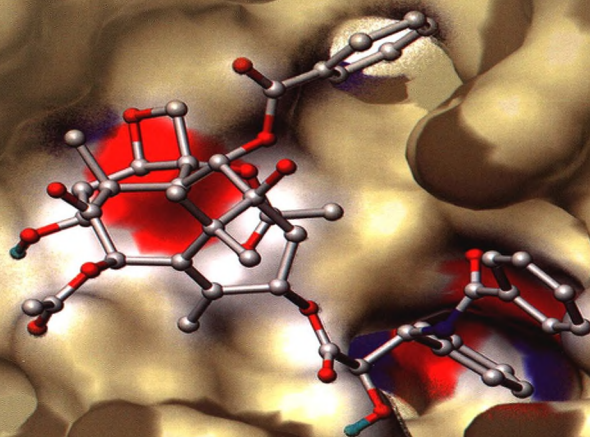




# 药 学 学 报

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### 聚焦抗新冠病毒药物研究

孙 静, 崔晓兰等

苦参碱氯化钠注射液对人冠状病毒肺炎寒湿疫毒袭肺证小鼠病证结合模型的治疗作用

### 综述

高宇雄, 钟大放

抗体药物LC-MS法生物分析进展



中国药学会  
中国医学科学院药物研究所



# 药 学 学 报

第 55 卷 第 3 期 2020 年 3 月

## 图 文 摘 要

### 聚焦抗新冠病毒药物研究

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#### 新型冠状病毒有关药物和生物制品研究进展

王赫然\*, 王茜

(科学技术部火炬高技术产业开发中心, 北京 100045)

本文综述了可能用于治疗新型冠状病毒肺炎的化学药、中药和生物制品的研究进展, 供有关部门、单位和科技人员参考。

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#### 浅析注册用于新冠肺炎治疗的临床试验药物

张超<sup>1</sup>, 陈姝冰<sup>2</sup>, 张洁<sup>1</sup>, 郭颖<sup>2\*</sup>

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截至 2020 年 2 月 14 日, 共有 14 个化学药物 (含 2 个临床在研药物) 注册用于治疗新冠肺炎的临床研究。本文在总结上述药物临床试验方案的基础上, 并分析了这些药物与抗新型冠状病毒相关的临床数据、实验结果和作用机制。



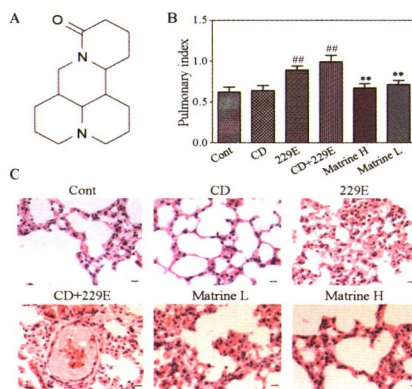
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#### 苦参碱氯化钠注射液对人冠状病毒肺炎寒湿疫毒袭肺证小鼠病证结合模型的治疗作用

孙静<sup>1</sup>, 赵荣华<sup>1</sup>, 郭姗姗<sup>1</sup>, 时宇静<sup>1</sup>, 包蕾<sup>1</sup>, 耿子涵<sup>1</sup>, 高英杰<sup>1</sup>, 刘建<sup>2</sup>, 李琼<sup>2</sup>, 崔晓兰<sup>1\*</sup>

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本文研究了苦参碱氯化钠注射液对人冠状病毒肺炎寒湿疫毒袭肺证小鼠病证结合模型的治疗作用, 为临床用药提供了实验室数据支持。



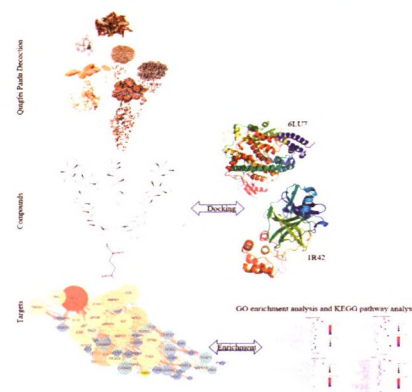
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#### 基于网络药理学和分子对接技术初步探索“清肺排毒汤”抗新型冠状病毒肺炎作用机制

吴昊<sup>1#</sup>, 王佳琪<sup>1#</sup>, 杨雨薇<sup>1</sup>, 李天怡<sup>1</sup>, 曹一佳<sup>1</sup>, 曲玉霞<sup>1</sup>, 靳玉洁<sup>2</sup>, 张晨宁<sup>1,2\*</sup>, 孙毅坤<sup>1\*</sup>

(1. 北京中医药大学中药学院, 北京 102488; 2. 十堰市太和医院, 湖北医药学院附属医院, 湖北 十堰 442000)

采用网络药理学技术初步探索了清肺排毒汤抗 COVID-19 的生物学机制, 并对复方中的关键化合物进行了分子对接预测。



### 综述

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#### 抑郁症发病与受体基因异常研究进展

王惠芹<sup>1,2</sup>, 王真真<sup>2</sup>, 陈乃宏<sup>1,2\*</sup>

(1. 湖南中医药大学药学院, 湖南省中药饮片标准化及功能工程技术研究中心, 湖南 长沙 410208; 2. 中国医学科学院药物研究所, 神经科学中心, 北京 100050)

受体基因异常是导致抑郁症发病的重要因素, 研究潜在的受体基因位点有望成为未来抑郁症治疗的新靶点。

Receptor	Receptor gene	Gene loci	Level	Type
GR	<i>NR3C1</i>	chr 5	Amygda ↓ <sup>[6]</sup> PFC ↓ <sup>[6]</sup>	DNAm <sup>[6]</sup>
NMDAR	<i>GRIN2B</i>	12p13.1	PFC ↑ <sup>[7]</sup>	rs1805502-rs890 G-T hypotype <sup>[8]</sup>
AMPA	<i>GRIN1</i>	-	DG ↓ <sup>[9]</sup>	rs4302506, rs4403097 SNP <sup>[9]</sup>
5-HT1A	-	5q11.2-13	CSF ↓ <sup>[10]</sup>	rs6295C(-1019)G <sup>[6]</sup>
GABRA2	<i>Gabra2</i>	-	PFC ↓ <sup>[6]</sup> Hip ↓ <sup>[6]</sup>	SNP <sup>[6]</sup>

