

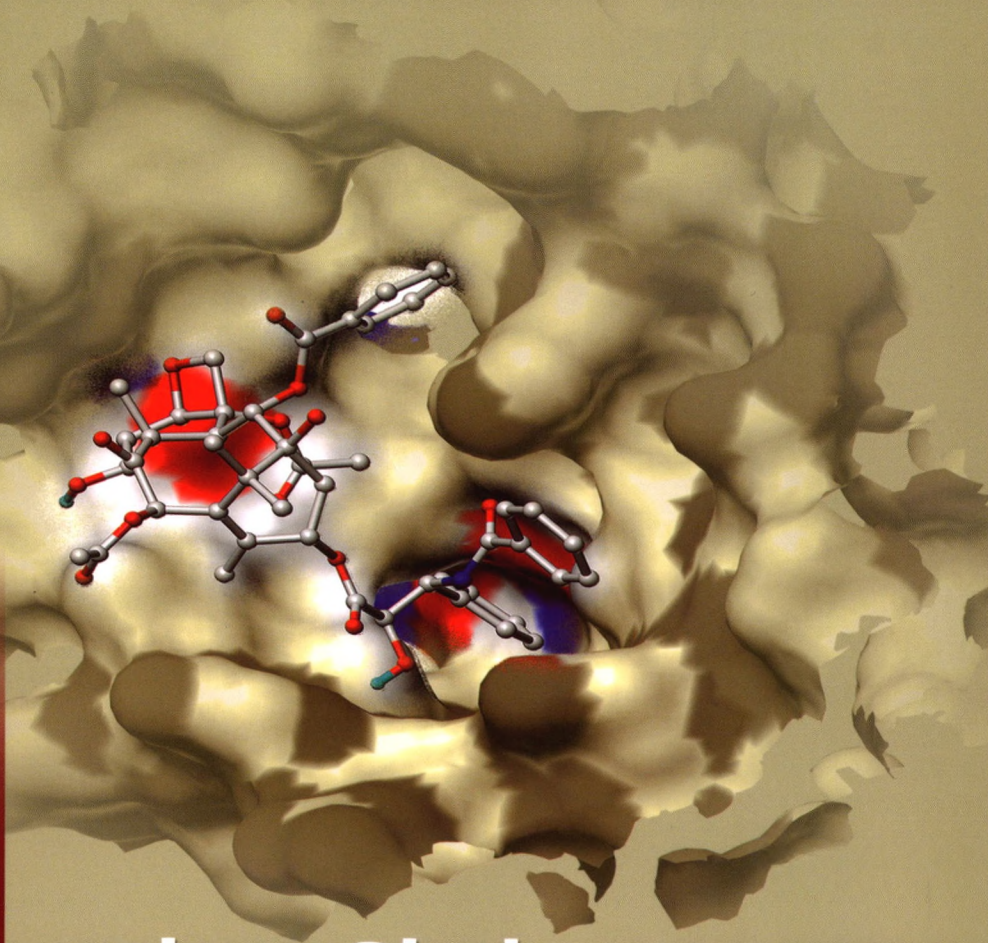


# 药 学 学 报

第56卷 第6期

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### 专家论坛

张 芳, 王晓良

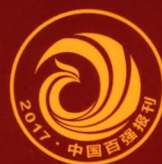
血液载脂蛋白作为神经退行性疾病  
潜在生物标志物的研究

万方数据

### 研究论文

徐 凡, 傅继华等

肾脏5-羟色胺合成和降解在高血糖  
诱导肾损伤时的作用研究



中国药学会  
中国医学科学院药物研究所

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第 56 卷 第 6 期 2021 年 6 月

图 文 摘 要

## 专家论坛

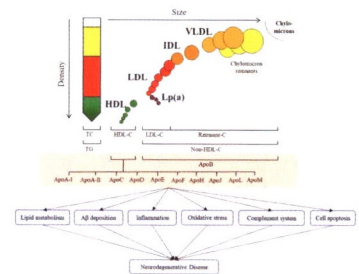
1513

### 血液载脂蛋白作为神经退行性疾病潜在生物标志物的研究

张芳, 王晓良\*

(中国医学科学院、北京协和医学院药物研究所, 北京 100050)

脂蛋白主要由血脂和载脂蛋白构成。载脂蛋白通过影响脂质代谢、A $\beta$ 聚集、氧化应激、补体系统和细胞凋亡等过程, 参与神经退行性疾病 (ND) 的发生发展。本篇综述主要探讨 ND 患者与非 ND 的对照组相比, 血液中哪些载脂蛋白发生变化, 以及这些发生变化的载脂蛋白能否作为神经退行性疾病的血液生物标志物。



## 综述

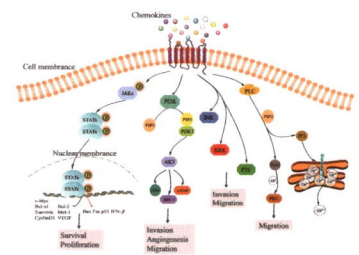
1521

### 趋化因子及其受体在乳腺癌中的研究进展

王婉玉, 吕晓希, 胡卓伟, 刘姗姗\*

(中国医学科学院、北京协和医学院药物研究所, 天然药物活性物质与功能国家重点实验室, 北京 100050)

趋化因子与受体结合后通过 JAK/STATs、PI3K/AKT、MAPK 和 PLC 等多种信号通路发挥其促肿瘤作用, 靶向抑制趋化因子及其受体, 或阻断趋化因子发挥作用的信号途径很可能成为治疗乳腺癌的新策略。



1532

### Torpor 发生机制最新研究进展

朱子玉, 姜剑伟, 张建军\*

(中国医学科学院、北京协和医学院药物研究所, 新药作用机制研究和药效评价北京市重点实验室, 北京 100050)

本文主要从 adcyap 神经元、瘦素、QRFP 神经元和交感神经系统等四方面就调控 torpor 状态发生的具体机制进行总结, 旨在为 torpor 发生机制的进一步研究提供思路。



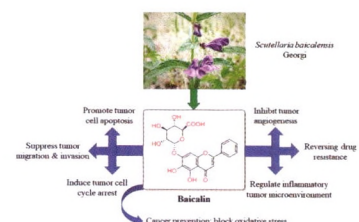
1537

### 黄芩苷的抗肿瘤作用研究进展

孔邦彦, 魏立彬, 郭青龙\*

(中国药科大学基础医学与临床药学学院, 江苏 南京 211198)

本文概述了国内外对黄芩苷抗肿瘤药理作用及机制的研究进展, 为黄芩苷的深入研究提供依据。



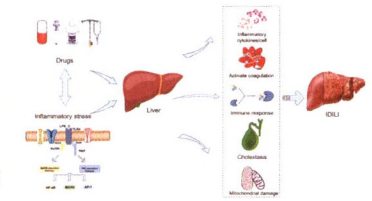
1544

炎症应激条件下特异质药物性肝损伤发生机制研究进展

蒋欣<sup>1</sup>, 李丹<sup>2</sup>, 斯陆勤<sup>1</sup>, 龚卫静<sup>3,4</sup>, 伍三兰<sup>3,4\*</sup>, 黄建耿<sup>1</sup>

