药用紫草醌类化合物及其药理活性研究进展

廖 梅[1*],吴凌凤[1],姜宏梁[2]

[1]嘉应学院医学院,梅州 514031;[2] 华中科技大学同济药学院,武汉 430030

摘 要:紫草是我国传统中药,收载于《中国药典》,有凉血,活血,解毒透疹之功效。紫草的化学成分分为脂溶性和水溶性两大部分,其中脂溶性的醌类化合物为其主要活性成分,包括紫草素类及其二聚体、紫草呋喃类、苯醌类及苯酚类等混源萜类化合物。研究表明药用紫草醌类化合物具有广泛的药理活性,如抗肿瘤、抗菌、抗病毒、抗炎等活性,近年来,尤其在抗肿瘤药物的研究和开发中,该类化合物已经受到国内外学者的极大关注。为了更好的研究和开发这类天然产物,该文综述了近年来药用紫草的醌类化合物和药理活性进展并讨论了这些化合物的研究前景,为药用紫草的深入研究和开发利用提供依据。

关键词:紫草;化学成分;药理活性;研究进展

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Reviews on natural quinones and their bioactivities of medicinal Zicao

LIAO Mei[1*],WU Ling-feng[1],JIANG Hong-liang[2]

[1]*School of Medicine,Jiaying University,Meizhou 514031,China*;

[2]*Tongji School of Pharmacy,Huazhong University of Science and Technology,Wuhan 430030,China*

Abstract:Medicinal Zicao is a traditional Chinese medicine that is recorded in the *Chinese Pharmacopoeia*. It is mainly used in clinical practice such as cooling blood,invigorating the circulation of blood,detoxification and clearing rash. The chemical components of medicinal Zicao mainly consist of liposoluble and water-soluble parts. Among them,liposoluble quinones are the main active components,including shikonins and its dimers,shikonofurans,benzoquinones,phenols and other meroterpenoids. It has been shown that these chemical components exhibit significant activities in cytotoxic,antioxidant,anti-inflammatory,antibacterial and antiviral effect,etc. In recent years,they have attracted wide attention,especially on the anti-tumor activity throughout the world. For further investigation of Zicao,the progress in the anti-tumor,antibacterial,antiviral,anti-inflammatory and other activities of shikonins,shikonin dimers,shikonofurans,benzoquinones,phenols and other meroterpenoids from medicinal Zicao in recent years have been reviewed and discussed. This article aims to assist discovery and identification of more natural quinones from Boraginaceae plants and provide reference for the development and utilization of medicinal Zicao.

Key words:medicinal Zicao;chemical components;pharmacological activities;review

药用紫草为紫草科(Boraginaceae)多年生草本植物,始载于《神农本草经》,列为中品,药用其根部。作为紫草入药的有紫草属(*Lithospermum*),软紫草属(*Arnebia*)和滇紫草属(*Onosma*)中多种植物[1,2],其中拟紫草属植物新疆紫草 *Arnebia euchroma*(Royle) Johnst(软紫草),内蒙紫草 *Arnebia guttata* Bunge(黄花软紫草)和紫草属植物紫草 *Lithospermum erythrorhizon* sieb. et zucc.(硬紫草)是我国药用紫草的主要来源。历届中国药典(1990 年、1995 年、2000 年版)中均收录了以上 3 种植物作为紫草入药,然而自 2005 版开始将硬紫草除去,只保留了前两者作为《中国药典》收录的基原植物。紫草味苦,性寒。有凉血、活血、解毒和透疹的功能,主治血热毒盛、斑疹紫黑、麻疹不透、疮疡、湿疹和水火烫伤等症。现代药理学证明,药用紫草在许多难治性疾

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*通信作者 Tel:86-015016269891;E-mail:yaoxueliaomei@163.com

病如肿瘤、艾滋病、过敏性紫癜、银屑病[3]等显现出非常好的疗效,已引起国内外学者的广泛关注,在资源、植物化学、药理学等方面的研究正逐渐深入[4]。

药用紫草的化学成分分为脂溶性和水溶性两大部分,其中脂溶性的醌类化合物为其主要活性成分,包括紫草素类、紫草素二聚体、紫草呋喃类、苯醌类及苯酚类。本文就近年来药用紫草的醌类化合物及其药理活性进行了综述,为该药材及近缘植物资源的进一步研究和开发提供参考。