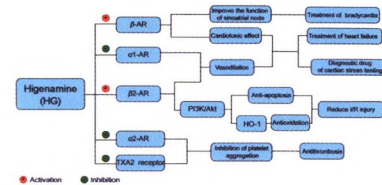
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#### 去甲乌药碱对心血管药理作用的研究进展

王玉红, 李聪, 江爽, 蒋建东\*

(中国医学科学院、北京协和医学院药物研究所, 北京 100050)

本文综述了去甲乌药碱对心血管药理作用的研究进展, 有助于该药物进一步研发及临床应用。



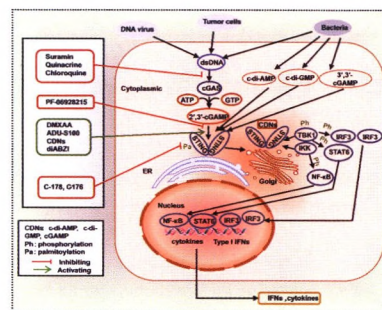
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#### cGAS-STING 在肿瘤转移中的研究进展

屠书梅<sup>1,2</sup>, 刘玉萍<sup>1,2</sup>, 陈彦<sup>1,2\*</sup>

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本文对环磷酸鸟苷-腺苷酸合成酶-干扰素基因刺激因子 (cGAS-STING) 信号通路在肿瘤发生发展及转移中发挥的双重作用及其相关激动剂和抑制剂的最新研究进展进行了综述。



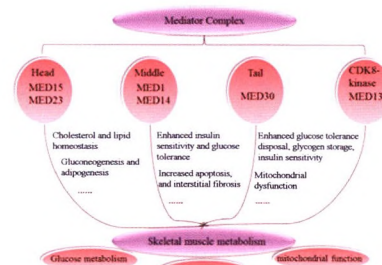
407

#### 中介复合体对骨骼肌代谢功能影响及机制研究进展

李娜, 殷琳, 杨秀颖, 杜冠华\*

(中国医学科学院、北京协和医学院药物研究所, 药物靶点研究与新药筛选北京市重点实验室, 北京 100050)

中介复合体通过调控相关转录因子的表达对骨骼肌代谢功能的影响及其机制研究进展。



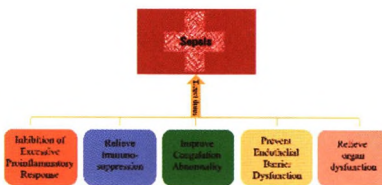
413

#### 治疗脓毒症药物研究进展

谢春阳, 王秀坤, 游雪甫\*

(中国医学科学院、北京协和医学院医药生物技术研究所, 抗感染药物研究北京市重点实验室, 北京 100050)

脓毒症是一种致死率高的难治性疾病, 临床上大多数治疗手段治标不治本, 缺乏有效治疗药物。脓毒症患者体内病理生理过程复杂, 导致研发治疗脓毒症的药物难度巨大。本文主要综述根据其病理生理过程设计的靶点药物。



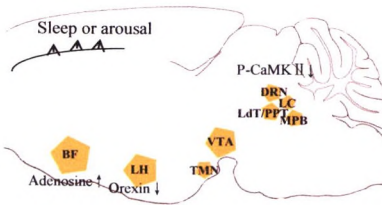
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#### 一氧化氮调控机体睡眠觉醒的研究进展

于凤婷, 张建军\*

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在机体内, 睡眠剥夺会导致脑中一氧化氮浓度升高, 一氧化氮能通过抑制上行网状激活系统的活性从而促进机体睡眠。





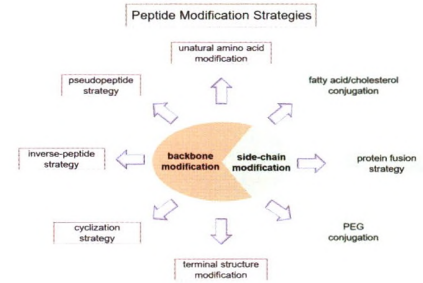
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先导化合物结构优化策略 (七)—— 肽类分子结构修饰与改造

彭晶晶<sup>1,2</sup>, 王江<sup>1,2</sup>, 戴文豪<sup>1</sup>, 谢雄<sup>1,2</sup>, 柳红<sup>1,2\*</sup>

(1. 中国科学院上海药物研究所, 新药研究国家重点实验室, 上海 201203;  
2. 中国科学院大学, 北京 100049)

本文综述了肽类分子的改造策略, 旨在提高多肽先导化合物的活性、稳定性、细胞渗透性和溶解性, 为多肽药物开发提供参考。



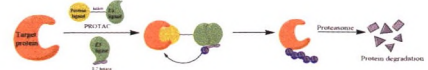
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小分子 PROTAC 在不同靶点研究中的应用

王媛<sup>1,2</sup>, 龙菁<sup>3</sup>, 唱祺<sup>1</sup>, 胡维稳<sup>4</sup>, 胡高云<sup>1</sup>, 李乾斌<sup>1\*</sup>

(1. 中南大学湘雅药学院药物化学系, 湖南 长沙 410012; 2. 北京大学药学院, 天然药物及仿生药物国家重点实验室, 北京 100191; 3. 中南大学湘雅医院皮肤科, 湖南长沙 410012; 4. 云南中医医院制剂室, 云南 昆明 650021)

PROTAC 分子具有将无法成药的蛋白质作为靶蛋白的潜力以及可能在药物耐药中发挥作用的优点, 本文总结了现有的 PROTAC 小分子在核蛋白、膜蛋白及胞浆蛋白等不同靶点研究中的应用。



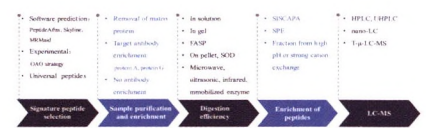
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抗体药物 LC-MS 法生物分析进展

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(中国科学院上海药物研究所, 上海 201203)