(1. 华中科技大学同济医学院药学院, 湖北 武汉 430030; 2. 深圳大学总医院, 广东 深圳 518000; 3. 华中科技大学同济医学院附属协和医院药学部, 湖北 武汉 430022; 4. 湖北省重大疾病精准用药临床医学研究中心, 湖北 武汉 430022)

药物与炎症相互作用影响炎症细胞因子、凝血系统、代谢物活性、胆汁淤积以及线粒体损伤等多种机制, 介导特异质药物性肝损伤 (IDILI) 的发生。



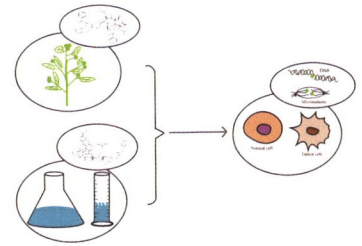
1551

传统抗肿瘤药物的临床应用现状与发展

徐焦<sup>1</sup>, 蒙凌华<sup>2</sup>, 卿晨<sup>1\*</sup>

(1. 昆明医科大学, 云南 昆明 650500; 2. 中国科学院上海药物研究所, 上海 201203)

传统抗肿瘤药物是肿瘤治疗的基石, 基于生物标志物的个性化治疗和不同方式之间的联合用药将进一步扩大细胞毒化疗药物的应用。



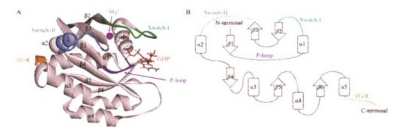
1562

KRAS 抑制剂的研 究进展

许俨钊, 文辉, 崔华清\*

(中国医学科学院、北京协和医学院药物研究所, 活性物质发现与适药化研究北京市重点实验室, 北京 100050)

本文主要介绍了 KRAS 抑制剂的研 究进展, 并根据作用模式进行分类总结。



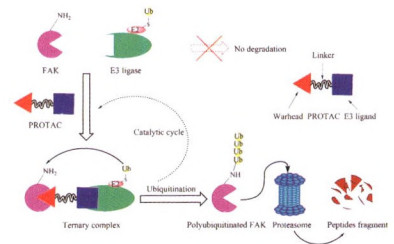
1571

基于 PROTAC 技术靶向降解 FAK 蛋白的研究进展

徐颖若, 张沁松, 吴菁艺, 鲍润菲, 曾申昕\*

(杭州医学院药学院, 浙江 杭州 310053)

PROTAC 技术是一种新兴的药物研 发策略, 快速、可逆选择性的降解 FAK 蛋白为研 究 FAK 靶点的成药性及相关药物的研 发提供新方法。



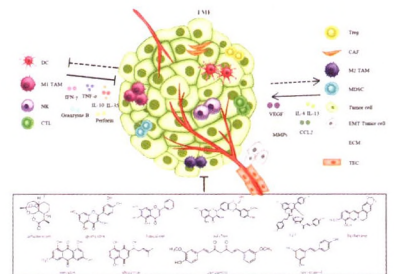
1580

天然产物靶向肿瘤微环境的研究进展

李玲, 汪哲, 谭宁华\*

(中国药科大学中药学院, 江苏 南京 211198)

天然产物靶向肿瘤微环境。



1591

烷基糖苷类吸收促进剂在药物递送系统中的应用与展望

李先福, 张志伟, 洪晓轩, 韩晓璐, 李蒙, 王增明\*, 郑爱萍\*

(军事科学院军事医学研 究院毒物药物研 究所, 北京 100850)

跨膜障碍是药物递送的难点。烷基糖苷可高效安全地解决这一问题, 具有广阔的应用前景。



## 研究论文

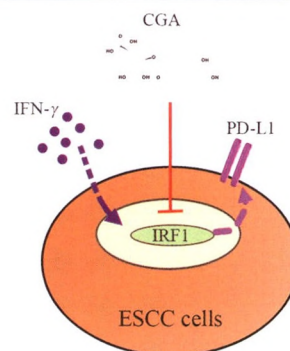
1599

### 绿原酸通过 IFN- $\gamma$ 信号通路抑制食管癌细胞中 PD-L1 的表达

詹芸, 李瑞, 李晓琳, 韩燕星, 蒋建东\*

(中国医学科学院、北京协和医学院药物研究所, 天然药物活性物质与功能国家重点实验室, 北京 100050)

IFN- $\gamma$  通过 IRF1 上调食管癌细胞中 PD-L1 的表达, 而绿原酸可以抑制这一过程。



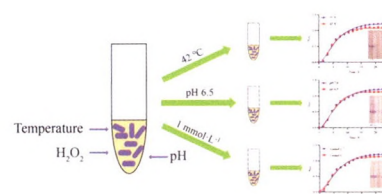
1606

### 温度、pH 值和 H<sub>2</sub>O<sub>2</sub> 对减毒沙门氏菌 VNP20009 的生长及生物膜形成的影响

李静<sup>1</sup>, 包斐斐<sup>1</sup>, 李家璜<sup>1,2,3\*</sup>, 华子春<sup>1,2,3\*</sup>

(1. 南京大学生命科学学院, 医药生物技术国家重点实验室, 江苏 南京 210023; 2. 中国药科大学生物药物学院, 江苏 南京 211198; 3. 常州南京大学高新技术研究院和江苏靶标生物医药研究所, 江苏 常州 213164)

本文研究了减毒沙门氏菌 VNP20009 在不同环境条件下的生长状态和生物膜形成, 为 VNP20009 的进一步改造及抗肿瘤应用提供理论指导。



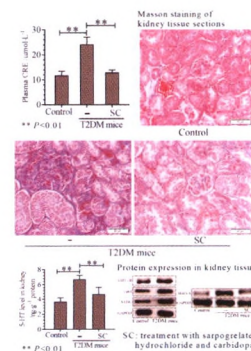
1612

### 肾脏 5-羟色胺合成和降解在高血糖诱导肾损伤时的作用研究

徐凡<sup>1#</sup>, 杨静<sup>1#</sup>, 金佳琦<sup>1</sup>, 张怡<sup>1</sup>, 梁秀睿<sup>1</sup>, 关晶<sup>1</sup>, 张誉馨<sup>1</sup>, 闪雪纯<sup>1</sup>, 张锐<sup>1</sup>, 赵希彤<sup>2</sup>, 郝宇轩<sup>3</sup>, 傅继华<sup>1\*</sup>

(1. 中国药科大学基础医学与临床药学学院, 江苏 南京 210009; 2. 中国药科大学中药学院, 江苏 南京 210009; 3. 中国药科大学药学院, 江苏 南京 210009)

糖尿病肾脏并发症致肾功能受损及肾小球病变, 主要原因是高血糖诱导了肾小球系膜细胞 5-HT<sub>2A</sub> 受体激活、5-HT 合成及降解增多。



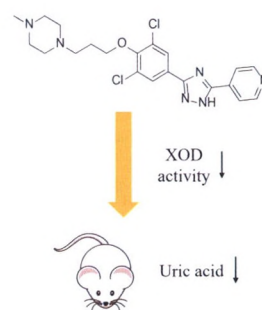
1621

### 基于靶点黄嘌呤氧化酶的化合物 CC18022 抗高尿酸血症作用的研究

李雪晨<sup>1#</sup>, 姜楠<sup>1#</sup>, 杨亚军<sup>2</sup>, 闫祯昕<sup>1</sup>, 张露<sup>2</sup>, 田金英<sup>1</sup>, 陈冬婷<sup>1</sup>, 肖志艳<sup>2</sup>, 叶菲<sup>1\*</sup>