1　紫草素类

1.1　抗肿瘤活性

紫草素类化合物包括紫草素或其对映异构体阿卡宁以及它们与小分子羧酸的成酯衍生物,其本质为羟基萘醌类化合物,同时紫草素类成分也是紫草科植物专属的特征性成分,到目前为止,仅在该科植物中报道过。早在 1922 年,日本化学家 Majima 和 Kuroda 首次以酯的形式从硬紫草中分离得到紫草素类化合物,并阐明紫草素具有 5,8-二羟基-1,4 萘醌的结构[5]。到了 1936 年,德国科学家 Brockmann 更正并最终确立了紫草素的现有结构,提出硬紫草中存在两种旋光异构体:紫草素和阿卡宁[6]。直到 1961 年,Arakawa 发现紫草素在水溶液中经臭氧和过氧化氢分解,产生苹果酸二甲酯,继而转化变为 D(+)-苹果酰胺,从而确定紫草素为 R 构型,阿卡宁则为 S 构型[7](见图 1)。此后,有学者通过圆二色谱和手性 HPLC 的方法测定了紫草素与阿卡宁的比例,并发现两者在不同植物种属中的比例并非恒定不变[8,9]。

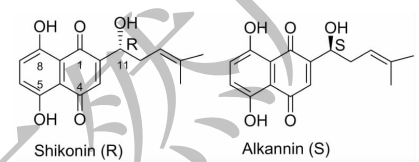


图 1　紫草素和阿卡宁的结构

Fig. 1　Structures of shikonin and alkannin

至今已从不同种属药用紫草中分离到 30 多种紫草素类化合物(见表 1)。从结构上看,这类成分都具有羟基萘醌母核,都含有异己烯侧链,差别在于其旋光性、侧链中羟基的位置和酰基的不同。紫草素及其衍生物作为紫草的主要有效成分,已经被证实具有抗肿瘤、抗菌、抗病毒、抗炎、促进伤口愈合、抗血栓、抗甲状腺功能亢进、抗免疫功能低下、降血糖、保肝护肝等多种生物活性,特别是其抗肿瘤作用,已被大量研究所证实[10-13],引起了学术界的广泛关注,其中,又以紫草素(**1**)的抗肿瘤活性研究报道最多。紫草素的抗肿瘤机制涉及多个靶点,包括诱导细胞凋亡、诱导细胞坏死、抑制拓扑异构酶、抑制蛋白酪氨酸激酶、抗肿瘤血管生成、影响肿瘤细胞信号传递等一系列的化学预防和治疗途径[14,15]。近年来,国内外学者对紫草素衍生物的抗肿瘤活性和作用机制研究越来越深入。例如:乙酰紫草素(**2**)通过诱导细胞自噬、程序性死亡和靶向 m-TOR/PI3K/Akt 信号通路抑制口腔癌顺铂耐药细胞系 KB-R 细胞的肿瘤发生[16],也能通过 ROS 介导的 Caspase 激活诱导 HepG2 cell 肝癌细胞凋亡[17]。异丁酰紫草素(**4**)能显著抑制人结肠癌细胞增殖,诱导早期凋亡,改变细胞的周期分布[18]。另有研究显示异丁酰紫草素、α-甲基丁酰紫草素(**7**)、异戊酰紫草素(**6**)和β,β-二甲基丙烯酸紫草素(**8**)对黑色素瘤细胞 SBcl2、WM35、WM9 和白血病细胞株 U937、WM164、Jurkat、Molt4、CCRF-CEM 等肿瘤细胞表现生长抑制活性,抑制 c-MYC 的表达,影响 AKT、ERK1/2 和 SAPK/JNK 的磷酸化,其活性均高于紫草素[19]。β,β-二甲基丙烯酰紫草素对人肺癌 A549[20]、人结肠癌 HCT-116[21]、胃癌 SGC-7901[22]、SMMC-7721[23]等肿瘤细胞显示体内或体外生长抑制活性。β-羟基异戊酰紫草素(**13**)对 U937 和肺癌细胞 DMS 114 等具有抑制作用[24],对人绒毛膜癌细胞株 BeWo 具有诱导细胞凋亡的作用[25]。本课题组在 LC-MS/MS 技术的指导下从新疆紫草二氯甲烷部位系统分离并鉴定了 19 个紫草素类化合物,体外抗肿瘤活性筛选结果显示,各化合物对 A549、HCT116、HepG2、HeLa 细胞体外增值均有不同程度的抑制作用,其中紫草素、1-methoxyacetylshikonin、α-甲基丁酰紫草素对 A549 的 IC_{50} 分别为 1.10、1.30 和 0.74 μmol/L,抗肿瘤活性明显,具有较好的开发利用前景。LC-MS/MS 进一步分析发现药用紫草中至少存在 73 种该类成分,有待进一步深入挖掘。