本文对抗体药物 LC-MS 法生物分析的进展进行综述, 重点介绍替代肽的选择、样品纯化与富集、提高酶解效率等策略。



研究论文

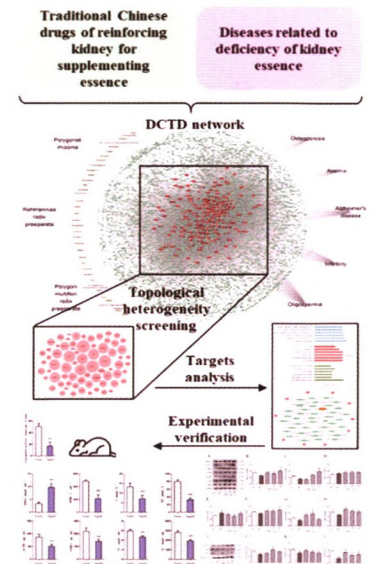
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补肾益精中药治疗肾精亏虚证相关疾病的生物学物质基础及作用机制的预测与验证

伍超, 韦佳慧, 陈涵, 阮陶仁, 李卓恒, 张继芬, 徐晓玉\*

(西南大学药学院·中医药学院, 重庆市高校中药新药筛选重点实验室, 国家中医药管理局中药药理学重点建设学科, 重庆 400715)

补肾益精中药治疗肾精亏虚证相关疾病的生物学基础及机制与调节细胞核内转录活性及促红细胞生成素 (EPO) 信号通路有关。



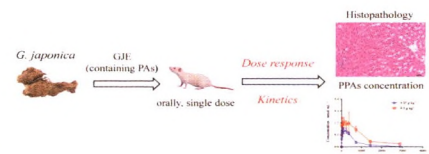
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大鼠灌胃菊三七生成吡咯蛋白加合物的药代动力学研究

陈岩<sup>1</sup>, 王汛江<sup>1</sup>, 熊芬<sup>1</sup>, 王蔚倩<sup>1</sup>, 杨莉<sup>1,2\*</sup>, 熊爱珍<sup>1\*</sup>, 王长虹<sup>1</sup>, 王峥涛<sup>1,2</sup>

(1. 上海中医药大学中药研究所, 中药标准化教育部重点实验室暨上海市复方中药重点实验室, 上海 201203; 2. 上海中药标准化研究中心, 上海 201203)

PPAs 含量随菊三七给药剂量增加呈剂量依赖性, 且与肝损伤程度相关; 其在大鼠体内的消除率随着菊三七给药剂量的增加明显减慢。



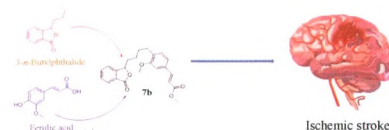
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## 丁苯酞衍生物的设计、合成及神经细胞保护和抗血小板聚集活性研究

张斌, 刘万冬, 李家明\*, 金凡, 钱诗虎

(安徽中医药大学药学院, 安徽 合肥 230012)

以丁苯酞为基本骨架设计合成了系列丁苯酞衍生物, 其中化合物 **7b** 表现出良好的神经细胞保护活和抗血小板聚集活性。



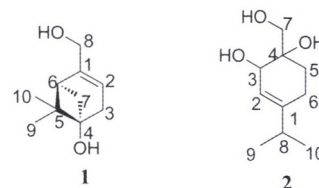
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## 姜皮中两个新的单萜类化合物

郭燕<sup>1</sup>, 王彦志<sup>1,2\*</sup>, 徐志贫<sup>1</sup>, 李曼倩<sup>1</sup>, 张晓娟<sup>1</sup>, 刘煜飞<sup>1</sup>, 胡雪雨<sup>1</sup>, 冯卫生<sup>1,2\*</sup>

(1. 河南中医药大学药学院, 河南 郑州 450046; 2. 呼吸疾病中医药防治省部共建协同创新中心, 河南 郑州 450046)

运用多种色谱分离技术从姜皮中分离鉴定了 7 个萜类化合物, 其中化合物 **1**、**2** 为新化合物, 命名为: (4*R*,6*S*)-1-(羟甲基)-5,5-二甲基二环[3.1.1]庚-2-烯-4-醇和 4-(羟甲基)-1-异丙基环己-2-烯-3,4-二醇, 化合物 **3**~**7** 均为首次从该植物中得到。



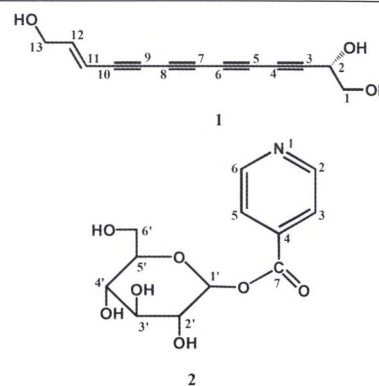
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## 小花鬼针草中 1 个新的聚炔和 1 个新的异烟酸葡萄糖酯苷

李传厚<sup>1,2</sup>, 朱彦军<sup>1</sup>, 于绍华<sup>1</sup>, 蒋海强<sup>1</sup>, 周洪雷<sup>1\*</sup>

(1. 山东中医药大学药学院, 山东 济南 250355; 2. 山东医学高等专科学校, 山东 临沂 276000)

从小花鬼针草 80%乙醇提取物的乙酸乙酯部位分离得到 11 个化合物, 其中化合物 **1** 和 **2** 为新化合物, 分别鉴定为(2*S*)-十三烷-(11*E*)-一炔-3,5,7,9-四炔-1,2,13-三醇 (**1**)、吡啶-4-甲酰-*O*-β-*D*-吡喃葡萄糖酯苷 (**2**)。



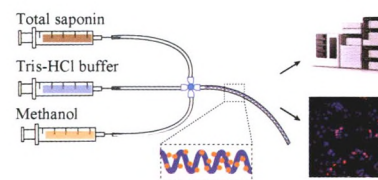
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## 基于中空纤维吸附靶酶的流体灌注系统用于苦丁茶总皂苷活性成分筛选

侯宇<sup>1</sup>, 郑娇<sup>2</sup>, 屠鹏飞<sup>1</sup>, 艾晓妮<sup>1\*</sup>, 姜勇<sup>1\*</sup>