(1. 中国医学科学院、北京协和医学院药物研究所, 新药作用机制研究与药效评价北京市重点实验室, 北京 100050; 2. 中国医学科学院、北京协和医学院药物研究所, 活性物质发现与适药化研究北京市重点实验室, 北京 100050)

化合物 CC18022 显著抑制黄嘌呤氧化酶活性并在高尿酸血症小鼠中发挥良好的降尿酸效果。



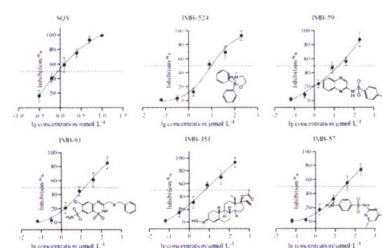
1627

### HIV-1 前体蛋白早成熟化小分子激活剂的筛选与评价

马铃<sup>1</sup>, 温佳佳<sup>1</sup>, 李晓宇<sup>1</sup>, 魏涛<sup>2\*</sup>, 岑山<sup>1\*</sup>

(1. 中国医学科学院、北京协和医学院医药生物技术研究所, 北京 100050; 2. 北京联合大学应用文理学院, 北京 100191)

本研究中的活性化合物可激活前体蛋白 Gag-Pol 中 HIV-1 蛋白酶, 诱导其早成熟化, 抑制 HIV-1 感染性, 为抗病毒药物的研发提供了思路。

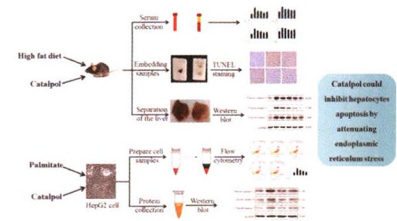


1634

**梓醇缓解内质网应激抑制非酒精性脂肪肝细胞凋亡**田香<sup>1,2</sup>, 熊琪<sup>1</sup>, 乐凯<sup>1</sup>, 周梅<sup>1</sup>, 林款<sup>1</sup>, 马宝苗<sup>1</sup>, 陈勇<sup>2\*</sup>, 茹琴<sup>1\*</sup>

(1. 江汉大学医学院, 武汉生物医学研究院, 湖北 武汉 430056; 2. 湖北大学中药生物技术省重点实验室, 药物高通量筛选技术国家地方联合工程研究中心, 湖北 武汉 430062)

梓醇能够通过缓解内质网应激抑制肝细胞凋亡, 从而发挥保护肝损伤的作用。

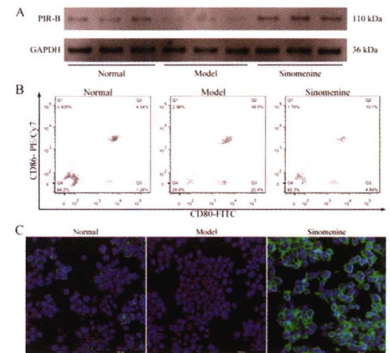


1644

**青藤碱增加配体免疫球蛋白受体 B 表达抑制巨噬细胞经典活化**卫智权<sup>1#</sup>, 包传红<sup>2#</sup>, 陈仪新<sup>2</sup>, 阎莉<sup>1\*</sup>

(1. 广西中医药大学, 广西高校壮医药基础与应用研究重点实验室, 广西 南宁 530001; 2. 广西中医药大学, 广西中药药效研究重点实验室, 广西 南宁 530200)

青藤碱可显著抑制巨噬细胞的经典活化, 其机制或许与其增强巨噬细胞 PIR-B 表达水平有关。

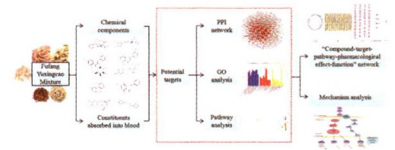


1653

**基于网络药理学的复方鱼腥草合剂清热解病毒效物质基础及作用机制研究**韩彦琪<sup>1,2#</sup>, 陈志霖<sup>3#</sup>, 刘耀晨<sup>4</sup>, 胡江宁<sup>5</sup>, 许浚<sup>1,2</sup>, 张洪兵<sup>1,2</sup>, 刘建庭<sup>1,2</sup>, 张杨<sup>1,2</sup>, 张铁军<sup>1,2\*</sup>, 刘昌孝<sup>1,2\*</sup>

(1. 天津市中药质量标志物重点实验室, 天津 300462; 2. 释药技术与药物代谢动力学国家重点实验室 (天津药物研究院), 天津 300462; 3. 浙江康恩贝中药有限公司, 浙江 丽水 323400; 4. 天津医科大学, 天津 300070; 5. 浙江康恩贝制药股份有限公司, 浙江 杭州 310052)

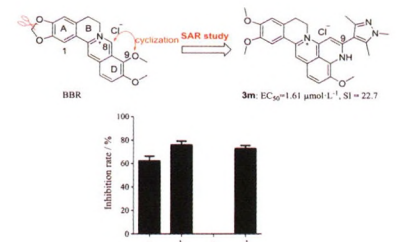
利用网络药理学方法整合体外细胞验证实验, 构建复方鱼腥草合剂“化合物-靶点-通路-药理作用-功效”网络图, 阐释其清热解病毒效的物质基础及网络调控机制。



1663

**N-环化小檗碱衍生物合成及抗 SARS-CoV-2 假病毒活性研究**范田运<sup>1</sup>, 吴佳静<sup>2</sup>, 李迎红<sup>1</sup>, 黄维金<sup>2</sup>, 郭茜茜<sup>1</sup>, 赵丽萍<sup>1</sup>, 汪燕翔<sup>1</sup>, 王佑春<sup>2</sup>, 宋丹青<sup>1\*</sup>

(1. 中国医学科学院、北京协和医学院医药生物技术研究所, 北京市抗感染重点实验室, 北京 100050; 2. 中国食品药品检定研究院, 北京 102629)

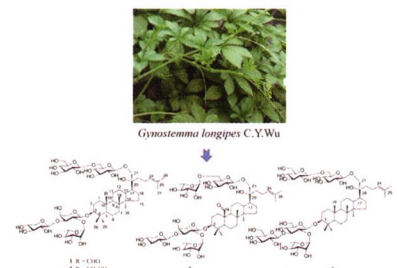
由小檗碱 (BBR) 衍生的化合物 **3m** 具有较强的抗 SARS-CoV-2 假病毒活性,  $EC_{50}$  值为  $1.61 \mu\text{mol}\cdot\text{L}^{-1}$ , SI 值为 22.2, 它可能是通过抑制吸附和膜融合等多种病毒入侵过程发挥抗病毒作用。

1670

**长梗绞股蓝中的四个新达玛烷型三萜皂苷**李齐<sup>1,2</sup>, 庞旭<sup>2</sup>, 卢彭信<sup>1,2</sup>, 张洁<sup>2</sup>, 张军<sup>3</sup>, 师东晓<sup>3</sup>, 马百平<sup>1,2\*</sup>

