发生全基因组复制事件（WGD），在72-85MYA发现一次唇形科共有的WGD；iv）结合转录组及UPLC分析发现黄芩素、汉黄芩素及其糖苷衍生物主要在黄芩和半枝莲的根中合成，而野黄芩素及其糖苷衍生物主要在黄芩和半枝莲的地上部位合成；v）黄酮类化合物生物合成途径相关基因在黄芩和半枝莲中保守存在，但苯丙氨酸解氨酶（PAL）和查尔酮合成酶（CHS）在黄芩中显著扩张，4-香豆酸辅酶A连接酶（4CL）在半枝莲中扩张；vi）黄酮羟化酶基因F6H和F8H在黄芩和半枝莲中均存在串联复制，基因组共线性显示半枝莲F8H串联复制区域发生大片段的重排。本研究揭示黄芩属植物全基因组进化及活性成分生物合成的分子机制，为黄芩的分子辅助育种及活性成分合成生物学研究奠定基础。

Wuzhi capsule regulates chloroacetaldehyde pharmacokinetics behavior and alleviates high-dose cyclophosphamide-induced nephrotoxicity and neurotoxicity in rats

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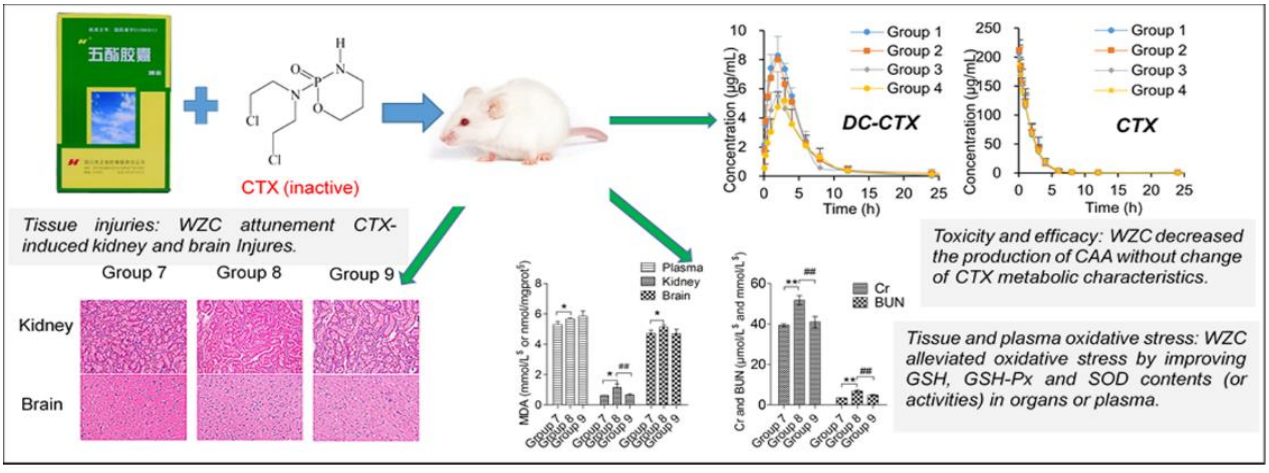
Abstract:

The objective of this study was to evaluate the effect of Wuzhi Capsule (WZC) on the pharmacokinetics of cyclophosphamide and its metabolites in SD rats, and the attenuation of chloroacetaldehyde (CAA) induced kidney and brain injuries, which was produced at equimolar with 2-dechloroethylcyclophosphamide (DCCTX). Rats were treated with single- or multiple-dose of WZC when giving HD-CTX, and the plasma concentration of CTX and its metabolites were quantitated by UHPLC-MS/MS. Single-dose, not multiple-dose of WZC co-administration (300 mg/kg) significantly reduced Cmax and AUC0 24 h of DC-CTX by 33.10% and 35.51%, respectively. Biochemical assay suggested oxidative stress was involved in kidney and brain injuries by HD-CTX, which were attenuated by single-dose WZC (300 mg/kg) pre-treatment, with incresed glutathione, glutathione peroxidase and superoxide dismutase contents/or activities in both tissues and plasma ($p < 0.05$). Meanwhile, WZC pre-treatment could also significantly decresed the plasma levels of creatinine, blood urea nitrogen, and malondialdehyde ($p < 0.05$). Additionally, WZC treatment improved the morphology and pathology condition of the kidneys and brains in rats. In conclusion, single-dose WZC co-administration decreased CAA production and exerted protective effect on CTX-induced oxidative stress in kidney and brain, whereas repetitive WZC co-administration with CTX was probably not recommended.



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公司简介
BRIEF INTRODUCTION OF COMPANY

广西梧州制药(集团)股份有限公司是中恒集团（股票代码：600252）控股的一家集研发、生产、销售于一体的现代综合型制药企业、是国家高新技术企业、中国医药制造业百强企业，是我国现代中药制造业前端的一颗璀璨明珠。

公司拥有“中华”、“晨钟”和“中恒”等知名商标品牌，以及注射用血栓通、妇炎净胶囊、中华跌打丸、结石通片等主导产品，在心脑血管、跌打损伤、妇科疾病、呼吸系统等治疗领域优势突出。尤其注射用血栓通，更成为国内中药注射剂治疗心脑血管疾病的典范。

梧州制药以中药现代化为己任，致力于实现医药健康领域的传承与创新。努力成为广西医药健康资源的整合者和国内有影响力的医药产业综合企业。

科技强企
STRENGTHENING THE ENTERPRISE BY SCIENCE AND TECHNOLOGY

梧州制药拥有广西医药产业工程院、广西天然药物现代制剂技术工程研究中心、广西药物提纯工程技术研究中心、广西千亿元研发中心、院士工作站等技术平台，配备了一支精湛、高效、专业的科技创新团队及国内高精尖的先进检测仪器，自主创新水平领先，具备开发多类新药、中药前沿技术、新工艺、新产品的研发和老产品二次开发的能力。同时，梧州制药与国内外高校、科研院所等单位加强产学研联合创新，成立有“暨大—广投中恒健康产业研究院”，以此为平台集聚来自全国的高尖端人才，助力企业提升创新研发水平。

近几年来，公司先后承担了多项国家重大新药创制、中药质量标准制定等国家级科研项目，取得了卓越的成果。