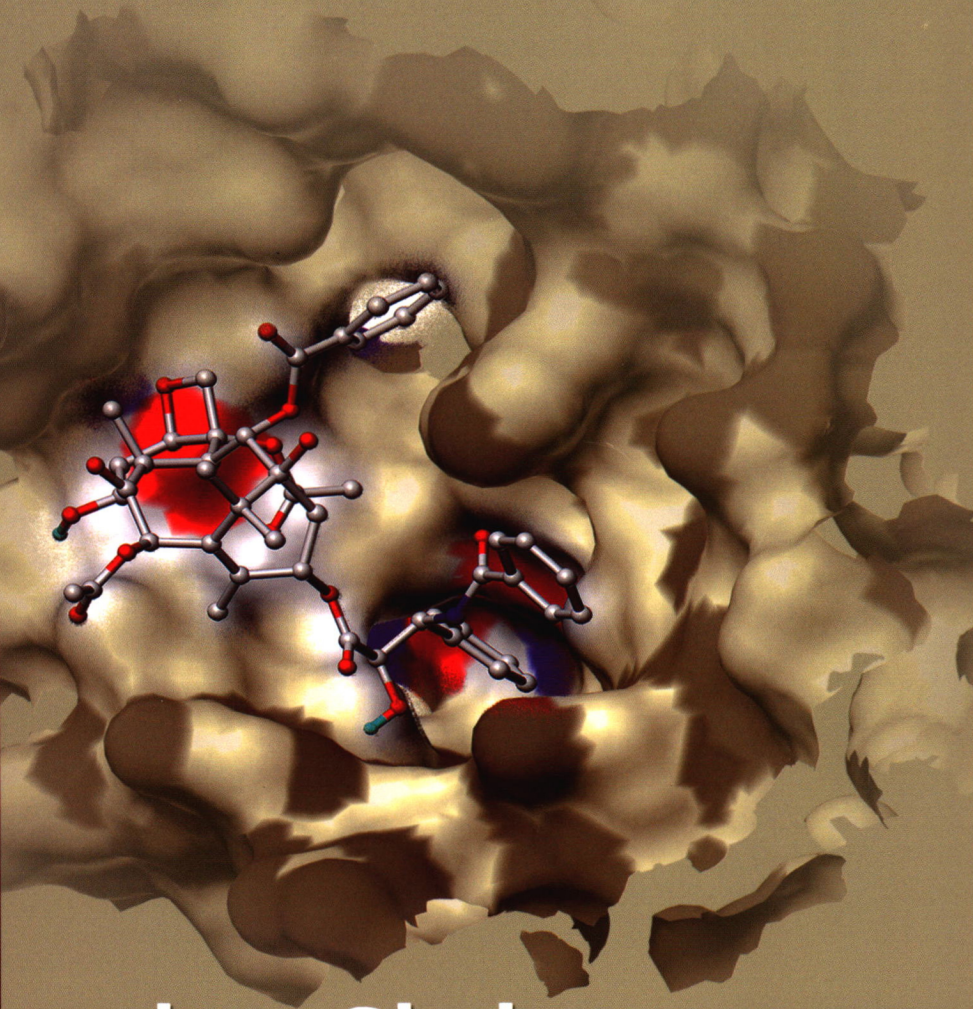


药 学 学 报

第58卷 第4期

Vol. 58 No. 4

2023 年 4 月



Acta Pharmaceutica Sinica

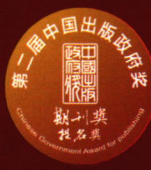
专题报道

崔丽莉, 张 勇

上市核酸药物及其脂质纳米递送载体
研究进展

黄芳华, 王庆利等

《纳米药物非临床安全性评价研究技
术指导原则》解读



中国药学会
中国医学科学院药物研究所

药 学 学 报

第 58 卷 第 4 期 2023 年 4 月

图 文 摘 要

专题报道: 纳米药物药代动力学研究

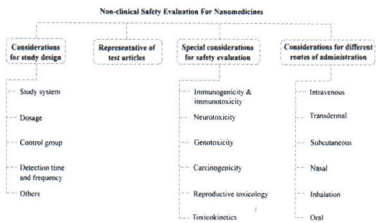
805

《纳米药物非临床安全性评价研究技术指导原则》解读

黄芳华¹, 邵雪¹, 耿兴超², 王庆利¹

(1. 国家药品监督管理局药品审评中心, 北京 100022; 2. 中国食品药品检定研究院国家药物安全评价监测中心, 北京 100176)

本品对《纳米药物非临床安全性评价研究技术指导原则(试行)》进行全面解读, 着重介绍纳米药物非临床安全性评价的关注要点, 并结合案例进行阐述。



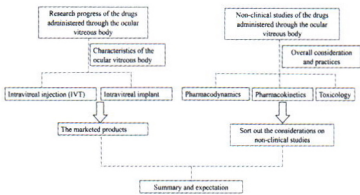
815

经眼玻璃体给药药物的研究进展及非临床研究的考虑要点

付淑军¹, 于冰¹, 廖琴², 孙涛¹

(1. 国家药品监督管理局药品审评中心, 北京 100022; 2. 昭衍(苏州)新药研究中心股份有限公司, 江苏 太仓 215421)

本文结合审评实践和已上市产品的研发案例, 总结了经眼玻璃体给药药物的研究进展及其非临床研究评价考虑要点。



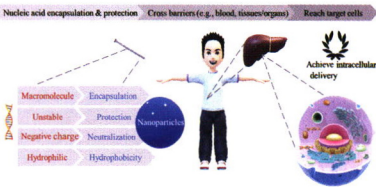
826

上市核酸药物及其脂质纳米递送载体研究进展

崔丽莉¹, 张勇

(吉林大学生命科学学院, 吉林 长春 130012)

核酸定制型纳米制剂及其递送屏障。



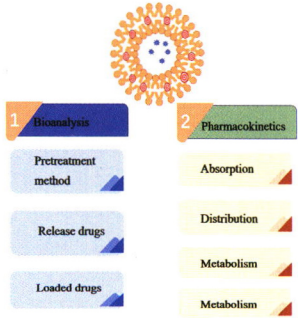
834

脂质体纳米药物制剂的生物分析方法及药代动力学研究进展

刘一¹, 张煜杰¹, 王梓榆², 尤建嵩², 尹磊¹, 史美云^{1,2}

(1. 大连理工大学生命科学与药学院, 辽宁 盘锦 124221; 2. 艾美诚信生物制药有限公司, 辽宁 大连 116100)

本篇综述介绍了脂质体纳米药物的前处理方法, 总结了脂质体纳米药物的分析测定方法及其药代动力学的研究进展, 希望能够为脂质体纳米药物制剂的研究开发提供参考。



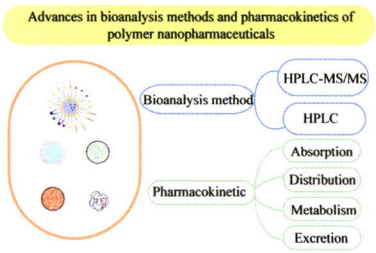
844

聚合物纳米药物制剂生物分析方法及药动力学研究进展

崔雨琪¹, 雷芳彬¹, 张霖茜², 尤建嵩², 尹磊¹, 史美云^{1,2}

(1. 大连理工大学生命科学与药学院, 辽宁 盘锦 124221; 2. 艾美诚信生物制药有限公司, 辽宁 大连 116600)

本文简要介绍了聚合物纳米药物制剂常用生物分析方法的特点及适用范围, 概述了聚合物纳米药物制剂在体内的药代动力学, 希望能够为聚合物纳米药物制剂的药代动力学研究、安全性和有效性评价提供借鉴和参考。



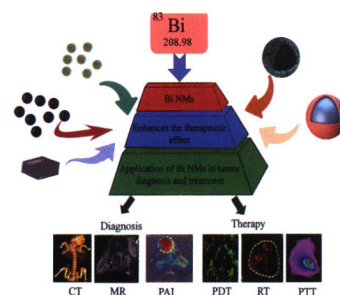
852

铋基纳米药物系统的抗肿瘤诊疗及生物安全性研究进展

王英杰, 高平, 孙萌, 李磊姣*

(长春理工大学化学与环境工程学院, 吉林 长春 130022)