(1. 广东药科大学, 广东 广州 510060; 2. 军事科学院军事医学研究院辐射医学研究所, 北京 100850; 3. 安康正大制药有限公司, 陕西 安康 725000)

从长梗绞股蓝总皂苷大极性部位分离得到 4 个新的达玛烷型三萜皂苷。



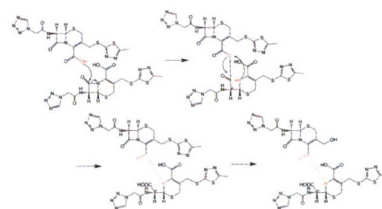
1677

**头孢唑林钠原料及制剂中的聚合物杂质研究**

张夏, 李进, 王晨, 刘颖, 姚尚辰, 尹利辉, 许明哲\*, 胡昌勤\*

(中国食品药品检定研究院, 国家药品监督管理局重点实验室化学药品质量研究与评价重点实验室, 北京 102629)

采用柱切换液相色谱-高分辨质谱联用法分析了 7 位侧链中不含活性基团氨基的头孢菌素—头孢唑林中的聚合物, 最终建立了最合理的聚合物检测方法。



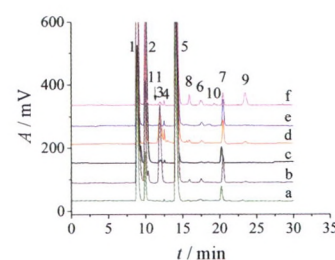
1683

**由硫酸卡那霉素注射液中杂质的变化探讨处方和灭菌工艺的合理性**

赵敬丹, 刘浩\*, 张含智

(上海市食品药品检验研究院, 上海 201203)

国内药品生产企业在处方筛选时应关注处方的合理性, 并特别关注药物和含活泼基团辅料的相容性, 确保产品的安全性。



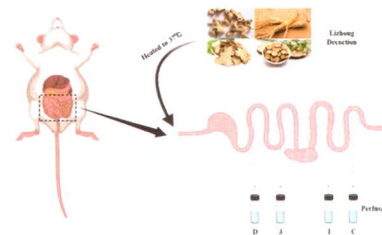
1689

**理中汤提取物中 5 种主要活性成分在体肠吸收特征研究**

万悦, 申雨檬, 邹俊凤, 陈孟君, 张智苗, 江曙\*, 钱大玮, 段金璇

(南京中医药大学, 江苏省中药资源产业化过程协同创新中心, 江苏 南京 210023)

通过建立大鼠在体单向肠灌流模型, 评价理中汤提取物中 5 种主要活性成分的吸收特点, 为理中汤口服给药剂型的改进和进一步开发提供一定的科学依据。



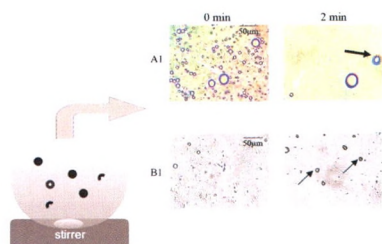
1696

**十一酸睾酮III型脂质制剂体外脂解过程及机制研究**

王雅蒙#, 邹丹璐#, 李钰, 柯学\*

(中国药科大学药学院, 江苏省纳米药物制备与生物学评价公共服务中心, 江苏 南京 210009)

利用体外脂解模型研究发现III型脂质制剂的油相含量、乳化剂种类及比例综合影响其体外脂解速率及程度。



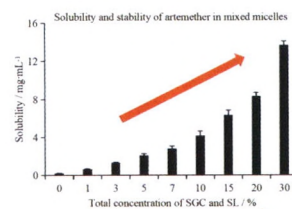
1704

**载蒿甲醚甘氨酸钠/大豆磷脂混合胶束的制备与稳定性评价**

肖光清<sup>1,2,3</sup>, 伍丽<sup>1</sup>, 熊婷<sup>1,2</sup>, 李海燕<sup>1</sup>, 朱卫丰<sup>2</sup>, 李东勳<sup>2</sup>, 张继稳<sup>1,2\*</sup>

(1. 中国科学院上海药物研究所, 上海 201203; 2. 江西中医药大学, 现代中药制剂教育部重点实验室, 江西 南昌 330004; 3. 广东省食品药品职业技术学校, 广东 广州 510663)

薄膜分散法制备的甘氨酸钠/大豆磷脂混合胶束可显著增加蒿甲醚的溶解度并提高蒿甲醚的稳定性。



ARM-loaded MM after storage for two months at 25°C

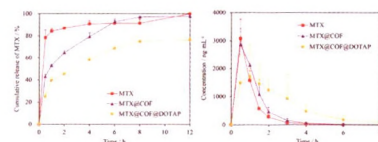
1712

## 交联环糊精金属有机骨架负载甲氨蝶呤缓释微粒的制备及体内外评价

王勤<sup>1,2</sup>, 王彩芬<sup>2</sup>, 伍丽<sup>2</sup>, 陈晓锦<sup>1,2</sup>, 孙宏宇<sup>2</sup>, 桂双英<sup>1</sup>, 张继稳<sup>1,2\*</sup>

(1. 安徽中医药大学, 安徽 合肥 230012; 2. 中国科学院上海药物研究所, 上海 201210)

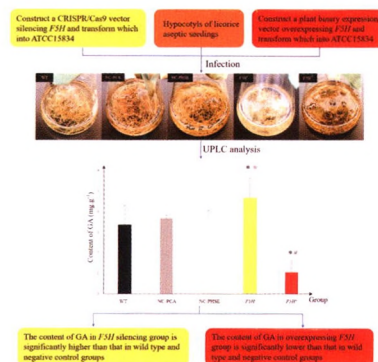
经阳离子脂质材料 (2,3-二油酰基-丙基)-三甲胺 (DOTAP) 包裹的 MTX@COF 载药微粒可延缓甲氨蝶呤的体内外释药。



1719

基于基因过表达及基因沉默解析 *F5H* 基因对甘草酸生物合成的调控研究张智新<sup>1</sup>, 汪逗逗<sup>1</sup>, 杨林<sup>1</sup>, 田少凯<sup>1</sup>, 肖瑶<sup>2\*</sup>, 刘颖<sup>1\*</sup>

(1. 北京中医药大学生命科学院, 北京 102488; 2. 北京中医药大学中药学院, 北京 102488)

通过基因过表达和沉默两个方面验证 *F5H* 基因对甘草酸生物合成的调控。

1727

## 重组人源葡萄糖醛酸转移酶表达系统的构建及应用

陈赅, 解可波\*, 陈日道, 陈大伟, 刘继梅, 韩耀天, 刘雨雨, 戴均贵\*

(中国医学科学院、北京协和医学院药物研究所, 中国医学科学院酶与天然药物生物催化重点实验室, 创新药物非临床药物代谢及 PK/PD 研究北京市重点实验室, 卫健委天然药物生物合成重点实验室, 天然药物活性物质与功能国家重点实验室, 北京 100050)