(1. 北京大学天然药物及仿生药物国家重点实验室, 北京 100191; 2. 北京中医药大学中药现代研究中心, 北京 100029)

运用基于中空纤维吸附靶酶的连续灌注系统从苦丁茶总皂苷中筛选得到两种脂肪酶抑制剂, 具有较好的抗动脉粥样硬化的活性。



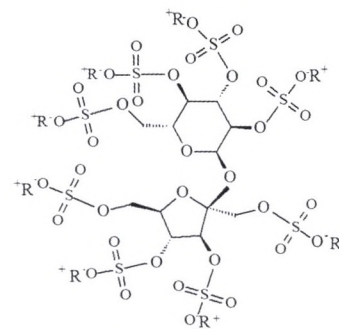
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## 两种测定盐酸伊立替康脂质体注射液中蔗糖八硫酸酯定量法的比较

王慧嘉<sup>1</sup>, 王远见<sup>1,2</sup>, 梁晨<sup>2</sup>, 蔡倩<sup>3</sup>, 徐洪胜<sup>4</sup>, 李清<sup>1\*</sup>

(1. 沈阳药科大学药学院, 辽宁 沈阳 110016; 2. 玻思韬控释药业有限公司, 广东 广州 510530; 3. 辽源市食品药品监督管理局, 吉林 辽源 136200; 4. 浙江莎普爱思药业股份有限公司, 浙江 嘉兴 314200)

两种测定盐酸伊立替康脂质体注射液中蔗糖八硫酸酯定量法的比较。



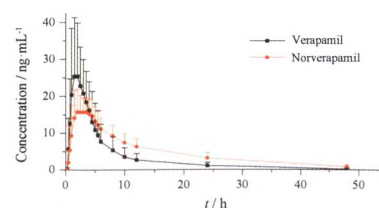
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## LC-MS/MS 法同时测定人血浆中维拉帕米和代谢产物去甲维拉帕米

丁春晓<sup>1,2</sup>, 耿雅杰<sup>2</sup>, 刘静媛<sup>2</sup>, 夏媛媛<sup>2</sup>, 刘万卉<sup>1</sup>, 司端运<sup>2\*</sup>

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本文建立了一种简便、灵敏的同时测定人血浆中维拉帕米和去甲维拉帕米浓度的液相色谱-串联质谱 (LC-MS/MS) 的分析方法, 经方法学验证后, 由伦理委员会批准用于健康人体口服维拉帕米片 (40 mg) 后的药代动力学研究。





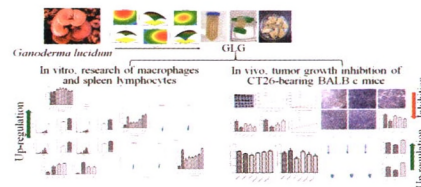
512

灵芝  $\beta$ -葡聚糖的碱提取及其抗肿瘤免疫调节研究

张锦锦<sup>1,2</sup>, 陈菲菲<sup>1,2</sup>, 严展鹏<sup>1,2</sup>, 李畅<sup>1,2</sup>, 孙娥<sup>1,2</sup>, 罗毅<sup>1\*</sup>, 谭晓斌<sup>1,2\*</sup>

(1. 南京中医药大学附属中西医结合医院, 江苏 南京 210028; 2. 江苏省中医药研究院, 国家中医药管理局中药释药系统重点研究室, 江苏 南京 210028)

响应面法优化灵芝颗粒性  $\beta$ -葡聚糖 (GLG) 的碱提取方式。GLG 能活化巨噬细胞, 促进脾淋巴细胞增殖, 促进 T 细胞抗肿瘤免疫应答。



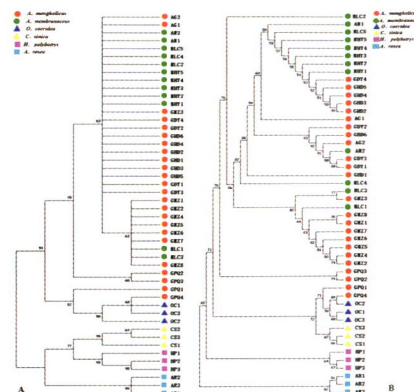
522

基于 ITS2 序列及二级结构对药用黄芪及混伪品的鉴别研究

刘亚令<sup>1#</sup>, 耿雅萍<sup>1#</sup>, 王芳<sup>1</sup>, 解潇冬<sup>1</sup>, 张鹏飞<sup>2</sup>, 梁建萍<sup>1</sup>, 刘德旺<sup>3\*</sup>

(1. 山西农业大学生命科学学院, 山西 晋中 030801; 2. 山西农业大学园艺学院, 山西 晋中 030801; 3. 内蒙古医科大学药学院, 内蒙古 呼和浩特 010059)

基于 ITS2 序列及二级结构对药用黄芪及混伪品进行了鉴别研究, 二级结构信息的加入, 使得构建的系统发育树不仅包含了基于一级结构得到的所有结论, 也解决了梳子状拓扑结构, 同时在分辨率与支持率上也有所提高。



新药发现与研究实例简析

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模拟天然产物的他米巴罗汀和贝沙罗汀

郭宗儒

(中国医学科学院、北京协和医学院药物研究所, 北京 100050)

## Focus on Anti Novel Coronavirus Drugs Research

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### Advances in research of novel coronavirus related drugs and biological products

WANG He-ran\*, WANG Xi

(Torch High Technology Industry Development Center, Ministry of Science and Technology, Beijing 100045, China)

We reviewed the advances in research of novel coronavirus related chemical drugs, Chinese traditional medicines and biological products, which could provide reference for relevant departments, units and scientists.

355

### Analysis of chemical drugs applied for clinical trial for the treatment of COVID-19

ZHANG Chao<sup>1</sup>, CHEN Shu-bing<sup>2</sup>, ZHANG Jie<sup>1</sup>, GUO Ying<sup>2\*</sup>

(1. National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin's Clinical Research Center for Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin 300060, China; 2. Beijing Key Laboratory of New Drug Mechanisms and Pharmacological Evaluation Study, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)



There were 14 chemical drugs, including 12 drugs on market and 2 in clinical trials, registered clinical trials for COVID-19 treatment by Feb. 14<sup>th</sup>, 2020. We summarize the medication regimens of the clinical trials, along with these drugs' clinical data, experimental results, and mechanism related to the activity against SARS-CoV-2.