本文综述了不同类型的铋基纳米材料 (Bi NMs) 在抗肿瘤领域应用方面的研究进展及其在体内的分布和清除途径等生物安全性问题。



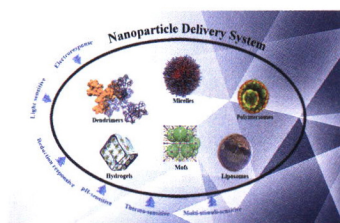
856

纳米载体作为药物递送系统的临床应用和药代动力学研究

肖箫 陈俊宇 李彩霞 呈满 黎建堂 史长阔 呈书庆 李文亮

(吉林医药学院, 药学院, 抗体中心, 吉林 吉林 132013)

本文就纳米载体在药物递送中的辅助作用及特点、种类及功能、药代动力学、应用前景、面临的挑战等方面进展做出综述分析。



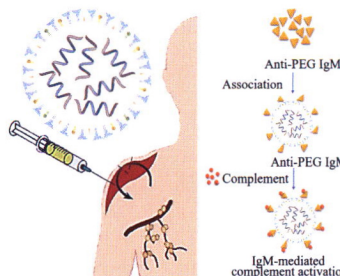
867

mRNA-LNP新冠疫苗过敏反应及其体内药代动力学

梁春苏, 左玮, 都丽萍, 张波

(中国医学科学院, 北京协和医院药剂科, 北京 100730)

mRNA-LNP 新冠疫苗过敏反应及其体内药代动力学。



专家论坛

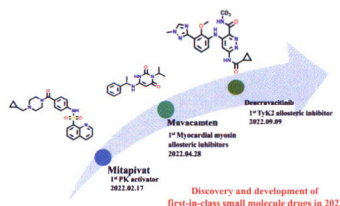
875

2022年首创性小分子药物研究实例浅析

王磊^{1,2}, 尤启冬^{1,2*}

(1. 中国药科大学, 江苏省药物分子设计与成药性优化重点实验室, 江苏 南京 210009; 2. 中国药科大学药学院, 药物化学系, 江苏 南京 210009)

本文简要介绍了2022年上市的首创性小分子药物研究概况,并选取了3例阐述其研发背景、研发过程和治疗应用,为更多首创性药物的研发提供思路与借鉴。



综述

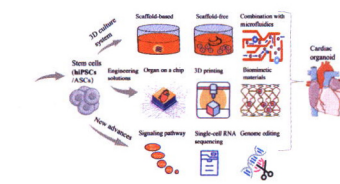
884

心脏类器官的研究进展及在药物发现研究中的应用

吴迪^{1,2},王守宝^{1*},杜冠华^{1*}

(1. 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; 2. 烟台大学, 分子药理和药物评价教育部重点实验室, 山东 烟台 264005)

心脏类器官是由干细胞经体外培养形成的一类具有心脏样结构和功能特性的微型三维结构,成为药物发现研究的重要技术手段。



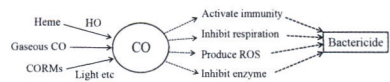
891

一氧化碳的抗菌机制及其释放分子作为抗感染药物的可行性

吴根福*

(浙江大学生命科学学院, 浙江 杭州 310058)

一氧化碳 (CO) 通过激活机体免疫、抑制细菌呼吸和酶活、产生氧化压力等途径杀灭细菌, CO 气体或 CO 释放分子 (CORMs) 有望作为感染性疾病的治疗药物。



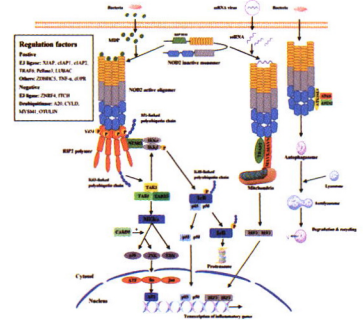
899

NOD2介导的信号通路及其与自身炎症性疾病关系以及抑制剂研究进展

杨熙玥, 叶菜英, 朱蕾*

(中国医学科学院基础医学研究所, 北京协和医学院基础学院药理系, 北京 100005)

本文阐述了NOD2受体介导的信号转导通路及其调节机制、NOD2与AIDs的关系以及NOD2通路抑制剂研究的最新进展。



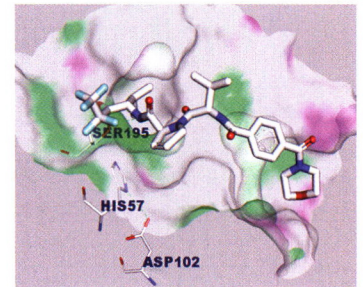
909

人中性粒细胞弹性蛋白酶抑制剂的研究进展

王中伟, 文辉, 王雨辰, 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)

人中性粒细胞弹性蛋白酶 (human neutrophil elastase, hNE) 的生物学功能及小分子抑制剂的研发现状。



研究论文

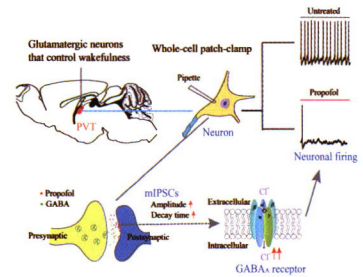
919

丙泊酚对丘脑室旁核谷氨酸能神经元活性的影响

王玉龙^{1#}, 易琼^{2#}, 徐薇³, 王锸², 黄志力³, 陈永权^{1*}, 王露^{3*}

(1. 皖南医学院弋矶山医院, 安徽 芜湖 241000; 2. 中南大学湘雅医院, 湖南 长沙 410008; 3. 复旦大学基础医学院, 医学神经生物学国家重点实验室, 脑科学前沿研究中心, 上海 200032)

丘脑旁核 (PVT) 参与控制觉醒和整合行为, 其在丙泊酚麻醉中的作用未知。本文利用全细胞膜片钳技术在成年小鼠急性脑片上发现丙泊酚呈浓度依赖和可逆性地抑制 PVT 谷氨酸能神经元活性, 该作用主要由突触后 GABA_A 受体介导, 表明 PVT 很可能是丙泊酚诱导麻醉的靶点。

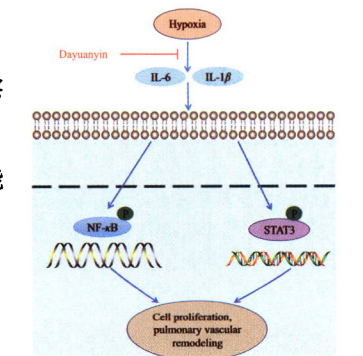


928

达原饮通过NF- κ B信号通路预防低氧性肺动脉高压作用及机制研究王建美^{1,2}, 王冉冉¹, 袁天翊¹, 秦雪梅², 杜冠华^{1*}

(1. 中国医学科学院、北京协和医学院药物研究所, 北京市药物靶点研究与新药筛选重点实验室, 北京 100050; 2. 山西大学中医药现代研究中心, 山西 太原 030006)

本研究对达原饮在低氧性肺动脉高压上的药效进行评价,达原饮改善肺动脉高压症状可能与核因子 κ B (NF- κ B) 信号通路相关。



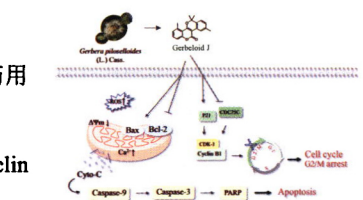
938

毛大丁草内酯J对乳腺癌细胞周期和凋亡的影响及机制研究

李靖荣¹, 李凌宇², 赵晨旭², 尚海², 张涛², 邹忠梅^{2*}, 宛蕾^{1*}

(1. 贵州医科大学基础医学院, 贵州 贵阳 550025; 2. 中国医学科学院、北京协和医学院, 药用植物研究所, 北京 100193)