成功构建了人源葡萄糖醛酸转移酶的酿酒酵母和杆状病毒感染的昆虫细胞表达系统, 首次实现了药物葡萄糖醛酸化代谢产物的毫克级规模制备。



## 新药论坛

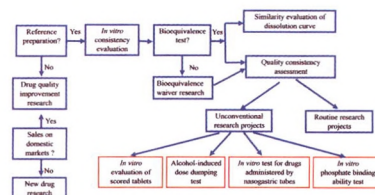
1739

## 口服固体仿制药体外一致性评价中的非常规研究及常见问题解析

赵娜, 石靖\*

(国家药品监督管理局药品审评中心, 北京 100022)

本文根据体外一致性评价的决策树, 论述了不同情况下体外研究项目的差异, 重点分析了非常规研究项目的关注点。



## 新药发现与研究实例简析

1745

## 首创的选择性雌激素受体调节剂他莫昔芬

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)

# ACTA PHARMACEUTICA SINICA

Volume 56 Number 6 2021 June

## Graphical Abstracts

### Professionals Forum

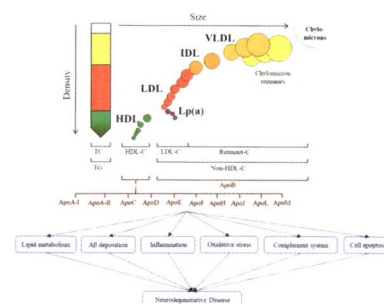
1513

#### Study on blood apolipoprotein as a potential biomarker of neurodegenerative diseases

ZHANG Fang, WANG Xiao-liang\*

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

Lipoproteins are mainly composed of blood lipids and apolipoproteins. Apolipoproteins participate in the occurrence and development of neurodegenerative disease (ND) by affecting lipid metabolism,  $A\beta$  deposition, oxidative stress, complement system, and cell apoptosis. This review mainly explores which apolipoproteins in the blood have changed in patients with neurodegenerative diseases compared with non-ND control groups, and whether these changed apolipoproteins can be used as blood biomarkers for neurodegenerative diseases.



### Reviews

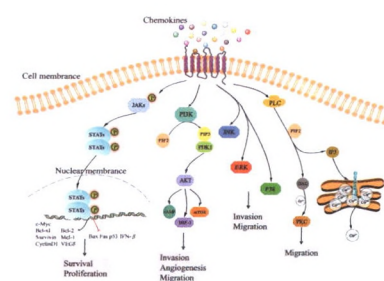
1521

#### Research progress of chemokines and their receptors in breast cancer

WANG Wan-yu, LÜ Xiao-xi, HU Zhuo-wei, LIU Shan-shan\*

(State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)

Chemokine-receptor interaction exerts the tumor-promoting effect through a variety of signaling pathways, such as JAK/STATs, PI3K/AKT, MAPK, and PLC. Targeting chemokines and chemokine receptors, or blocking chemokine signalings may become a new strategy for the treatment of breast cancer.



1532

#### The latest research progress of torpor occurrence mechanism

ZHU Zi-yu, JIANG Jian-wei, ZHANG Jian-jun\*

(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)

This article summarizes the specific mechanisms regulating the occurrence of torpor from four aspects: adcyap neurons, leptin, QRFP neurons, and sympathetic nervous system, aiming to provide ideas for further research on the mechanism of torpor.





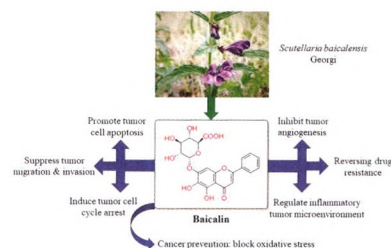
1537

**Progress in antitumor activity of baicalin**

KONG Bang-yan, WEI li-bin, GUO Qing-long\*

*(School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, Nanjing 211198, China)*

This article reviewed the research progress of baicalin on its antitumor pharmacology and possible mechanisms at home and abroad, and provided the basis for its further research.

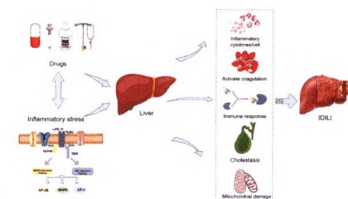


1544

**Research progress in mechanisms of idiosyncratic drug-induced liver injury mediated by inflammatory stress**JIANG Xin<sup>1</sup>, LI Dan<sup>2</sup>, SI Lu-qin<sup>1</sup>, GONG Wei-jing<sup>3,4</sup>, WU San-lan<sup>3,4\*</sup>, HUANG Jian-geng<sup>1</sup>

*(1. School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China; 2. Shenzhen University General Hospital, Shenzhen 518000, China; 3. Department of Pharmacy, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China; 4. Hubei Province Clinical Research Center for Precision Medicine for Critical Illness, Wuhan 430022, China)*

Drugs interact with inflammation and mediate the occurrence of idiosyncratic drug-induced liver injury (IDILI) through a variety of mechanisms, which can affect the production of inflammatory cytokines, coagulation system, the activity of metabolites, cholestasis, mitochondrial damage, and others.

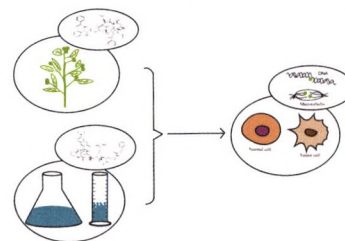


1551

**The clinical application and development of traditional antitumor drugs**XU Jiao<sup>1</sup>, MENG Ling-hua<sup>2</sup>, QING Chen<sup>1\*</sup>

*(1. Kunming Medical University, Kunming 650500, China; 2. Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China)*

Traditional antitumor drugs are the cornerstone of tumor therapy. Personalized therapy based on biomarkers and combination of different methods will further expand the application of cytotoxic chemotherapy drugs.



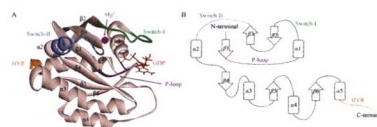
1562

**Research progress of KRAS inhibitors**

XU Yan-zhao, WEN Hui, CUI Hua-qing\*

*(Beijing Key Laboratory of Active Substance Discovery and Druggability Evaluation, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)*

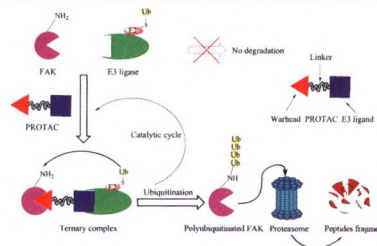
KRAS inhibitors were introduced and classified according to the mode of action in this review.



1571

**Recent progress in targeting degradation of FAK based on PROTAC**XU Ying-ruo, ZHANG Qin-song, WU Jing-yi, BAO Run-fei, ZENG Shen-xin\*  
*(College of Pharmacy, Hangzhou Medical College, Hangzhou 310053, China)*

PROTAC technology is an emerging strategy for drug development, which rapid and reversible for selectively degrading FAK provides a novel method for studying the druggability and corresponding drug discovery of FAK.



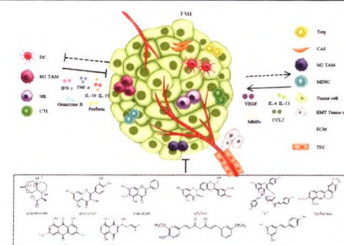
1580

**Advances in natural products that target the tumor microenvironment**

LI Ling, WANG Zhe, TAN Ning-hua\*

*(School of Traditional Chinese Pharmacy, China Pharmaceutical University, Nanjing 211198, China)*

Natural products targeting tumor microenvironment.