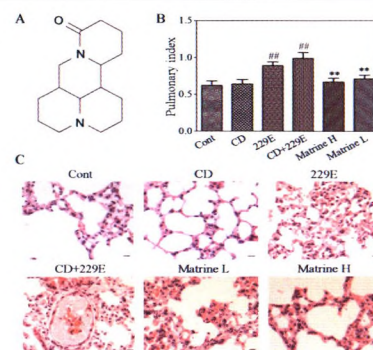
366

### Effect of matrine sodium chloride injection on a mouse model combining disease with syndrome of human coronavirus pneumonia with cold-dampness pestilence attacking the lung

SUN Jing<sup>1</sup>, ZHAO Rong-hua<sup>1</sup>, GUO Shan-shan<sup>1</sup>, SHI Yu-jing<sup>1</sup>, BAO Lei<sup>1</sup>, GENG Zi-han<sup>1</sup>, GAO Ying-jie<sup>1</sup>, LIU Jian<sup>2</sup>, LI Qiong<sup>2</sup>, CUI Xiao-lan<sup>1\*</sup>

(1. Biosecurity Laboratory, Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, Beijing 100700, China; 2. Hubei Kangqing Pharmaceutical Co., Ltd., Jingmen 448000, China)

This study on the effect of matrine sodium chloride injection on a mouse model combining disease with syndrome of human coronavirus pneumonia with cold-dampness pestilence attacking the lung provided laboratory data support for its clinical use.



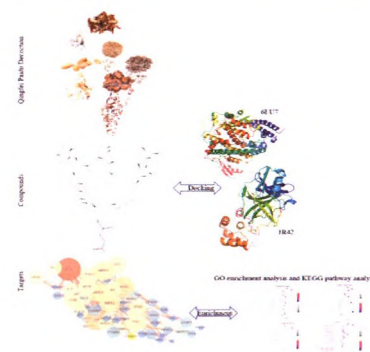
374

### Preliminary exploration of the mechanism of Qingfei Paidu decoction against novel coronavirus pneumonia based on network pharmacology and molecular docking technology

WU Hao<sup>1#</sup>, WANG Jia-qi<sup>1#</sup>, YANG Yu-wei<sup>1</sup>, LI Tian-yi<sup>1</sup>, CAO Yi-jia<sup>1</sup>, QU Yu-xia<sup>1</sup>, JIN Yu-jie<sup>2</sup>, ZHANG Chen-ning<sup>1,2\*</sup>, SUN Yi-kun<sup>1\*</sup>

(1. School of Chinese Materia Medica, Beijing University of Chinese Medicine, Beijing 102488, China; 2. Taihe Hospital, Hubei University of Medicine, Shiyan 442000, China)

The biological mechanism of Qingfei Paidu decoction against COVID-19 was preliminarily predicted using network pharmacology technology, and the key compounds of the Chinese medicinal materials were predicted by molecular docking.





## Reviews

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### Advance in relationship between receptor gene abnormality and depression

WANG Hui-qin<sup>1,2</sup>, WANG Zhen-zhen<sup>2</sup>, CHEN Nai-hong<sup>1,2\*</sup>

(1. Hunan Engineering Technology Center of Standardization and Function of Chinese Herbal Decoction Pieces, College of Pharmacy, Hunan University of Chinese Medicine, Changsha 410208, China; 2. Neuroscience Center, Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing 100050, China)

Receptor	Receptor gene	Gene loci	Level	Type
GR	<i>NR3C1</i>	chr 5	Amygda <sup>[10]</sup> PFC <sup>[10]</sup>	DNAm <sup>[10]</sup>
NMDAR	<i>GRIN2B</i>	12p13.1	PFC <sup>[17]</sup>	rs1805502-rs890 G-T hypotype <sup>[10]</sup>
AMPA	<i>GRIA</i>	-	DG <sup>[10]</sup>	rs4302506, rs4403097 SNP <sup>[10]</sup>
5-HT1A	-	5q11.2-13	CSF <sup>[10]</sup>	rs62955C(-1019)G <sup>[10]</sup>
GABRA2	<i>Gabra2</i>	-	PFC <sup>[10]</sup> Hip <sup>[10]</sup>	SNP <sup>[10]</sup>

Receptor gene abnormalities are crucial factors leading to the onset of depression. The study of potential receptor gene loci is expected to be a new target for the treatment of depression in the future.

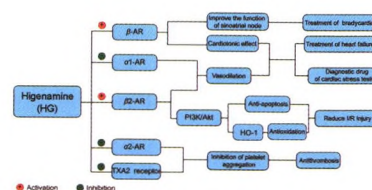
392

### Advances in pharmacological effects of higenamine on cardiovascular system

WANG Yu-hong, LI Cong, JIANG Shuang, JIANG Jian-dong\*

(Institute of Materia Medica, Chinese Academy of Medical Science and Peking Union Medical College, Beijing 100050, China)

In this paper, the research progress of the pharmacological effects of higenamine on cardiovascular is reviewed, which will help the development and clinical application of higenamine in the future.



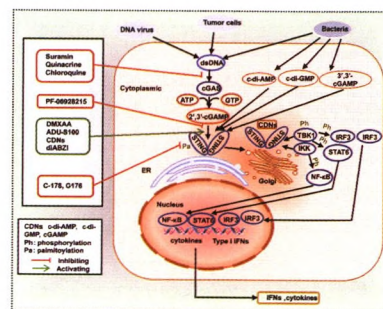
398

### Research progress of cGAS-STING in tumor metastasis

TU Shu-mei<sup>1,2</sup>, LIU Yu-ping<sup>1,2</sup>, CHEN Yan<sup>1,2\*</sup>

(1. Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing 210028, China; 2. Multi-component of Traditional Chinese Medicine and Microecology Research Center, Jiangsu Provincial Academy of Chinese Medicine, Nanjing 210028, China)

In this paper, recent advances in the research of the dual roles of cyclic GMP-AMP synthase-stimulator of interferon gene (cGAS-STING) signaling pathway in tumorigenesis, development and metastasis and the related agonists and inhibitors were reviewed.