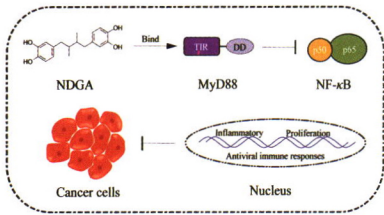
毛大丁草内酯J能够显著诱导乳腺癌细胞周期阻滞并发生凋亡,其作用机制与调控P21/cyclin B1/CDC25C通路及激活线粒体凋亡通路有关,可作为一种潜在的抗乳腺癌先导化合物。



946
去甲二氢愈创木酸靶向MyD88抗肿瘤研究

王月^{1,2}, 屈祎^{1,2}, 柯细松^{1,2}, 张雪^{1,2*}
(1. 上海中医药大学交叉科学研究院, 上海 201203; 2. 上海市中药化学生物学前沿基地, 上海 201203)

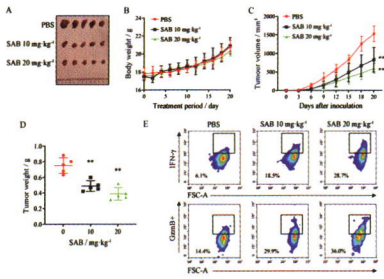
MyD88是介导肿瘤发生发展的关键蛋白, 去甲二氢愈创木酸 (NDGA) 与MyD88直接结合并且抑制NF-κB信号通路和肿瘤细胞增殖。



954
靶向USP2下调PD-L1表达的丹酚酸B抗肿瘤免疫作用研究

况泽安¹, 董靖雯¹, 孙翠翠¹, 殷明晓¹, 刘璐², 邓洪斌¹, 刘晓嘉^{3*}, 冯艳春^{4*}
(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. 青岛市妇女儿童医院, 山东 青岛 266034; 3. 北京市临床药学研究所、北京友谊医院, 北京 100050; 4. 中国食品药品检定研究院, 北京 102629)

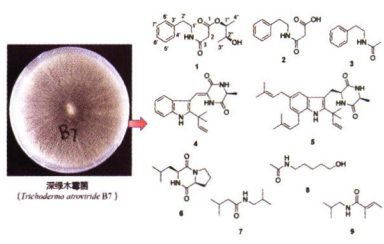
本研究发现天然活性小分子化合物丹酚酸B (salvianolic acid B, SAB) 通过直接结合去泛素化酶USP2并抑制其活性, 诱导肿瘤细胞中PD-L1发生泛素-蛋白酶体途径降解, 促进T细胞对肿瘤细胞的杀伤活性, 从而发挥抗肿瘤作用。研究结果为将SAB发展成为靶向USP2-PD-L1轴的抗肿瘤免疫治疗药物提供了依据。



963
火把花内生真菌Trichoderma atroviride B7生物碱类成分研究

李文渊^{1,2}, 王莹¹, 匡策¹, 郭凯³, 刘燕^{1,3}, 黎胜红^{1,3*}
(1. 中国科学院昆明植物研究所, 植物化学与西部植物资源持续利用国家重点实验室, 云南 昆明 650201; 2. 郑州工业应用技术学院, 河南省水环境与健康工程技术研究中心, 河南 郑州 451150; 3. 成都中医药大学, 省部共建西南特色中药资源国家重点实验室/中医药创新研究院, 四川 成都 611137)

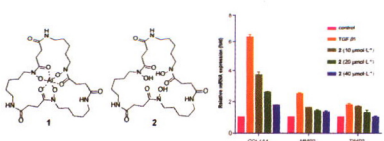
从火把花内生真菌Trichoderma atroviride B7固体发酵提取物中分离鉴定9个生物碱。其中化合物1为新化合物, 化合物2~9首次从木霉属真菌中发现。



967
海洋来源链霉菌IMB18-531与枝孢菌IMB19-099共培养代谢产物研究

李莎莎^{1*}, 李琴^{1,2*}, 李翎铭¹, 商悦¹, 何红伟¹, 陈淑珍¹, 舒积成², 甘茂罗^{1*}
(1. 中国医学科学院、北京协和医学院医药生物技术研究所, 国家新药微生物筛选实验室, 北京 100050; 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)

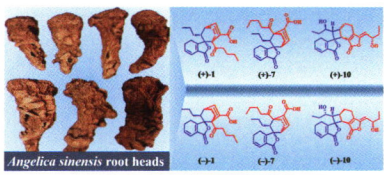
从海洋来源链霉菌IMB18-531与枝孢菌IMB19-099的共培养产物中分离得到一个新的铁载体螯合物铝草菌素E (1)。去铁胺E (2) 显示出抗肝纤维化活性, 能够抑制肝纤维化相关基因COL1A1、MMP2和TIMP2的表达。



975
当归头水提取物中的二聚鞣类成分

夏召, 陈有哲, 徐成博, 朱承根, 雷小强, 郭庆兰*, 石建功*
(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)

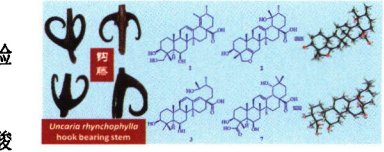
从"归头"水煎提取物中分离、拆分得到10对二聚鞣类对映体 (+)-/(-)-1~(+)-/(-)-10, 确定了绝对构型并讨论了相关化合物的相对构型确定。



992
钩藤水提取物中的微量三萜酸类

张卿, 雷小强, 李若斐, 孙华, 徐成博, 朱承根, 郭庆兰*, 石建功*
(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)

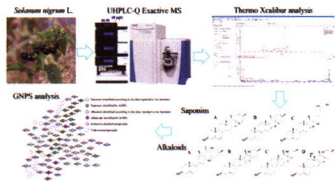
从中药钩藤水煎煮提取物中分离得到8个微量三萜酸类新成分1~8, 依次命名为钩藤酸Q~X; 2和7的结构得到单晶X-射线衍射分析的确证。



1003
基于UHPLC-Q Exactive MS的分子网络技术快速分析龙葵叶物质成分

董现龙, 杨琳娇, 秦雪梅, 李震宇*
(山西大学化学生物学与分子工程教育部重点实验室, 中医药现代研究中心, 山西 太原 030006)

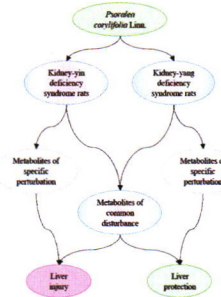
本研究基于UHPLC-Q Exactive MS和分子网络技术快速分析龙葵叶物质成分。共鉴定化合物157个, 其中35个化合物为首次在龙葵中报道的化合物, 包括6个生物碱类化合物、20个皂苷类化合物和9个黄酮类化合物。



1014
补骨脂"大燥伤肝"的客观性及生物学机制研究

张明亮^{1,2}, 赵旭³, 李伟霞², 王晓艳², 陈毓龙², 孔德鑫², 吴承钊¹, 陈小菲², 柏兆方³, 牛明³, 王伽伯⁴, 赵艳玲³, 肖小河³, 唐进法^{2*}
(1. 成都中医药大学药学院, 四川 成都 611137; 2. 河南中医药大学第一附属医院, 河南 郑州 450000; 3. 中国人民解放军总医院第五医学中心, 北京 100039; 4. 首都医科大学中医药学院, 北京 100069)

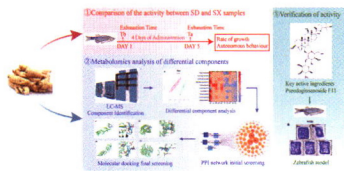
本研究从"性本大燥"药性理论出发, 通过构建肾阳虚证与肾阴虚证模型动物, 发现肾阳虚证与肾阴虚证可能分别是补骨脂发挥肝保护与肝损害的易感证候, 代谢组学检测进一步发现这可能与其调控体内相关氨基酸代谢和鞘脂代谢等有关。



1024
基于代谢组学和斑马鱼模型探究西洋参抗疲劳的关键活性成分

刘慧茹^{1,2}, 汪海洋², 王喆², 陈立国², 程贵东², 马智慧^{1,2}, 王松松¹, 李正国^{1,3}, 韩利文^{2*}
(1. 山东中医药大学药学院, 山东 济南 250355; 2. 山东第一医科大学药学院与制药科学学院, 山东省医学科学院药物研究所, 卫生部生物技术药物重点实验室, 山东 济南 250000; 3. 山东省济宁市食品药品检验检测研究院, 山东 济宁 272027)