1591

**Application and prospect of alkyl polyglycosides absorption enhancers in drug delivery system**

LI Xian-fu, ZHANG Zhi-wei, HONG Xiao-xuan, HAN Xiao-lu, LI Meng, WANG Zeng-ming\*, ZHENG Ai-ping\*

(Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences, Academy of Military Sciences, Beijing 100850, China)



Transmembrane barrier is a difficult problem in drug delivery. Alkyl polyglycoside can solve this problem efficiently and safely, and have a broad application prospect.

**Original Articles**

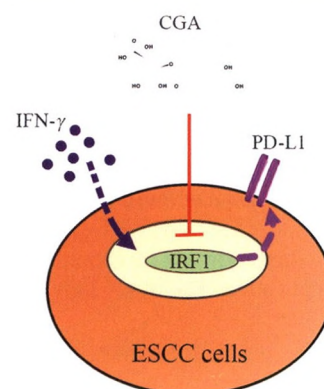
1599

**Chlorogenic acid down-regulates the expression of PD-L1 in esophageal squamous cell carcinoma via IFN-γ signaling pathway**

ZHAN Yun, LI Rui, LI Xiao-lin, HAN Yan-xing, JIANG Jian-dong\*

(State Key Laboratory of Bioactive Substances and Function of Natural Medicine, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)

IFN-γ up-regulates the expression of PD-L1 in ESCC cells via IRF1, which can be suppressed by chlorogenic acid (CGA).

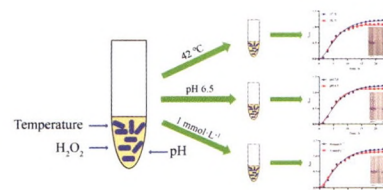


1606

**Effects of temperature, pH, and H<sub>2</sub>O<sub>2</sub> on the growth and biofilm formation of attenuated *Salmonella* VNP20009**

LI Jing<sup>1</sup>, BAO Fei-fei<sup>1</sup>, LI Jia-huang<sup>1,2,3\*</sup>, HUA Zi-chun<sup>1,2,3\*</sup>

(1. State Key Laboratory of Pharmaceutical Biotechnology, School of Life Sciences, Nanjing University, Nanjing 210023, China; 2. College of Biopharmaceuticals, China Pharmaceutical University, Nanjing 211198, China; 3. High-Tech Research Institute of Nanjing University at Changzhou and Jiangsu Target Pharma Laboratories Inc., Changzhou 213164, China)



This study has discovered the growth characteristics and formation of bacterial biofilm of attenuated *Salmonella* VNP20009 under various environmental stresses. The results provide theoretical guidance for the in-depth modification and further anti-tumor application of VNP20009.

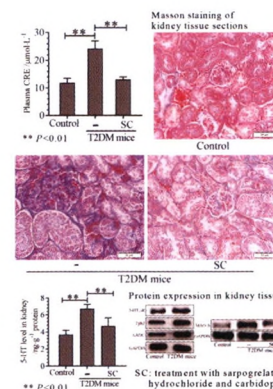
1612

**The role of renal 5-hydroxytryptamine synthesis and degradation in hyperglycemia-induced kidney injury**

XU Fan<sup>1#</sup>, YANG Jing<sup>1#</sup>, JIN Jia-qi<sup>1</sup>, ZHANG Yi<sup>1</sup>, LIANG Xiu-rui<sup>1</sup>, GUAN Jing<sup>1</sup>, ZHANG Yu-xin<sup>1</sup>, SHAN Xue-chun<sup>1</sup>, ZHANG Rui<sup>1</sup>, ZHAO Xi-tong<sup>2</sup>, HAO Yu-xuan<sup>3</sup>, FU Ji-hua<sup>1\*</sup>

(1. School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, Nanjing 210009, China; 2. School of Chinese Materia Medica, China Pharmaceutical University, Nanjing 210009, China; 3. School of Pharmacy, China Pharmaceutical University, Nanjing 210009, China)

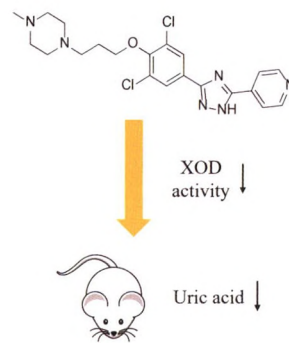
Diabetic complications in kidney leading to abnormal renal function and glomerular lesions, is mainly due to hyperglycemia-induced the activation of 5-HT<sub>2A</sub> receptor and increase of 5-HT synthesis and degradation.



1621

**The anti-hyperuricemic effects of compound CC18022 targeting xanthine oxidase**LI Xue-chen<sup>1#</sup>, JIANG Nan<sup>1#</sup>, YANG Ya-jun<sup>2</sup>, YAN Zhen-xin<sup>1</sup>, ZHANG Lu<sup>2</sup>,  
TIAN Jin-ying<sup>1</sup>, CHEN Dong-ting<sup>1</sup>, XIAO Zhi-yan<sup>2</sup>, YE Fei<sup>1\*</sup>*(1. 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; 2. Beijing Key Laboratory of Active Substance Discovery and Druggability Evaluation, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)*

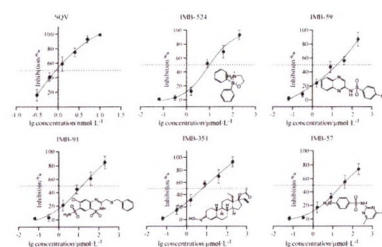
Compound CC18022 significantly inhibited xanthine oxidase activity and exhibited favorable serum uric acid-lowering effect in hyperuricemic mice.



1627

**Screening and evaluation of small molecule activators for premature activation of HIV-1 precursors**MA Ling<sup>1</sup>, WEN Jia-jia<sup>1</sup>, LI Xiao-yu<sup>1</sup>, WEI Tao<sup>2\*</sup>, CEN Shan<sup>1\*</sup>*(1. Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China; 2. College of Applied Arts and Science of Beijing Union University, Beijing 100191, China)*

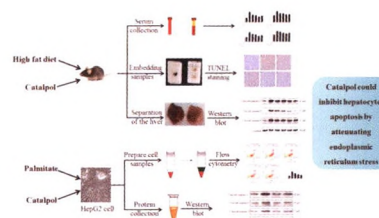
In this study, the compounds are able to activate HIV-1 PR and inhibit HIV-1 replication. This study provides ideas for the research and development of antiviral drugs.