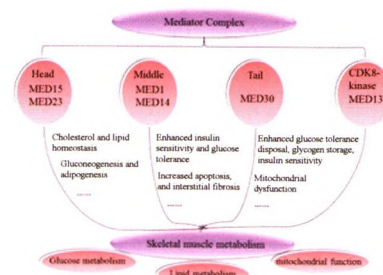
407

### Mediator complexes regulate skeletal muscle metabolic function: a review

LI Na, YIN Lin, YANG Xiu-ying\*, DU Guan-hua\*

(Beijing Key Laboratory of Drug Target Identification and Drug Screening, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)

The effect and mechanism of mediator complex on skeletal muscle metabolism by regulating the expression of transcription factors.



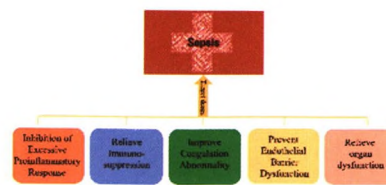
413

### Research progress in drugs for treating sepsis

XIE Chun-yang, WANG Xiu-kun, YOU Xue-fu\*

(Beijing Key Laboratory of Antimicrobial Agents, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)

Sepsis is a refractory disease with high mortality. Most of the clinical treatments are not cured, and there is no effective treatment. The pathophysiological process in patients with sepsis is complicated, which makes it difficult to develop drugs for treating sepsis. This paper mainly reviews the research progress of targeted drugs based on its pathophysiological processes.





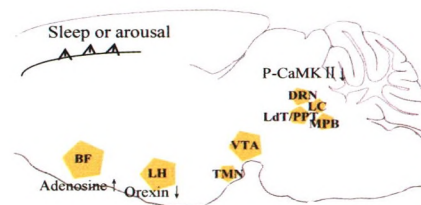
421

**Advances in research on the role of nitric oxide in regulating sleep and arousal**

YU Feng-ting, ZHANG Jian-jun\*

(Beijing Key Laboratory of New Drug Mechanism and Pharmacological Evaluation Study, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)

In body, sleep deprivation increases the concentration of nitric oxide in the brain, which promotes sleep by inhibiting the activity of the ascending reticular activation system.



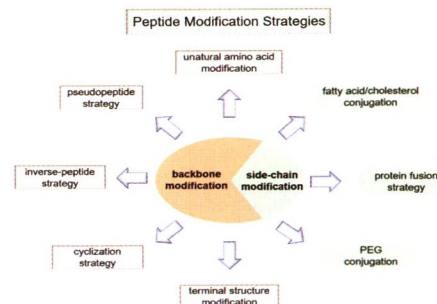
427

**Lead compound optimization strategy (7) — modification strategies for peptides**

PENG Jing-jing<sup>1,2</sup>, WANG Jiang<sup>1,2</sup>, DAI Wen-hao<sup>1</sup>, XIE Xiong<sup>1,2</sup>, LIU Hong<sup>1,2\*</sup>

(1. State Key Laboratory of Drug Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China; 2. University of Chinese Academy of Sciences, Beijing 100049, China)

This review summarized modification strategies of peptides, which is aimed to improve activity, stability, cell permeability, and solubility of peptide lead compound and provide reference for medicinal chemists in peptide drug development.

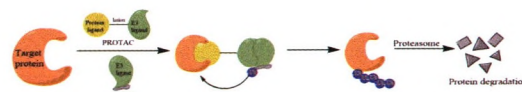


446

**The application of small molecule PROTAC in researches of different targets**

WANG Yuan<sup>1,2</sup>, LONG Jing<sup>3</sup>, CHANG Qi<sup>1</sup>, HU Wei-wen<sup>4</sup>, HU Gao-yun<sup>1</sup>, LI Qian-bin<sup>1\*</sup>

(1. Department of Medicinal Chemistry, Xiangya School of Pharmaceutical Sciences, Central South University, Changsha 410012, China; 2. State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing 100191, China; 3. The Department of Dermatology, Xiangya Hospital, Central South University, Changsha 410012, China; 4. Pharmaceutical Department, Yunnan Provincial Hospital Of Traditional Chinese Medicine, Kunming 650021, China)



The protein proteolysis-targeting chimeras (PROTAC) have the potential to use non-proprietary proteins as target proteins and to play roles in drug resistance. This review summarizes the application of small molecule PROTAC in previous studies of different targets, such as nuclear proteins, membrane proteins and cytoplasmic proteins.

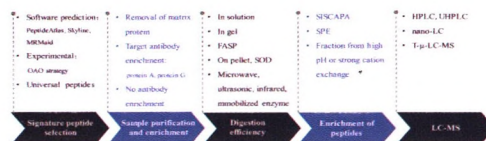
453

**Advances in bioanalysis of antibody drugs by LC-MS**

GAO Yu-xiong, ZHONG Da-fang\*

(Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China)

This paper reviews the progress of bioanalysis of antibody drugs by LC-MS method, with emphasis on the selection of signature peptides, sample purification and enrichment, and improvement of digestion efficiency and so on.





## Original Articles

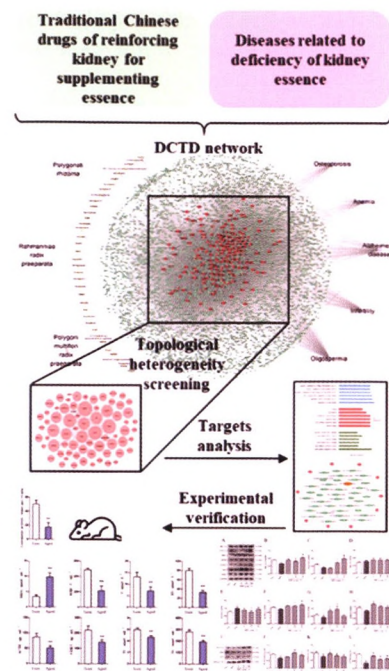
463

### Prediction and verification of biological basis and mechanism for traditional Chinese drugs of reinforcing kidney for supplementing essence in treating diseases related to deficiency of kidney essence

WU Chao, WEI Jia-hui, CHEN Han, RUAN Tao-ren, LI Zhuo-heng, ZHANG Ji-fen, XU Xiao-yu\*

(Chongqing Key Laboratory of New Drug Screening from Traditional Chinese Medicine, Pharmacology of Chinese Materia Medica - the Key Discipline Constructed by the State Administration of Traditional Chinese Medicine, College of Pharmaceutical Sciences and Chinese Medicine, Southwest University, Chongqing 400715, China)

The biological basis and mechanisms of traditional Chinese drugs of reinforcing kidney for supplementing essence on deficiency of kidney essence may be related to the regulation of nuclear transcriptional activity and erythropoietin (EPO) signaling pathway.