1.2　抗菌活性

文献报道紫草素类化合物对多种细菌表现抗菌活性[26-28]。紫草素对多种常见菌株包括革兰阳性菌、革兰阴性菌以及真菌显示出抗菌作用,对金黄色葡萄球菌、大肠埃希菌、白色念珠菌、蜡状芽孢杆菌、沙门氏菌、伤寒杆菌等的生长有显著抑制作用,抗菌能力与左氧氟沙星相当[29]。紫草素及其衍生物对于具有 NorA 外泵蛋白的多药耐药金葡菌菌株、标

准金黄色葡萄球菌、耐甲氧西林金葡菌株的耐药菌株、大肠杆菌、枯草杆菌等具有明显抑制作用[30]；在一项以生物活性为导向的提取分离实验中显示乙酰阿卡宁及乙酰紫草素、异戊酰紫草素、α-甲基丁酰阿卡宁及 α-甲基丁酰紫草素，异丁酰阿卡宁和 β,β-二甲基丙烯酰紫草素(**8**)，对耐甲氧西林金黄色葡萄球菌(MRSA)和耐万古霉素肠球菌(F935、CKU-17)表现抑菌活性[27]。它们抗 MRSA 的最低抑菌浓度为 1.56 ~ 3.13 μg/mL，作用强于紫草素和阿卡宁(MIC = 6.25 μg/mL)，抗 F935 和 CKU-17 的活性也优于紫草素和阿卡宁。研究表明紫草素对抗 MRSA 的作用机制与肽聚糖的亲和力、细胞膜的通透性、以及 ATP 结合盒(ABC)转运蛋白活性有关[26]。以上研究表明紫草素及其衍生物作为一种潜在而有效的天然抗生素，具有极大的开发利用前景。

1.3 抗病毒活性

紫草对单纯疱疹病毒、乙型肝炎病毒、人类乳头瘤病毒、带状疱疹病毒及甲型肝炎病毒等均有抗病毒作用[31-33]。关于紫草抗病毒的有效成分尚未达成共识，目前认为发挥作用的主要是紫草素及其衍生物。研究表明紫草素具有抗腺病毒的作用，作用方式是抑制腺病毒的复制，其机制可能与减少细胞凋亡、抑制腺病毒六邻体蛋白表达有关，该结果提示紫草素具有成为天然、高效、低毒的抗腺病毒药物的潜力[34]。Luo 等[35]采用血细胞凝集反应及细胞病变法研究左旋紫草素的抗副流感病毒作用，结果显示其在实验所用的质量浓度范围内毒性较低，且具有一定的体外抗副流感病毒的作用。这一研究结果为紫草素的抗病毒作用又增添了新的内容，也为其在临床上的进一步广泛应用提供了有价值的实验依据。Cocchi 等[36]研究了紫草素对趋化因子受体功能和 HIV-1 复制的影响，结果显示，紫草素在纳摩尔浓度下能够抑制单核细胞的趋化性。在巨噬细胞中，紫草素还能显著下调 HIV-1 辅助受体 CCR5 的表达和 mRNA 水平。此外，紫草素还能抑制人外周血单个核细胞中多药耐药病毒株和儿科临床 HIV 分离株的复制，IC_{50} 为 96 ~ 366 nmol/L；紫草素还有效抑制单核细胞/巨噬细胞中 HIV Ba-L 分离株的复制，IC_{50} 为 470 nmol/L，提示紫草素发挥抗 HIV-1 作用与其干扰趋化因子受体的表达和功能有关。因此，紫草素作为天然存在的低分子量泛趋化因子受体抑制剂，有望开发为新型抗 HIV 治疗剂。