1634

**Catalpol inhibits cell apoptosis through alleviating endoplasmic reticulum stress in nonalcoholic fatty liver disease**TIAN Xiang<sup>1,2</sup>, XIONG Qi<sup>1</sup>, YUE Kai<sup>1</sup>, ZHOU Mei<sup>1</sup>, LIN Kuan<sup>1</sup>, MA Bao-miao<sup>1</sup>,  
CHEN Yong<sup>2\*</sup>, RU Qin<sup>1\*</sup>*(1. Wuhan Institute of Biomedical Sciences, School of Medicine, Jiangnan University, Wuhan 430056, China; 2. Hubei Province Key Laboratory of Biotechnology of Chinese Traditional Medicine, National and Local Joint Engineering Research Center of High-throughput Drug Screening Technology, Hubei University, Wuhan 430062, China)*

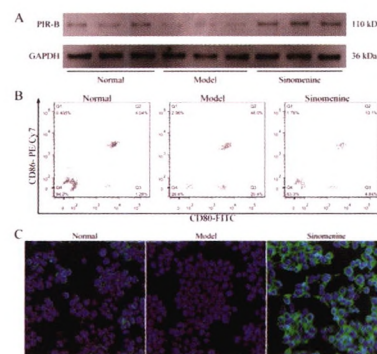
Catalpol could inhibit hepatocytes apoptosis and had a significant protective effect on liver injury, and its mechanism might be related to the relief of endoplasmic reticulum stress.



1644

**Sinomenine promotes paired immunoglobulin-like receptor B expression to restrain macrophage classic activation**WEI Zhi-quan<sup>1#</sup>, BAO Chuan-hong<sup>2#</sup>, CHEN Yi-xin<sup>2</sup>, YAN Li<sup>1\*</sup>*(1. Guangxi University Key Laboratory of Basic and Applied Research on Zhuang Medical Prescriptions, Guangxi Traditional Chinese Medicine University, Nanning 530001, China; 2. Guangxi Key Laboratory of Efficacy Study on Chinese Materia Medica, Guangxi Traditional Chinese Medicine University, Nanning 530200, China)*

Sinomenine can significantly inhibit the classical activation of macrophages, and its mechanism may be related to its enhanced PIR-B expression level of macrophages.

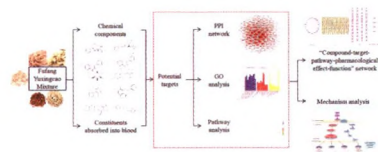


1653

### Pharmacodynamic material basis and mechanism of Fufang Yuxingcao Mixture for the treatment of heat-clearing and detoxification based on network pharmacology

HAN Yan-qi<sup>1,2#</sup>, CHEN Zhi-lin<sup>3#</sup>, LIU Yao-chen<sup>4</sup>, HU Jiang-ning<sup>5</sup>, XU Jun<sup>1,2</sup>, ZHANG Hong-bing<sup>1,2</sup>, LIU Jian-ting<sup>1,2</sup>, ZHANG Yang<sup>1,2</sup>, ZHANG Tie-jun<sup>1,2\*</sup>, LIU Chang-xiao<sup>1,2\*</sup>

(1. Tianjin Key Laboratory of Quality Marker of Traditional Chinese Medicine, Tianjin 300462, China; 2. State Key Laboratory of Drug Delivery and Pharmacokinetics, Tianjin Institute of Pharmaceutical Research, Tianjin 300462, China; 3. Zhejiang CONBA Chinese Medicine Co., LTD., Lishui 323400, China; 4. Tianjin Medical University, Tianjin 300070, China; 5. Zhejiang CONBA Pharmaceutical Co., LTD., Hangzhou 310052, China)



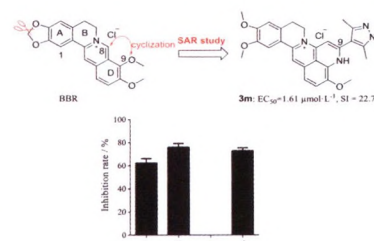
“Compound-target-pathway-pharmacological action-effect” network of Fufang Yuxingcao Mixture (FYM) was established by network pharmacology integrated with cell validation assay to explain the pharmacodynamic material basis and network regulation mechanism of FYM for the treatment of heat-clearing and detoxification.

1663

### Synthesis and evaluation of *N*-cycloberberine derivatives as a novel class of anti-SARS-CoV-2 pseudovirus agents

FAN Tian-yun<sup>1</sup>, WU Jia-jing<sup>2</sup>, LI Ying-hong<sup>1</sup>, HUANG Wei-jin<sup>2</sup>, GUO Xi-xi<sup>1</sup>, ZHAO Li-ping<sup>1</sup>, WANG Yan-xiang<sup>1</sup>, WANG You-chun<sup>2</sup>, SONG Dan-qing<sup>1\*</sup>

(1. Beijing Key Laboratory of Antimicrobial Agents, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China; 2. National Institute for Food and Drug Control, Beijing 102629, China)



Compound **3m**, derived from berberine (BBR), showed potent activity against SARS-CoV-2 pseudovirus with EC<sub>50</sub> value of 1.61 μmol·L<sup>-1</sup> and SI value of 22.2, might act by of inhibiting multiple process of viral invasion, including adsorption and membrane fusion.

1670

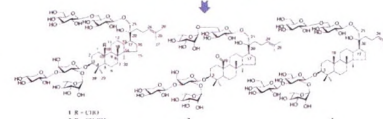
### Four new dammarane-type triterpenoid saponins from *Gynostemma longipes* C.Y.Wu

LI Qi<sup>1,2</sup>, PANG Xu<sup>2</sup>, LU Peng-xin<sup>1,2</sup>, ZHANG Jie<sup>2</sup>, ZHANG Jun<sup>3</sup>, SHI Dong-xiao<sup>3</sup>, MA Bai-ping<sup>1,2\*</sup>

(1. Guangdong Pharmaceutical University, Guangzhou 510060, China; 2. Institute of Radiation Medicine, Academy of Military Medical Science, Academy of Military Sciences, Beijing 100850, China; 3. AnKang Chia Tai Pharmaceutical Co. Ltd., Ankang 725000, China)



*Gynostemma longipes* C.Y.Wu



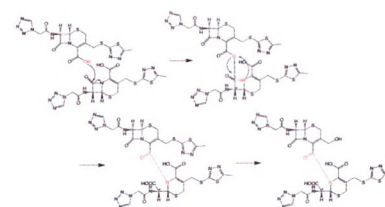
Four new dammarane-type triterpenoid saponins were isolated from the polar part of total saponins of *G. longipes*.

1677

### Research on polymer impurities in cefazolin sodium raw materials and products

ZHANG Xia, LI Jin, WANG Chen, LIU Ying, YAO Shang-chen, YIN Li-hui, XU Ming-zhe\*, HU Chang-qin\*

(Key Laboratory of State Drug Administration-Key Laboratory of Research and Evaluation of Chemical Drug Quality, National Institutes for Food and Drug Control, Beijing 102629, China)



This study analyzed the polymers in cefazolin, which does not contain the active amino groups at the C-7 side chain, and finally developed the most suitable analysis method for controlling polymers in cefazolin.

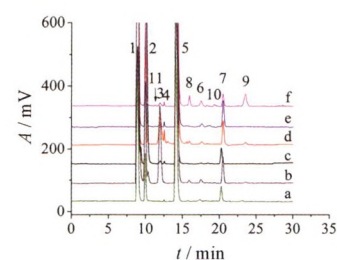
1683

**Formulation and sterilization assessment of kanamycin sulfate injection based on impurity profiles**

ZHAO Jing-dan, LIU Hao\*, ZHANG Han-zhi

*(Shanghai Institute for Food and Drug Control, Shanghai 201203, China)*

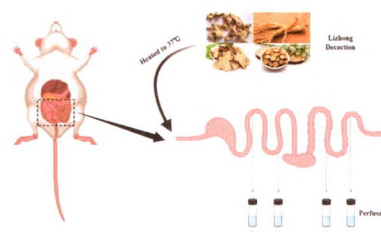
Attention should be paid on formula optimization in domestic factory, especially when the active pharmaceutical ingredients with primary amine group, which is crucial to the safety and efficacy of the preparations.