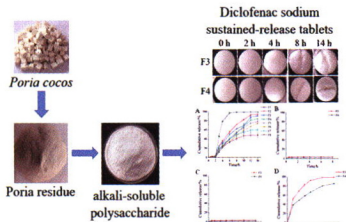
本研究采用"代谢组学结合斑马鱼模型"的策略筛选具有抗疲劳作用的西洋参关键活性物质, 为西洋参抗疲劳研究提供新的物质基础。



1033
茯苓碱溶性多糖的理化性质评价及其在双氯芬酸钠缓释片中的应用研究

毛荣¹, 方文悠¹, 孙娟¹, 高松¹, 刘军玲², 陈胜麒^{1,3}, 胡容峰^{1,4,5*}, 李庆林^{1,3*}
(1. 安徽中医药大学, 药物制剂技术与应用安徽省重点实验室, 安徽 合肥 230012; 2. 安徽省食品药品检验研究院, 安徽 合肥 230051; 3. 安徽中医药大学, 新安医学教育部重点实验室, 安徽 合肥 230038; 4. 省部共建安徽道地中药材品质提升协同创新中心, 安徽 合肥 230012; 5. 安徽中医药大学, 中药复方安徽省重点实验室, 安徽 合肥 230012)

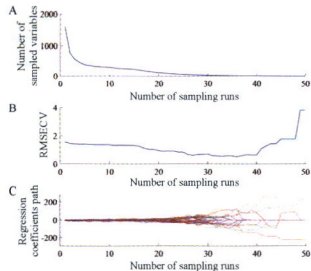
本研究表明从茯苓残渣中提取得到的碱溶性多糖可作为缓释材料用于制备缓释片。



1041
基于偏最小二乘回归的红外光谱波段筛选用于甘露醇-氯化钙共晶的定量分析

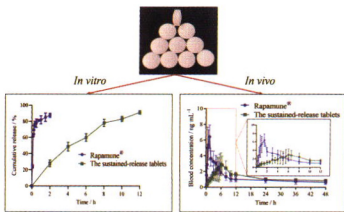
李祖頔¹, 张珂¹, 张泽飞², 钱帅¹, 魏元锋¹, 张建军², 高缘^{1*}
(1. 中国药科大学药学院, 江苏 南京 211198; 2. 中国药科大学药学院, 江苏 南京 211198)

基于偏最小二乘回归的红外光谱法将光谱数据降维与波段筛选相结合定量分析甘露醇-氯化钙共晶, 可实现共晶辅料的质量控制。



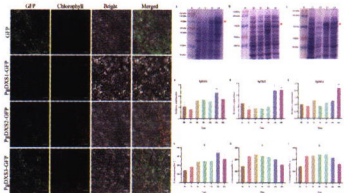
1049
基于介孔硅固化自微乳的西罗莫司缓释片的制备与评价
黄雯婷^{1,2}, 刘志宏¹, 张灵娜³, 曾令军¹, 张倩², 宋洪涛^{1*}
(1. 中国人民解放军联勤保障部队第九〇〇医院, 福建 福州 350025; 2. 福建医科大学药学院, 福建 福州 350108; 3. 福建省药品审评与监测评价中心, 福建 福州 350003)

西罗莫司自微乳-介孔硅缓释片, 以市售西罗莫司片作为参比制剂, 结果表明其在体外及体内均缓慢释药, 有望减轻药物毒副作用, 为其他难溶性药物的增溶及缓释制剂的研发提供参考。



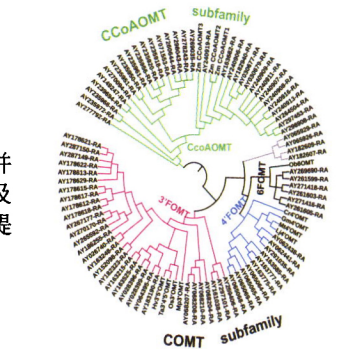
1059
桔梗 *DXS* 基因的原核表达、亚细胞定位和酶活性分析
董楠¹, 余函纹¹, 刘梦丽¹, 李景¹, 陈博文¹, 常相伟¹, 王举涛¹, 查良平^{1*}, 桂双英^{1,2,3,4*}
(1. 安徽中医药大学药学院, 安徽 合肥 230012; 2. 安徽省中医药科学院药物制剂研究所, 安徽 合肥 230012; 3. 现代药物制剂安徽省教育厅工程技术研究中心, 安徽 合肥 230012; 4. 药物制剂技术与应用安徽省重点实验室, 安徽 合肥 230012)

本研究成功克隆出桔梗 *DXS* 基因, 并进行原核表达、亚细胞定位研究, 检测其基因表达水平及经茉莉酸甲酯 (MeJA) 处理后的基因表达和酶活性变化。



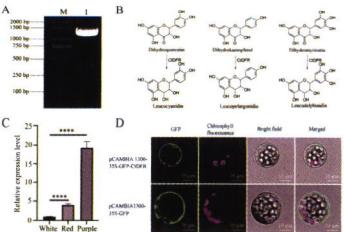
1069
艾叶类黄酮 *O*-甲基转移酶基因家族的鉴定及表达分析
彭赛男, 李宇琨, 罗丹丹, 陈昌婕, 周佳, 李佳怡, 郑佳, 刘大会*, 苗玉焕*
(湖北中医药大学, 中药资源中心, 湖北 武汉 430065)

本研究对艾叶类黄酮 *O*-甲基转移酶 (*FOMT*) 基因家族进行了全基因组水平的挖掘和鉴定, 并进行系统发育、染色体定位、基因序列特征、亚细胞定位预测、蛋白结构、基因结构分析及表达模式的分析和验证, 为进一步深入研究 *FOMT* 功能和甲基化黄酮类化合物的生物合成提供理论依据。



1079
管花肉苁蓉花中二氢黄酮醇 4-还原酶的克隆、表达分析和酶活性鉴定
邱海玲^{1,2}, 王方明³, 高博闻⁴, 米芯雨^{1,2}, 张泽坤^{1,2}, 杜宇^{1,2}, 史社坡^{1,2}, 屠鹏飞^{3*}, 王晓晖^{1,2*}
(1. 北京中医药大学中药学院, 北京 102488; 2. 北京中医药大学中药学院中药现代研究中心, 北京 100029; 3. 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; 4. 包头医学院, 内蒙古 包头 014060)

本研究从管花肉苁蓉花中克隆得到一条新的 *CtDFR* 基因, *CtDFR* 基因在红、紫色花中高表达, 在白色花中低表达。 *CtDFR* 蛋白能将二氢山柰酚、二氢槲皮素、二氢杨梅素还原为无色天竺葵素、无色矢车菊素、无色飞燕草素, 主要定位于细胞质。



新药发现与研究实例简析

1090
新作用机制治疗原发性胆汁性胆管炎药物奥贝胆酸
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)

Special Reports: Study on Pharmacokinetics of Nanomedicine

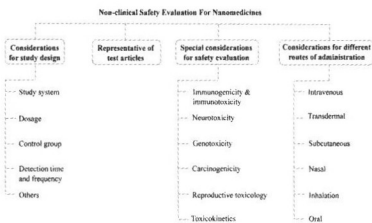
805

Interpretation of guidance on non-clinical safety evaluation for nanomedicines

HUANG Fang-hua¹, SHAO Xue¹, GENG Xing-chao², WANG Qing-li^{1*}

(1. Center for Drug Evaluation, National Medical Products Administration, Beijing 100022, China; 2. National Center for Safety Evaluation of Drugs, National Institutes for Food and Drug Control, Beijing 100176, China)

This article interprets comprehensively *Guidance on Non-clinical Safety Evaluation for Nanomedicines (interim)*, focuses on the key points of non-clinical safety evaluation for nanomedicines, and expounds combined with some cases.