1.4 抗炎活性

紫草、紫草素及其衍生物治疗烧烫伤、湿疹、银屑病、过敏性紫癜、关节炎、静脉炎、妇科炎症、急性肺损伤、重症急性胰腺炎伴肺损伤或肝损伤、局部脑缺血等多种疾病的实验研究正逐步深入，多认为其抗炎机制与 NF-κB、IL-1β、IL-6、TNF-α、NO、CCR、COX-2、IL-22、IL-17 等密切相关[37]。例如：紫草素、乙酰紫草素、β,β-二甲基丙烯酰紫草素的抗炎作用可能是通过抑制 LPS 刺激的 RAW 264.7 细胞 ERK 磷酸化，下调 NF-kappaB 的活化，从而抑制 iNOS 蛋白的表达[38]；亦能通过 TLR4 介导的信号通路活化 NF-κB，抑制 IL-1β、IL-6、TNF-α 和 NO 的分泌，并促进 IL-10 的分泌[39,40]，降低巨噬细胞中高迁移率族蛋白的表达；或者封锁 NF-κB-P65 从细胞质到细胞核的易位，抑制炎症反应相关酶体活性[41]等途径发挥抗炎疗效；此外，紫草素还可以抑制 IL-22 介导的细胞增殖以及抑制角质形成细胞分泌促炎性反应因子 S100A7、S100A8，从而减轻炎性反应[42]。

另外，紫草素对某些特异性的炎症模型如急性肺损伤[43]、胶原性关节炎[44]、类风湿性关节炎[45]、缺血性脑血管损伤[46]亦表现很好的保护作用。

研究表明紫草素可显著降低急性肺损伤(ALI)小鼠体内 PBMC 促炎症因子 TNF-α、IL-1β、IL-8 的产生和中性粒细胞的浸润，减轻病理学改变，减轻肺水肿，降低肺组织匀浆中的 MPO 活性和 NO 浓度，使肺组织中 iNOS、COX-2 和核蛋白中 NF-κB 水平下降，提示紫草素对 LPS 诱导的 ALI 具有保护作用，其机制可能与紫草素抑制 NF-κB、iNOS 和 COX-2 有关[43]。一项探讨紫草素对晚期胶原性关节炎的作用研究显示紫草素能够免疫干预已发病的胶原性关节炎小鼠，降低关节炎评分，阻止软骨破坏，其机制可能为紫草素通过抑制 Th1 细胞因子的表达发挥抗炎症作用[44]。此外，紫草素可通过抑制 COX-2 mRNA 基因表达，减少炎症性细胞因子的产生而发挥其对类风湿关节炎的免疫抗炎作用，这为开发紫草素成为 COX-2 抑制剂提供实验基础[45]。紫草素在缺血性脑血管病中发挥神经保护作用的机制可能为下调 TLR4、p-p38MAPK、NF-κB、TNF-α、MMP-9 的表达，上调 claudin-5 的表达，改善血脑屏障渗透性[46]。在一项探讨紫草素对单侧输尿管梗阻性肾病诱导的小鼠纤维化模型的治疗作用和潜在调控机制研究中，结果显示紫草素治疗后，肾功能改善，病理染色显示肾小管损伤明显改善，纤维化减少；免疫

印迹结果显示紫草素能够抑制 TGF-β/Smad 信号通路中关键蛋白 Smad 3 活化,上调 Smad 7 表达,而 TGF-β 和长链非编码 Erbb4-IR 的基因表达均呈现剂量依赖性下降,提示紫草素可有效减轻肾脏纤维化,其机制可能与调节 Smad3/Erbb4-IR 轴相关[47]。

1.5　其它活性

紫草素及其衍生物还表现一些其它药理活性。在一项考察乙酰紫草素,异丁酰紫草素和β-羟基异戊酰紫草素(**13**)对人胆固醇酰基转移酶(hACAT)的抑制活性研究,发现异丁酰紫草素对 hACAT-2 的抑制活性(IC_{50} = 57.5 μM)强于 hACAT-1,而乙酰紫草素和β-羟基异戊酰紫草素对 hACAT-1 和 hACAT-2 的抑制活性均很弱,而紫草素衍生化后活性较强[48]。Gwon 等[49]采用高脂饮食喂养 C57BL/6J 小鼠建立动物肥胖模型,研究发现硬紫草乙醇提取物能减轻肥胖小鼠体重、白脂肪组织重量、血清甘油三酯和总胆固醇水平和肝脏脂质水平,并减少促进脂肪生成的基因表达;而乙酰紫草素(**2**)能抑制脂肪细胞分化,减少 3T3-L1 细胞内成脂转录因子的表达。Chen 等[50]研究显示紫草素对于 Aβ_{25-35}诱导的阿尔兹海默病细胞(AD)具有保护作用,可以有效减少细胞凋亡,增加细胞活力,改善线粒体功能。同时还可以抑制 AD 细胞内 ROS 的累积,减少氧化应激导致的细胞死亡,可作为预防和治疗 AD 的神经保护候选物。Singh 等[51]从亚历山大软紫草 *Arnebia hispidissim*a 中分离得到 teracrylshikonin(**9**)、乙酰紫草素、arnebin-5(**19**)和 arnebin-6(**20**)并发现它们对前列腺素的生物合成有抑制作用。