1689

**The intestinal absorption characteristics of five active components in Lizhong Decoction**

WAN Yue, SHEN Yu-meng, ZOU Jun-feng, CHEN Meng-jun, ZHANG Zhi-miao, JIANG Shu\*, QIAN Da-wei, DUAN Jin-ao

*(Jiangsu Collaborative Innovation Center of Chinese Medicinal Resources Industrialization, Nanjing University of Chinese Medicine, Nanjing 210023, China)*

The intestinal absorption properties of five effective components in Lizhong decoction (LZD) extracts were investigated by *in situ* single-pass intestinal perfusion model in rats, which provided a scientific basis for the improvement and further development of oral administration of LZD.

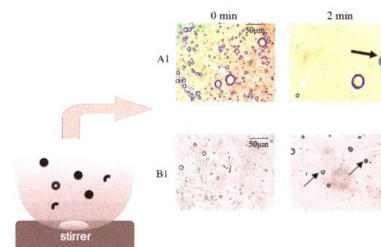
1696

***In vitro* lipolysis process and lipolysis mechanism of testosterone undecanoate type III lipid formulations**

WANG Ya-meng#, ZOU Dan-lu#, LI Yu, KE Xue\*

*(School of Pharmacy, China Pharmaceutical University, Jiangsu Public Technical Service Center for Nanometer Drug Preparation and Biological Evaluation, Nanjing 210009, China)*

By using the *in vitro* lipolysis model, the study found that the lipolysis rate and extent of type III lipid formulations are greatly influenced by the proportion of oil phase and surfactant, and the surfactant structure.

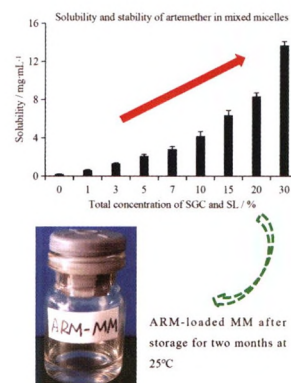


1704

**Preparation and stability evaluation of artemether-loaded mixed micelles composed of the sodium glycocholate and soybean lecithin**XIAO Guang-qing<sup>1,2,3</sup>, WU Li<sup>1</sup>, XIONG Ting<sup>1,2</sup>, LI Hai-yan<sup>1</sup>, ZHU Wei-feng<sup>2</sup>, LI Dong-xun<sup>2</sup>, ZHANG Ji-wen<sup>1,2\*</sup>

*(1. Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China; 2. Key laboratory of Modern Preparation Chinese Materia Medica of Ministry of Education, Jiangxi University of Chinese Medicine, Nanchang 330004, China; 3. Guangdong Food and Drug Vocational-Technical School, Guangzhou 510663, China)*

Obvious enhancement of solubility of artemether with an enhancement of its stability in mixed micelles composed of the sodium glycocholate and soybean lecithin prepared by film dispersion method.

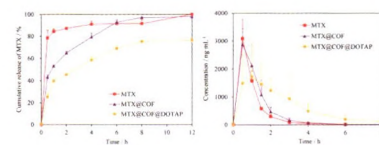


1712

**Preparation and evaluation of methotrexate sustained-release particles using crosslinked cyclodextrin metal-organic frameworks**

WANG Qin<sup>1,2</sup>, WANG Cai-fen<sup>2</sup>, WU Li<sup>2</sup>, CHEN Xiao-jin<sup>1,2</sup>, SUN Hong-yu<sup>2</sup>, GUI Shuang-ying<sup>1</sup>, ZHANG Ji-wen<sup>1,2\*</sup>

(1. Anhui University of Chinese Medicine, Hefei 230012, China; 2. Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201210, China)



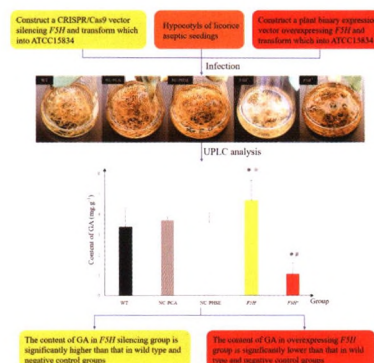
Methotrexate loaded crosslinked cyclodextrin metal-organic framework (COF) particles coated with (2,3-dioleoyl-propyl)-trimethylamine (DOTAP) delayed the *in vitro* and *in vivo* release kinetics.

1719

**Ferulate 5-hydroxylase gene (F5H) regulation of glycyrrhizic acid biosynthesis determined by gene overexpression and knockout**

ZHANG Zhi-xin<sup>1</sup>, WANG Dou-dou<sup>1</sup>, YANG Lin<sup>1</sup>, TIAN Shao-kai<sup>1</sup>, XIAO Yao<sup>2\*</sup>, LIU Ying<sup>1\*</sup>

(1. School of Life Sciences, Beijing University of Chinese Medicine, Beijing 102488, China; 2. School of Chinese Pharmacy, Beijing University of Chinese Medicine, Beijing 102488, China)



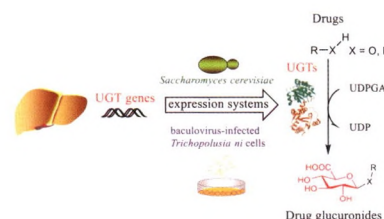
Verification of the regulation of *F5H* on glycyrrhizic acid (GA) biosynthesis through gene overexpressing and knockout.

1727

**Construction and application of recombinant human UDP-glucuronosyltransferases expression systems**

CHEN Yun, XIE Ke-bo\*, CHEN Ri-dao, CHEN Da-wei, LIU Ji-mei, HAN Yao-tian, LIU Yu-yu, DAI Jun-gui\*

(CAMS Key Laboratory of Enzymes and Natural Drug Biocatalysis, Beijing Key Laboratory of Non-Clinical Drug Metabolism and PK/PD Study, NHC Key Laboratory of Natural Drug Biosynthesis, State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing 100050, China)



The human UDP-glucuronosyltransferases expression systems of *Saccharomyces cerevisiae* and baculovirus-infected *Trichoplusia ni* cells were successfully constructed, and used for milligram-scale synthesis of drug glucuronide metabolites for the first time.

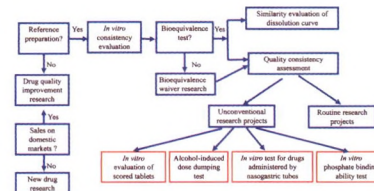
**New Drug Forum**

1739

**The analysis of unconventional research projects and common problems in the *in vitro* consistency evaluation of oral solid generic drugs**

ZHAO Na, SHI Jing\*

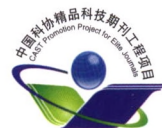
(Center for Drug Evaluation, National Medical Products Administration, Beijing 100022, China)



Based on the decision tree of *in vitro* consistency evaluation, this article discussed the differences of *in vitro* evaluation research projects under different conditions, and selective analyzed the concerns of unconventional research projects.

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