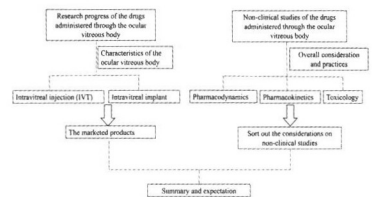
815

Research progress and considerations on non-clinical studies of the drugs administered through the ocular vitreous body

FU Shu-jun^{1#}, YU Bing^{1#}, LIAO Qin², SUN Tao^{1*}

(1. Center for Drug Evaluation, National Medical Products Administration, Beijing 100022, China; 2. Joynn Laboratories (Suzhou), Taicang 215421, China)

This article combines review practices and cases of marketed products to sort out the research progress and considerations on non-clinical studies of ophthalmic drugs dosing through the ocular vitreous body.



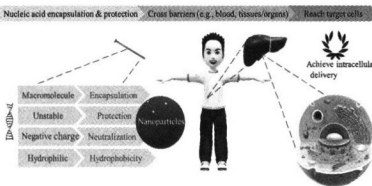
826

Advances in approved nucleic acid drugs and lipid nanoparticle system

CUI Li-li¹, ZHANG Yong

(School of Life Sciences, Jilin University, Changchun 130012, China)

Nucleic acid-customized nanomedicine and its delivery barriers.



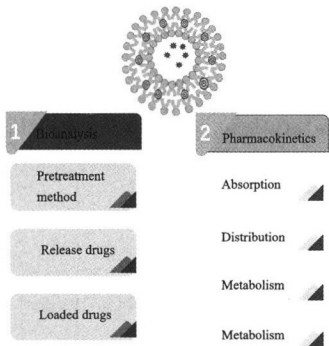
834

Research progress in bioanalysis and pharmacokinetics of liposome nanomedicine

LIU Yi^{1#}, ZHANG Yu-jie^{1#}, WANG Zi-yu², YOU Jian-song², YIN Lei^{1#}, SHI Mei-yun^{1,2*}

(1. School of Life and Pharmaceutical Sciences, Dalian University of Technology, Panjin 124221, China; 2. Aim Honesty Biopharmaceutical Co. Ltd., Dalian 116100, China)

This review introduces the pretreatment methods of liposome nano pharmaceutical preparations, summarizes the biological analytical methods and pharmacokinetics of liposomes. We hope this review will provide a reference for the development of liposome nano drug delivery systems.



844

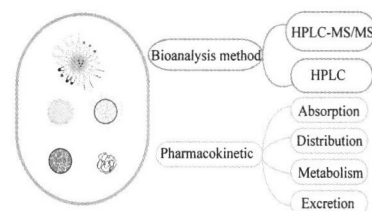
Advances in bioanalysis methods and pharmacokinetics of polymer nanopharmaceuticals

CUI Yu-qi^{1#}, LEI Fang-bin^{1#}, ZHANG Lin-qian², YOU Jian-song², YIN Lei^{1*},
SHI Mei-yun^{1,2*}

(1. School of Life and Pharmaceutical Sciences, Dalian University of Technology, Panjin 124221, China; 2. Aim Honesty Biopharmaceutical Co. Ltd., Dalian 116600, China)

The bioanalysis and pharmacokinetics of polymer nanomedicines were briefly introduced and discussed in this review. We hope this review will provide reference for the pharmacokinetics study, safety and effectiveness evaluation of polymer nanomedicines.

Advances in bioanalysis methods and pharmacokinetics of polymer nanopharmaceuticals



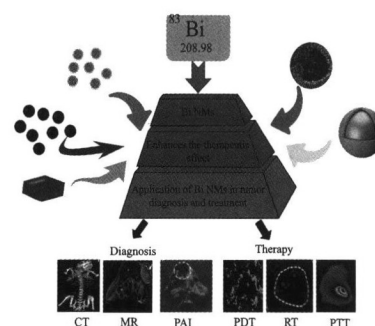
852

Advance on anti-tumor theranostics and biosafety of bismuth-based nanomedicine

WANG Ying-jie, GAO Ping, SUN Meng, LI Lei-jiao^{*}

(School of Chemistry and Environmental Engineering, Changchun University of Science and Technology, Changchun 130022, China)

This paper reviewed the application of different types of bismuth-based nanomaterials (Bi NMs) in the field of anti-tumor and biosafety including the distribution and clearance pathways of Bi NMs *in vivo*.



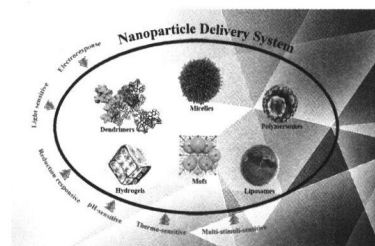
856

Clinical application and pharmacokinetic study of nanocarriers in drug delivery system

XIAO Xiao, CHEN Jun-yu, LI Cai-xia, WU Man, LI Jian-dang, SHI Chang-kuo,
WU Shu-qing, LI Wen-liang^{*}

(School of Pharmacy, Antibody Center, Jilin Medical University, Jilin 132013, China)

This paper reviewed and analyzed the research progress of nano carriers in drug delivery, including their auxiliary role and characteristics, types and functions, pharmacokinetics, application prospects and challenges.



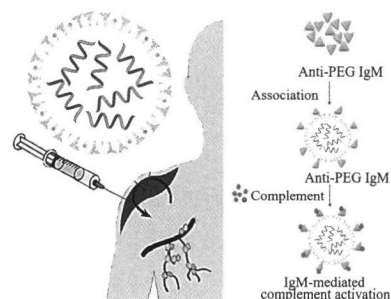
867

Allergic reactions of COVID-19 vaccine based on mRNA-LNP and its pharmacokinetics *in vivo*

LIANG Chun-su, ZUO Wei, DU Li-ping, ZHANG Bo^{*}

(Department of Pharmacy, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China)

Allergic reactions to lipid nanoparticle-based COVID-19 vaccines and its pharmacokinetics *in vivo*.



Professionals Forum

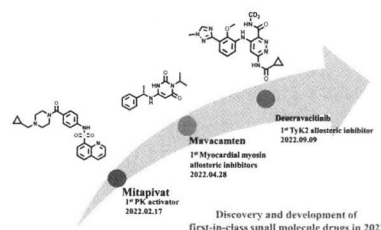
875

First-in-class small molecule drugs in 2022

WANG Lei^{1,2}, YOU Qi-dong^{1,2*}

(1. Jiangsu Key Laboratory of Drug Design and Optimization, China Pharmaceutical University, Nanjing 210009, China; 2. Department of Medicinal Chemistry, School of Pharmacy, China Pharmaceutical University, Nanjing 210009, China)

We briefly introduced three representative first-in-class small molecule drugs approved in 2022. Background of drug development, research process and therapeutic application were stated to provide new horizon for discovery and development of more first-in-class small molecule drugs.



Reviews

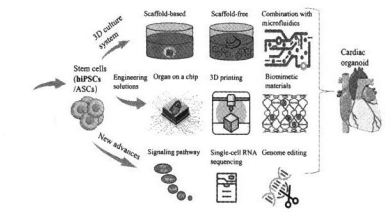
884

Advances in research of heart organoid and its application in drug discovery

WU Di^{1,2}, WANG Shou-bao^{1*}, DU Guan-hua^{1*}

(1. 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; 2. Key Laboratory of Molecular Pharmacology and Drug Evaluation (Yantai University), Ministry of Education, Yantai University, Yantai 264005, China)

Heart organoid, formed by the self-updating and specific differentiation of stem cells during the *in vitro* culture, is a miniature with the structure and function similar to human heart, and becomes an important technical means for drug discovery and other medical research.



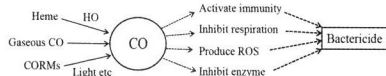
891

The bactericidal mechanisms of carbon monoxide and the feasibility of carbon monoxide-releasing molecules as anti-infective drugs

WU Gen-fu

(College of Life Sciences, Zhejiang University, Hangzhou 310058, China)

Carbon monoxide (CO) has bactericidal effect by activating body immunity, inhibiting bacterial respiration and enzyme activities, and generating oxidative pressure. Gaseous CO and CO releasing molecules (CORMs) are anticipated to be used as therapeutic drugs for infectious diseases.