2　紫草素二聚体类

早在 1949 年,Toribara 等[52]在水解欧紫草 *Alkanna tinctoria* 的阿卡宁提取物时发现阿卡宁/紫草素二聚体存在,它们与阿卡宁的单聚物有不同的理化性质,如颜色变深、光学活性消失、分子量变大、无升华现象。然而直到近代,Assimopoulou 和 Spyros 等[53,54]开始采用空间排阻色谱和 HPLC-DAD-MS 对紫草素/阿卡宁的聚合物进行分析并分离到一个二聚物,初步确定了其化学结构。迄今已报道了 4 个此类化合物,分别为 6-(11′-deoxyalkannin)-alkannin/shikonin(含两个非对映异构体)、6-(11′-deoxyalkannin)-alkannin/shikonin acetate、6-(11′-deoxyalkannin)-alkannin/shikonin β,β-dimethylacrylate(**29** ~ **31**)。结构研究显示它们只是侧链上 11′-C 简单地与另一萘醌结构母核的 6-C 相连,2 个单体间未成环。

此外,文献检索表明还存在另一类紫草素二聚体。1994 年,Piccione 等[55]采用紫草素经人体肠细菌 *Bacteroides fragillis* subsp. Thetaotus 生物转化之后得到四个新的紫草素二聚体 shikometabolins A-D(**32** ~ **35**)。此后,我国学者 Yang 等[56]从硬紫草 *Lithospermum erythrorhizon* 提取物中分离得到 shikometabolin A(**32**)、shikometabolin E(**36**)和 shikometabolin F(**37**),并发现他们具有明显的神经氨酸酶抑制活性。本课题组 LC-MS/MS 分析研究表明新疆紫草、内蒙紫草和硬紫草中均存在紫草素二聚体类化合物[57,58]。以上研究表明紫草素二聚体类化合物在经过高温、光照或生物转化时有可能发生聚合,提示该类成分可能不稳定,紫草药材应选择适当的储存条件。

3　紫草呋喃类

课题组前期研究表明紫草呋喃类成分为呋喃对苯二酚类衍生物,比紫草素类成分的极性稍大,在各种属紫草根中含量低微,目前仅在硬紫草和新疆紫草中分离得到过[59]。早在 1982 年,日本学者 Yoshizaki 等[60]就从硬紫草 *Lithospermum erythrorhizon* 根中分离得到了 5 个紫草呋喃类化合物 shikonofurans A-E(**39** ~ **43**),没有报道其活性数据。直到 2005 年 Choi 等[61]报道 shikonofurans E 具有微弱的单胺氧化酶抑制活性(IC_{50} = 59.1 μM),而同等条件下乙酰紫草素和紫草素的抑制活性相对较强(IC_{50} 分别为 10.0 和 13.3 μM)。此后,Ji 等[62]研究发现 shikonofuran D、shikonofuran E、shikonofuran C 对唾液酸糖基水解酶 GH 33 和 GH 34 显示较强抑制活性,其中 shikonofuran E 对 GH33 的活性最强(IC_{50} = 0.24 μM)。酶动力学实验显示它们均为竞争性、可逆性的弱结合抑制剂。2019 年,Ahn 等[63]从硬紫草 *Lithospermum erythrorhizon* 根中分离得到一个新的呋喃对苯二酚衍生物 shikonofuran J(**44**)以及已知化合物 shikonofuran D 和 shikonofuran E。结果显示它们均能抑制 TNF-α 诱导的 HaCaT 细胞中 IL-6 的产生,其中 shikonofuran D 和 shikonofuran E 的抑制作用较强,其 IC_{50}值分别为 13.5 和 6.0 μM,并能显著降低 IL-6 基因表达。Shikonofuran E 对 TNF-α 预处理的角质形成细胞具有毒性(< 50%,40 μm)。Cao 等[64]研究发现 shikonofuran E 在脂多糖刺激的 RAW 264.7 巨噬细胞中能通过下调 MAPK 和 NF-κB 信号通路发挥抗炎作用。