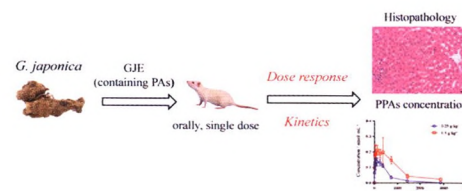


473

### Kinetic study of pyrrolizidine alkaloid-derived pyrrole-protein adducts in rats after intragastric administration of *Gynura japonica*

CHEN Yan<sup>1</sup>, WANG Xun-jiang<sup>1</sup>, XIONG Fen<sup>1</sup>, WANG Wei-qian<sup>1</sup>, YANG Li<sup>1,2\*</sup>, XIONG Ai-zhen<sup>1\*</sup>, WANG Chang-hong<sup>1</sup>, WANG Zheng-tao<sup>1,2</sup>

(1. The Ministry of Education Key Laboratory for Standardization of Chinese Medicines and the State Administration of Traditional Chinese Medicine Key Laboratory for New Resources and Quality Evaluation of Chinese Medicines, Institute of Chinese Materia Medica, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China; 2. Shanghai R & D Center for Standardization of Traditional Chinese Medicines, Shanghai 201203, China)

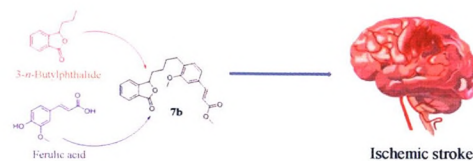


The contents of PPAs increased dose-dependently with the dose of GJE and positively correlated with the severity of liver injury. The elimination rate of PPAs in rats was significantly prolonged with the increase of doses.

478

### Design, synthesis, and neuroprotective and anti-platelet aggregation research of 3-*n*-butylphthalide derivatives

ZHANG Bin, LIU Wan-dong, LI Jia-ming\*, JIN Fan, QIAN Shi-hu  
(College of Pharmacy, Anhui University of Chinese Medicine, Hefei 230012, China)



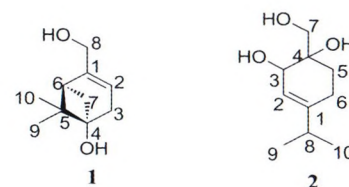
A series of butylphthalide derivatives were designed and synthesized using butylphthalide as the basic skeleton. Among them, compound **7b** exhibited potent neurocyte protective activity and anti-platelet aggregation activity.



484

**Two new monoterpenoids of *Zingiber officinale* peel**GUO Yan<sup>1</sup>, WANG Yan-zhi<sup>1,2\*</sup>, XU Zhi-pin<sup>1</sup>, LI Man-qian<sup>1</sup>, ZHANG Xiao-juan<sup>1</sup>, LIU Yu-fei<sup>1</sup>, HU Xue-yu<sup>1</sup>, FENG Wei-sheng<sup>1,2\*</sup>

(1. School of Pharmacy, Henan University of Chinese Medicine, Zhengzhou 450046, China; 2. Co-construction Collaborative Innovation Center for Chinese Medicine and Respiratory Diseases by Henan &amp; Education Ministry of P. R. China, Zhengzhou 450046, China)



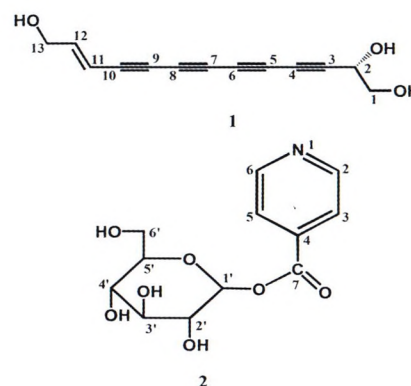
The chemical constituents of *Zingiber officinale* peel were isolated and purified by various chromatographic separation techniques. Seven terpenoids were identified by physicochemical properties and spectral data. Compounds **1**, **2** are new compounds, named: (4*R*,6*S*)-1-(hydroxymethyl)-5,5-dimethylbicyclo[3.1.1]hept-2-en-4-ol and 4-(hydroxymethyl)-1-isopropylcyclohex-2-ene-3,4-diol, and compounds **3-7** were obtained from this plant for the first time.

489

**A new polyacetylene and a new isonicotinic acid glucoside from *Bidens parviflora* Willd.**LI Chuan-hou<sup>1,2</sup>, ZHU Yan-jun<sup>1</sup>, YU Shao-hua<sup>1</sup>, JIANG Hai-qiang<sup>1</sup>, ZHOU Hong-lei<sup>1\*</sup>

(1. College of Pharmaceutical Science, Shandong University of Traditional Chinese Medicine, Jinan 250355, China; 2. Shandong Medical College, Linyi 276000, China)

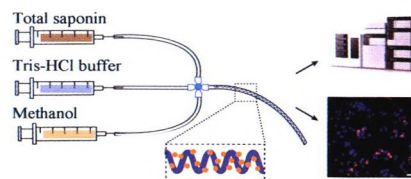
Eleven compounds were isolated from the ethyl acetate fraction of 80% ethanol extract from *Bidens parviflora* Willd. Compounds **1** and **2** are new compounds, named as (2*S*)-11*E*-tetradecene-3,5,7,9-tetrayne-1,2,13-triol (**1**), pyridine-4-formyl-*O*- $\beta$ -*D*-glucopyranoside (**2**).