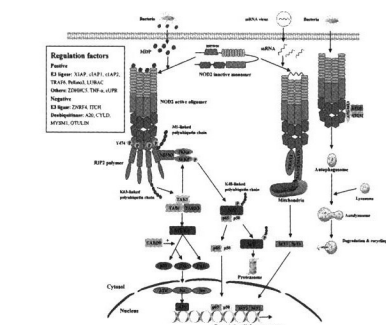
899

Research progress of NOD2-mediated signaling pathways and relationship with autoinflammatory diseases and its inhibitors

YANG Xi-yue, YE Cai-ying, ZHU Lei*

(Department of Pharmacology, Institute of Basic Medical Sciences CAMS, School of Basic Medicine PUMC, Beijing 100005, China)

This review presents the recent progress of NOD2 receptor-mediated signal transduction pathways and its regulation mechanisms, the relationship between NOD2 and AIDs, and the inhibitors of NOD2 pathway.



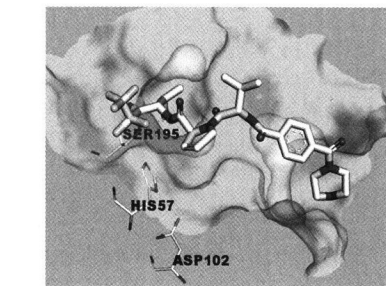
909

Research progress on the development of human neutrophil elastase inhibitors

WANG Zhong-wei, WEN Hui, WANG Yu-chen, 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)

The biological functions of human neutrophil elastase (hNE) and the current progress of inhibitor development against hNE.



Original Articles

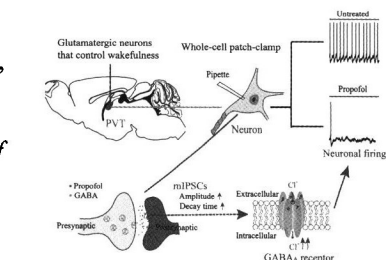
919

Effects of propofol on glutamatergic neuronal activity in paraventricular thalamus

WANG Yu-long^{1#}, YI Qiong^{2#}, XU Wei³, WANG E², HUANG Zhi-li³, CHEN Yong-quan^{1*}, WANG Lu^{3*}

(1. Yijishan Hospital, Wannan Medical College, Wuhu 241000, China; 2. Xiangya Hospital, Central South University, Changsha 410008, China; 3. State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science, School of Basic Medical Sciences, Shanghai Medical College of Fudan University, Shanghai 200032, China)

How the paraventricular thalamus (PVT) contributes to propofol anesthesia remains unknown. Using whole-cell patch-clamp recordings in acute brain slices of adult mice, the present study found that propofol inhibited PVT glutamatergic neurons in a concentration-dependent and reversible manner by potentiating postsynaptic GABA_A receptors, suggesting a potential role of the PVT in propofol anesthesia.

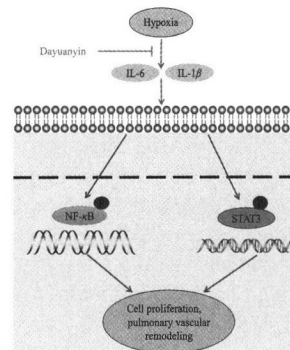


928

The preventive effect and mechanism of Dayuanyin in hypoxic pulmonary hypertension through NF- κ B signaling pathwayWANG Jian-mei^{1,2}, WANG Ran-ran¹, YUAN Tian-yi¹, QIN Xue-mei², DU Guan-hua^{1*}

(1. Beijing Key Lab of Drug Target Identification and Drug Screening, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100050, China; 2. Modern Research Center for Traditional Chinese Medicine, Shanxi University, Taiyuan 030006, China)

Evaluation of the effect of Dayuanyin in hypoxic pulmonary hypertension in this paper, the improvement of pulmonary hypertension symptoms by Dayuanyin maybe relate to nuclear factor kappa B (NF- κ B) signaling pathway.

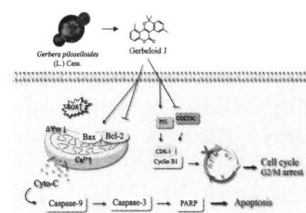


938

Effect and mechanism of gerbeloid J from *Gerbera piloselloides* (L.) Cass. on cycle and apoptosis of breast cancer cellsLI Jing-rong¹, LI Ling-yu², ZHAO Chen-xu², SHANG Hai², ZHANG Tao², ZOU Zhong-mei^{2*}, WAN Lei^{1*}

(1. School of Basic Medical Sciences, Guizhou Medical University, Guiyang 550025, China; 2. Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union College, Beijing 100193, China)

Gerbeloid J, a promising candidate for treating breast cancer, caused cell cycle arrest and apoptosis in breast cancer cells via regulating the P21/CDC25C/CDK-1/cyclin B1 pathway and activating the mitochondrial apoptosis pathway.



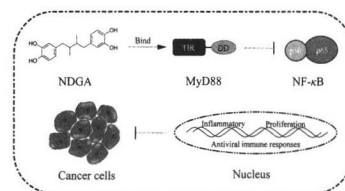
946

Research on the anti-tumor effect of nordihydroguaiaretic acid targeting MyD88WANG Yue^{1,2}, QU Yi^{1,2}, KE Xi-song^{1,2}, ZHANG Xue^{1,2*}

(1. Institute of Interdisciplinary Integrative Medicine Research, Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China; 2. Shanghai Frontiers Science Center of TCM Chemical Biology, Shanghai 201203, China)

MyD88 is a key protein that mediates tumorigenesis and development.

Nordihydroguaiaretic acid (NDGA) binds to MyD88, inhibits NF- κ B signaling pathway and proliferation of tumor cells.

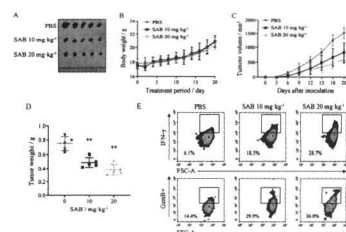


954

Salvianolic acid B exerts its anti-tumor immunity by targeting USP2 and reducing the PD-L1 levelKUANG Ze-an¹, DONG Jing-wen¹, SUN Cui-cui¹, YIN Ming-xiao¹, LIU Lu², DENG Hong-bin¹, LIU Xiao-jia^{3*}, FENG Yan-chun^{4*}

(1. Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China; 2. Qingdao Women and Children's Hospital, Qingdao 266034, China; 3. Beijing Institute of Clinical Pharmacy, Beijing Friendship Hospital, Beijing 100050, China; 4. National Institutes for Food and Drug Control, Beijing 102629, China)

Our study reveals that salvianolic acid B (SAB) exerts its anti-tumor activity by direct binding and inhibiting the activity of USP2 and promoting the ubiquitin-proteasome pathway degradation of PD-L1 proteins, thus enhancing the cytotoxicity of T cells toward cancer cells. Our results provide a potential application of SAB in tumor immunotherapy drug targeting USP2-PD-L1 axis.

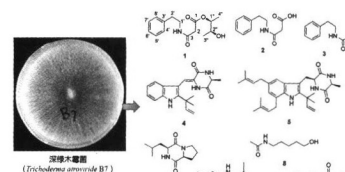


963

Study on alkaloids of endophytic *Trichoderma atroviride* B7 from *Colquhounia coccinea* var. *mollis*LI Wen-yuan^{1,2}, WANG Ying¹, KUANG Ce¹, GUO Kai³, LIU Yan^{1,3}, LI Sheng-hong^{1,3*}

(1. State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, China; 2. Henan Engineering Research Center of Water Environment and Health, Zhengzhou University of Industrial Technology, Zhengzhou 451150, China; 3. State Key Laboratory of Southwestern Chinese Medicine Resources, and Innovative Institute of Chinese Medicine and Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China)

Nine compounds were isolated from the crude extract of the solid culture of endophyte *Trichoderma atroviride* B7 of *Colquhounia coccinea* var. *mollis*. Among them, compound 1 is a new compound, and compounds 2–9 are firstly isolated from *Trichoderma* spp.