4 其他混源萜类

Dong 等[65]从昆明紫草 *Onosma paniculatum* 甲醇提取物中分离到 4 个新的萘醌类化合物 shikometabolin G(**38**)以及 naphthofuranin A-C (**45 ~ 47**),其中化合物 **46**、**47** 对 NO 的生成具有良好抑制作用(IC_{50} = 0.4 ~ 16.5 μM),提示它们具有潜在的抗炎作用。Yao 等[66]从新疆紫草 *Arnebia euchroma* 中分离出几个单萜苯酚及苯醌类化合物(**48 ~ 51**)。Wang 等[67]从新疆紫草 *Arnebia euchroma* 根中分离到 7 个对苯二酚类化合物(**52 ~ 59**)。并评价了各化合物对人肝癌细胞系 SMMC-7721、HepG2、QGY-7703 和 HepG2/ADM 的细胞毒性,结果显示各化合物对各细胞均显示一定细胞毒性,其中化合物 **55**、**56**、**59** 活性显著。

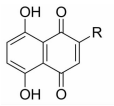
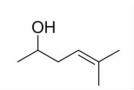
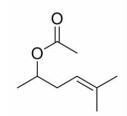
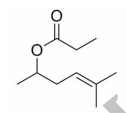
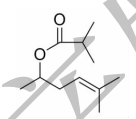
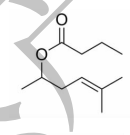
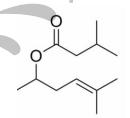
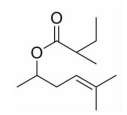
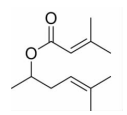
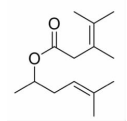


图 2 紫草素类化合物的结构骨架

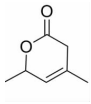
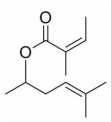
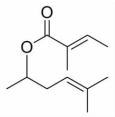
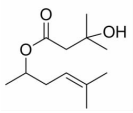
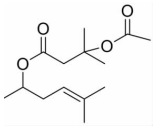
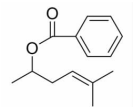
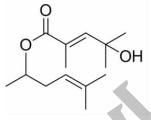
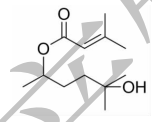
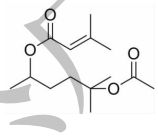
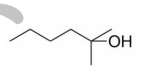
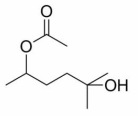
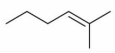
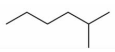
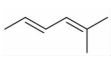
Fig. 2 Structure skeleton of shikonins

表 1 药用紫草中已分离得到的醌类化合物

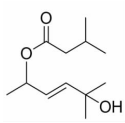
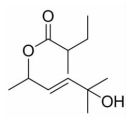
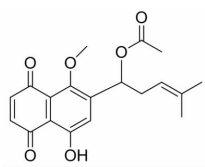
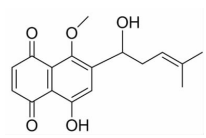
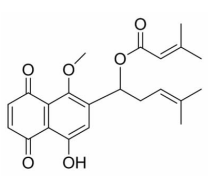
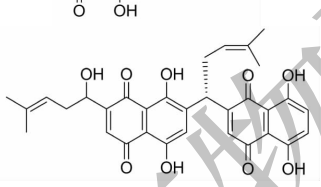
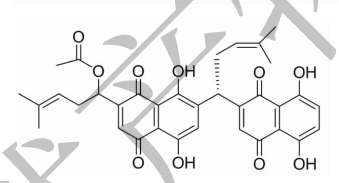
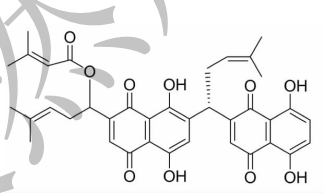
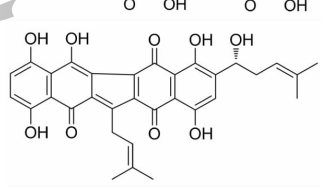
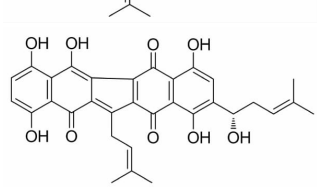
Table 1 Natural quinones isolated from medicinal Zicao