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**Perfusion enzyme affinity selection system based on hollow fiber for screening active compounds from total saponins of Kudingcha**HOU Yu<sup>1</sup>, ZHENG Jiao<sup>2</sup>, TU Peng-fei<sup>1</sup>, AI Xiao-ni<sup>1\*</sup>, JIANG Yong<sup>1\*</sup>

(1. State Key Laboratory of Natural and Biomimetic Drugs, Peking University, Beijing 100191, China; 2. Modern Research Center for Traditional Chinese Medicine, Beijing University of Chinese Medicine, Beijing 100029, China)



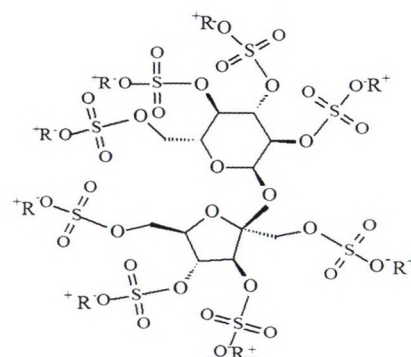
Two small molecular lipase inhibitors were found from the total saponin of Kudingcha through the hollow fiber-based perfusion enzyme affinity selection system, and they are proved to have good anti-atherosclerotic activities.

501

**Comparison of two methods for the determination of sucrose octasulfate concentration in irinotecan hydrochloride liposomes**WANG Hui-jia<sup>1</sup>, WANG Yuan-jian<sup>1,2</sup>, LIANG Chen<sup>2</sup>, CAI Qian<sup>3</sup>, XU Hong-sheng<sup>4</sup>, LI Qing<sup>1\*</sup>

(1. School of Pharmacy, Shenyang Pharmaceutical University, Shenyang 110016, China; 2. Bostal Drug Delivery Co., Ltd., Guangzhou 510530, China; 3. Liaoyuan Food and Drug Administration, Liaoyuan 136200, China; 4. Zhejiang Shapuaisi Pharmaceutical Co., Ltd., Jiaxing 314200, China)

Comparison of the two quantitation methods for determination of sucrose octasulfate in irinotecan hydrochloride liposome injection.



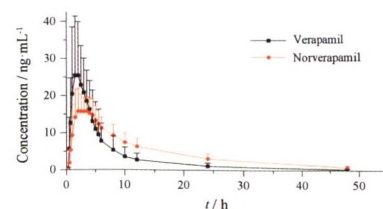


506

### Simultaneous determination of verapamil and its metabolite norverapamil in human plasma by liquid chromatography-tandem mass spectrometry

DING Chun-xiao<sup>1,2</sup>, GENG Ya-jie<sup>2</sup>, LIU Jing-yuan<sup>2</sup>, XIA Yuan-yuan<sup>2</sup>,  
LIU Wang-hui<sup>1</sup>, SI Duan-yun<sup>2\*</sup>

(1. Yantai University, Yantai 264005, China; 2. State Key Laboratory of Drug Delivery Technology and Pharmacokinetics, Tianjin Institute of Pharmaceutical Research, Tianjin 300193, China)



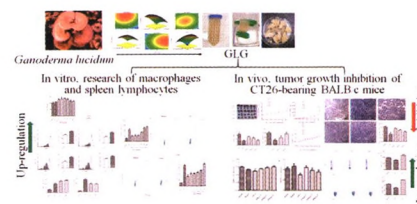
A simple and sensitive method for simultaneous determination of verapamil and norverapamil concentrations in human plasma by liquid chromatography-tandem mass spectrometry (LC-MS/MS) has been developed, this method was used for pharmacokinetic study of oral verapamil tablets (40 mg) in healthy people after approved by the ethics committee.

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### Alkali extraction of *Ganoderma lucidum* $\beta$ -glucan and its anti-tumor immune regulation

ZHANG Jin-jin<sup>1,2</sup>, CHEN Fei-fei<sup>1,2</sup>, YAN Zhan-peng<sup>1,2</sup>, LI Chang<sup>1,2</sup>, SUN E<sup>1,2</sup>,  
LUO Yi<sup>1\*</sup>, TAN Xiao-bin<sup>1,2\*</sup>

(1. Affiliated Hospital of Integrated Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine, Nanjing 210028, China; 2. Key Laboratory of New Drug Delivery Systems of Chinese Materia Medica, Jiangsu Provincial Academy of Chinese Medicine, Nanjing 210028, China)



Response surface analysis for the optimization of alkaline extraction condition for *Ganoderma lucidum* particulate  $\beta$ -glucan (GLG). Resident macrophages were activated by GLG. GLG could promote the proliferation of spleen lymphocytes and antitumor immune responses of T lymphocyte in mice.

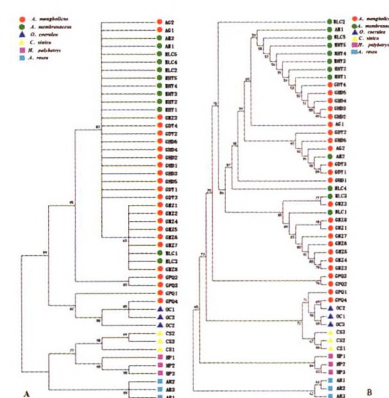
522

### Identification of *Astragalus* and its adulterants based on ITS2 sequence and secondary structure

LIU Ya-ling<sup>1#</sup>, GENG Ya-ping<sup>1#</sup>, WANG Fang<sup>1</sup>, XIE Xiao-dong<sup>1</sup>,  
ZHANG Peng-fei<sup>2</sup>, LIANG Jian-ping<sup>1</sup>, LIU De-wang<sup>3\*</sup>

(1. College of Life Science, Shanxi Agricultural University, Jinzhong 030801, China; 2. College of Horticulture, Shanxi Agricultural University, Jinzhong 030801, China; 3. College of Pharmacy, Inner Mongolia Medical University, Hohhot 010059, China)

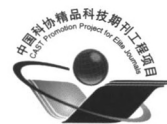
Identification of *Astragalus* and its adulterants was studied based on ITS2 sequence and secondary structure. With the addition of secondary structure information, the constructed phylogenetic tree not only contains all the conclusions based on the primary structure, but also solves the comb topological structure, at the same time, the distinguish ability and approval rating were also improved.





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