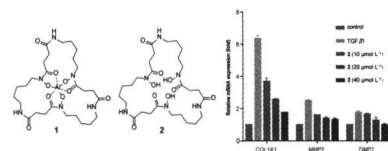


967

Identification of the metabolites from co-cultures of marine *Streptomyces* sp. IMB18-531 and *Cladosporium* sp. IMB19-099

LI Sha-sha^{1#}, LI Qin^{1,2#}, LI Yi-ming¹, SHANG Yue¹, HE Hong-wei¹,
CHEN Shu-zhen¹, SHU Ji-cheng^{2*}, GAN Mao-luo^{1*}

(1. Laboratory for Screening New Microbial Drugs, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China; 2. Key Laboratory of Modern Preparation of Traditional Chinese Medicines, Ministry of Education, Jiangxi University of Traditional Chinese Medicine, Nanchang 330004, China)



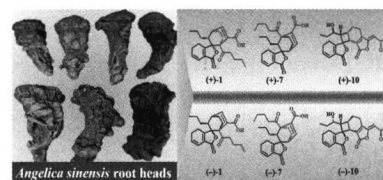
A new siderophore chelate aluminioxamine E (1) was identified from the co-cultures of marine-derived *Streptomyces* sp. IMB18-531 and *Cladosporium* sp. IMB19-099. Desferrioxamine E (2) showed inhibitory activities against the expression of the liver fibrosis related genes *COL1A1*, *MMP2*, and *TIMP2*.

975

Dimeric phthalides from an aqueous extract of the *Angelica sinensis* root head

XIA Zhao, CHEN You-zhe, XU Cheng-bo, ZHU Cheng-gen, LEI Xiao-qiang,
GUO Qing-lan*, SHI Jian-gong*

(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)



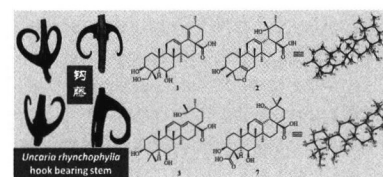
Ten pairs dimeric phthalide racemates [(+)-/(-)-1-(+)-/(-)-10] were isolated and chiral separated from an aqueous extract of the *Angelica sinensis* root head (Guitou). Their structures including absolute configurations were elucidated and determination of their relative configurations were discussed.

992

Minor triterpenoid acids from an aqueous extract of *Uncaria rhynchophylla*

ZHANG Qing, LEI Xiao-qiang, LI Ruo-fei, SUN Hua, XU Cheng-bo,
ZHU Cheng-gen, GUO Qing-lan*, SHI Jian-gong*

(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)



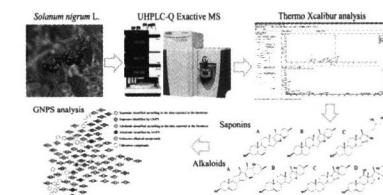
Eight minor triterpenoid acids (1–8) were isolated from an aqueous decoction of *Uncaria rhynchophylla*, named successively uncarinic acids Q–X, while the structures of 2 and 7 were confirmed by single crystal X-ray diffraction.

1003

Rapid identification of the chemical compounds in the leaves of *Solanum nigrum* L. based on UHPLC-Q Exactive MS and molecular network technology

DONG Xian-long, YANG Lin-jiao, QIN Xue-mei, LI Zhen-yu*

(Modern Research Center for Traditional Chinese Medicine, the Key Laboratory of Chemical Biology and Molecular Engineering of Ministry of Education, Shanxi University, Taiyuan 030006, China)



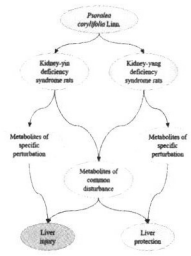
In this study, the material composition of the leaves of *Solanum nigrum* L. was rapidly analyzed based on UHPLC-Q Exactive MS and molecular network technology. Results: A total of 157 compounds were identified, of which 35 compounds were first reported in *S. nigrum* L., including 6 alkaloids, 20 saponins, and 9 flavonoids.

1014

Study on the objectivity and biological mechanism of *Psoralea corylifolia* Linn.'s 'Great dryness damages the liver'

ZHANG Ming-liang^{1,2,3}, ZHAO Xu³, LI Wei-xia², WANG Xiao-yan², CHEN Yu-long², KONG De-xin², WU Cheng-zhao¹, CHEN Xiao-fei², BAI Zhao-fang³, NIU Ming³, WANG Jia-bo⁴, ZHAO Yan-ling^{3*}, XIAO Xiao-he^{3*}, TANG Jin-fa^{2*}

(1. School of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China; 2. The First Affiliated Hospital of Henan University of Traditional Chinese Medicine, Zhengzhou 450000, China; 3. The Fifth Medical Center of Chinese PLA General Hospital, Beijing 100039, China; 4. School of Traditional Chinese Medicine, Capital Medical University, Beijing 100069, China)



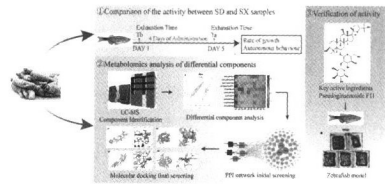
According to the drug property theory of Great dryness damages the liver, the study constructed the model animals of kidney-yang deficiency syndrome and kidney-yin deficiency syndrome, and found that kidney-yang deficiency syndrome and kidney-yin deficiency syndrome may be the susceptible syndrome of *Psoralea corylifolia* Linn. for liver protection and liver damage, respectively. The metabonomics further found that this may be related to the regulation of related amino acid metabolism and sphingolipid metabolism.

1024

Exploring the key anti-fatigue components of American ginseng based on metabolomics and zebrafish models

LIU Hui-ru^{1,2}, WANG Hai-yang², WANG Zhe², CHEN Li-guo², CHENG Gui-dong², MA Zhi-hui^{1,2}, WANG Song-song¹, LI Zheng-guo^{1,3*}, HAN Li-wen^{2*}

(1. College of Pharmacy, Shandong University of Traditional Chinese Medicine, Jinan 250355, China; 2. School of Pharmacy and Pharmaceutical Sciences & Institute of Materia Medica, Shandong First Medical University & Shandong Academy of Medical Sciences, NHC Key Laboratory of Biotechnology Drugs (Shandong Academy of Medical Sciences), Jinan 250000, China; 3. Jining Food and Drug Inspection and Testing Research Institute, Jining 272027, China)



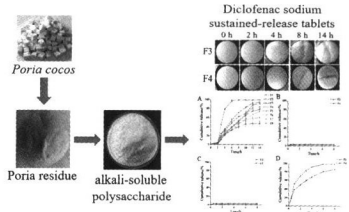
In this study, the strategy of "metabolomics combined with zebrafish model" was adopted to screen the key active substances with anti-fatigue effect of American ginseng, providing a new material basis for the study of anti-fatigue of American ginseng.

1033

Evaluation of the physicochemical properties of alkali-soluble polysaccharide from *Poria* and its application in diclofenac sodium sustained-release tablets

MAO Rong¹, FANG Wen-you¹, SUN Juan¹, GAO Song¹, LIU Jun-ling², CHEN Sheng-qi^{1,3}, HU Rong-feng^{1,4,5*}, LI Qing-lin^{1,3*}

(1. Anhui Province Key Laboratory of Pharmaceutical Preparation Technology and Application, Anhui University of Chinese Medicine, Hefei 230012, China; 2. Anhui Food and Drug Inspection and Research Institute; Hefei 230051, China; 3. Key Laboratory of Xin'an Medicine, the Ministry of Education, Anhui University of Chinese Medicine, Hefei 230038, China; 4. MOE-Anhui Joint Collaborative Innovation Center for Quality Improvement of Anhui Genuine Chinese Medicinal Materials, Hefei 230012, China; 5. Anhui Province Key Laboratory of Chinese Medicinal Formula, Anhui University of Chinese Medicine, Hefei 230012, China)



In this study, we showed that alkali-soluble polysaccharides extracted from *Poria* residues can be used as sustained-release materials for the preparation of sustained-release tablets.

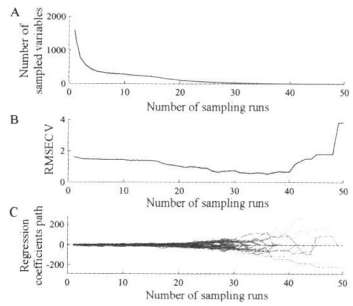
1041

Infrared spectral band screening based on partial least squares is used for the quantitative analysis of mannitol-calcium chloride cocrystal

LI Zu-di¹, ZHANG Ke², ZHANG Ze-fei², QIAN Shuai¹, WEI Yuan-feng¹, ZHANG Jian-jun², GAO Yuan^{1*}

(1. School of Traditional Chinese Pharmacy, China Pharmaceutical University, Nanjing 211198, China; 2. School of Pharmacy, China Pharmaceutical University, Nanjing 211198, China)

Based on partial least squares regression, infrared spectroscopy combines spectral data dimensionality reduction with band screening to quantitatively analyze mannitol-calcium chloride cocrystal, which can realize the quality control of cocrystal excipients.

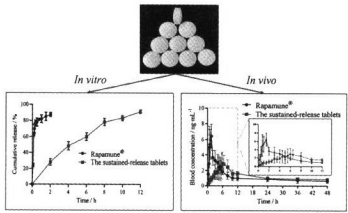


1049

Preparation and evaluation of sirolimus sustained release tablets based on mesoporous silicon loaded self-microemulsion

HUANG Wen-ting^{1,2}, LIU Zhi-hong¹, ZHANG Ling-na³, ZENG Ling-jun¹, ZHANG Qian^{2*}, SONG Hong-tao^{1*}

(1. 900TH Hospital of Joint Logistics Support Force, Fuzhou 350025, China; 2. Department of Pharmacy, Fujian Medical University, Fuzhou 350108, China; 3. Fujian Medical Products Administration, Fuzhou 350003, China)



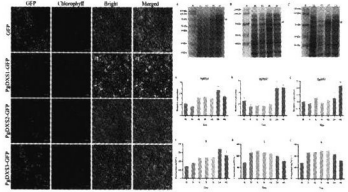
The experimental results indicated that sirolimus self-microemulsion-mesoporous silicon sustained-release tablets which used the commercial sirolimus tablets as references released slowly *in vitro* and *in vivo* and was expected to alleviate the toxicity of the drug, providing a reference for the solubilization of other insoluble drugs and the research and development of sustained-release preparations.

1059

Prokaryotic expression, subcellular localization and enzymatic activity analysis of DXS gene from *Platycodon grandiflorum*

DONG Nan¹, YU Han-wen¹, LIU Meng-li¹, LI Jing¹, CHEN Bo-wen¹, CHANG Xiang-wei¹, WANG Ju-tao¹, ZHA Liang-ping^{1*}, GUI Shuang-ying^{1,2,3,4*}

(1. School of Pharmacy, Anhui University of Chinese Medicine, Hefei 230012, China; 2. Institute of Pharmaceutics, Anhui Academy of Chinese Medicine, Hefei 230012, China; 3. Engineering Technology Research Center of Modernized Pharmaceutics, Anhui Education Department (AUCM), Hefei 230012, China; 4. Anhui Province Key Laboratory of Pharmaceutical Technology and Application (AUCM), Hefei 230012, China)



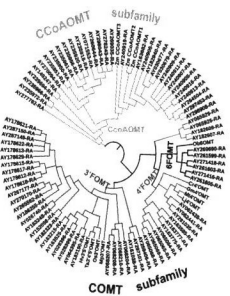
In this study, the *DXS* gene of *Platycodon grandiflorum* was successfully cloned and its prokaryotic expression and subcellular localization were studied. The gene expression level and the changes of gene expression and enzyme activity after methyl jasmonate (MeJA) treatment were detected.

1069

Identification and expression analysis of flavonoid *O*-methyltransferases gene family in *Artemisia argyi*

PENG Sai-nan, LI Yu-kun, LUO Dan-dan, CHEN Chang-jie, ZHOU Jia, LI Jia-yi, ZHENG Jia, LIU Da-hui*, MIAO Yu-huan*

(Hubei University of Chinese Medicine, Resource Center for Chinese Materia Medica, Wuhan 430065, China)



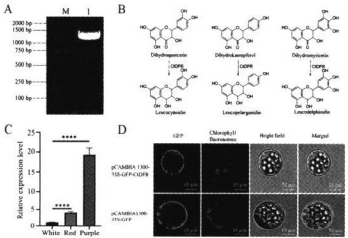
This paper carried out the whole genome mining and identification of flavonoid *O*-methyltransferase (*FOMT*) genes in *Artemisia argyi* and performed phylogenetic, chromosomal localization, gene sequence characterization, subcellular localization prediction, protein structure, gene structure analysis, and expression pattern analysis, which provided a theoretical basis for further research on the function of *FOMTs* and the biosynthesis of methylated flavonoids in *Artemisia argyi*.

1079

Cloning, expression analysis and enzyme activity verification of dihydroflavonol 4-reductase from *Cistanche tubulosa* (Schenk) Wight flower

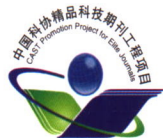
QIU Hai-ling^{1,2}, WANG Fang-ming³, GAO Bo-wen⁴, MI Xin-yu^{1,2}, ZHANG Ze-kun^{1,2}, DU Yu^{1,2}, SHI She-po^{1,2}, TU Peng-fei^{3*}, WANG Xiao-hui^{1,2*}

(1. School of Chinese Pharmacy, Beijing University of Chinese Medicine, Beijing 102488, China; 2. Modern Research Center for Traditional Chinese Medicine, School of Chinese Materia Medica, Beijing University of Chinese Medicine, Beijing 100029, China; 3. State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Science, Peking University, Beijing 100191, China; 4. Baotou Medical College, Baotou 014060, China)



A new *CtDFR* gene was isolated from *Cistanche tubulosa* (Schenk) Wight. *CtDFR* was highly expressed in red and purple flowers, and low expressed in white flowers. The *CtDFR* protein could reduce dihydrokaempferol, dihydroquercetin, dihydromyricetin to leucopelargonidin, leucocyanidin, leucodelphinidin and was mainly localized in the cytoplasm.

ACTA PHARMACEUTICA SINICA
Volume 58 Number 4 2023 April



期刊基本参数: CN 11-2163/R*1953*m*A4*288*zh*P*¥100.00* *32*2023-04

本期责任编辑 岳 瑞

药学报 (YAOXUE XUEBAO) (月刊, 1953 年 7 月创刊) 主管单位: 中国科学技术协会 主办单位: 中国药学会 (http://www.cpa.org.cn) 中国医学科学院药物研究所 (http://www.imm.ac.cn) 编辑出版: 药学报编辑部 (100050 北京市先农坛街 1 号) 电话/传真: 86-10-63026192, 63035012; 电子信箱: yxxb@imm.ac.cn ; 网址: http://www.yxxb.com.cn 主编: 王晓良 印刷: 北京科信印刷有限公司 国内订购: 全国各地邮电局 发行范围: 公开发行 国 内: 北京报刊发行局 国 外: 中国国际图书贸易集团有限公司 (北京市 399 信箱, 100044)	ACTA PHARMACEUTICA SINICA (Monthly, Founded in 1953 July) Directed by: China Association for Science and Technology Sponsored by: Chinese Pharmaceutical Association (http://www.cpa.org.cn) Institute of Materia Medica, Chinese Academy of Medical Sciences (http://www.imm.ac.cn) Edited and Published by: Editorial Office of Acta Pharmaceutica Sinica (1 Xiannongtan Street, Beijing 100050). Tel / Fax: 86-10-63026192, 63035012; E-mail: yxxb@imm.ac.cn ; http://www.yxxb.com.cn Editor-in-chief: WANG Xiao-liang Printed by: Beijing Kexin Printing Co., Ltd. Domestic subscriptions: Local Post Offices Distribution Domestic: Beijing Post Offices Foreign: China International Book Trading Corporation, PO Box 399, Beijing 100044, China
--	---

ISSN 0513-4870	2023 年 第 58 卷 第 4 期	2023 年 4 月 12 日出版	邮发代号: 2-233
CN 11-2163/R	2023, Vol. 58, No. 4	Publication Date: 2023-04-12	Code number: M105
			国内定价: 每期 100.00 元



万方数据