编号 No.	R	化合物 Compound	参考文献 Reference
1		紫草素 或阿卡宁	*Arnebia euchroma*[27] *Lithospermum erythrorhizon*[68] *Arnebia gutatta*[69]
2		乙酰紫草素 或乙酰阿卡宁	*Arnebia euchroma*[27] *Lithospermum erythrorhizon*[70] *Arnebia gutatta*[69]
3		丙酰紫草素 或丙酰阿卡宁	*Lithospermum erythrorhizon*[71] *Arnebia euchroma*[72]
4		异丁酰紫草素 或异丁酰阿卡宁	*Arnebia euchroma*[27] *Lithospermum erythrorhizon*[48] *Arnebia gutatta*[69]
5		丁酰紫草素 或丁酰阿卡宁	*Arnebia euchroma*[73]
6		异戊酰紫草素 或异戊酰阿卡宁	*Arnebia euchroma*[27] *Lithospermum erythrorhizon*[71] *Arnebia gutatta*[69]
7		α-甲基丁酰紫草素 或 α-甲基丁酰阿卡宁	*Arnebia euchroma*[27] *Lithospermum erythrorhizon*[71] *Arnebia gutatta*[69]
8		β,β-二甲基丙烯酰紫草素 或 β,β-二甲基丙烯酰阿卡宁	*Arnebia euchroma*[74] *Arnebia gutatta*[69] *Lithospermum erythrorhizon*[75]
9		Teracrylshikonin	*Arnebia euchroma* [74] *Arnebia densiflora*[76] *Arnebia hispidissima*[51]

续表 1(Continued Tab. 1)

编号 No.	R	化合物 Compound	参考文献 Reference
10		5,8-dihydroxy-2-(4-methyl-6-oxo-5,6-dihydro-2H-pyran-2-yl)-[1,4]naphthoquinone	*Onosma echioides*[77]
11		Angelylshikonin	*Echium italicum* L.[78]
12		Tigloylshikonin	*Lithospermum erythrorhizon*[79]
13		β-羟基异戊酰紫草素或β-羟基异戊酰阿卡宁	*Lithospermum erythrorhizon*[48] *Arnebia euchroma*[24,25]
14		β-Acetoxy-isovalerylshikonin or β-acetoxy-isovalerylalkannin	*Arnebia gutatta*[69] *Arnebia euchroma*[69] *Lithospermum erythrorhizon*[69]
15		Benzoylshikonin	*Moltkiopsis ciliata*[80]
16		Anthraquinone I	*Lithospermum erythrorhizon*[81]
17		β,β-Dimethylacryl-hydroxyalkannin	*Arnebia euchroma*[82]
18		Acetylarnebin-2	*Onosma heterophylla*[83]
19		Arnebin-5	*Arnebia hispidissima*[51]
20		Arnebin-6	*Arnebia hispidissima*[51]
21		Deoxyshikonin or Deoxyalkannin	*Lithospermum erythrorhizon*[84] *Arnebia gutatta*[69]
22		Alkannan	*Lithospermum erythrorhizon*[85]
23		Anhydroalkannin	*Arnebia euchroma*[86]

续表 1(Continued Tab. 1)

编号 No.	R	化合物 Compound	参考文献 Reference
24		Lithospermidin-A	*Lithospermum erythrorhizon*[87]
25		Lithospermidin-B	*Lithospermum erythrorhizon*[87]
26		1-Methoxyacetylshikonin	*Arnebia euchroma*[88] *Echium lycopsis*[89]
27		Onosone B	*Onosoma hispidum*[90]
28		Onosone A	*Onosoma hispidum*[90]
29		6-(11′-Deoxyalkannin)-alkannin/shikonin	*Alkanna tinctoria*[53]
30		6-(11′-Deoxyalkannin)-alkannin/shikonin acetate	*Alkanna tinctoria*[53]
31		6-(11′-Deoxyalkannin)-alkannin/shikonin β,β-dimethylacrylate	*Alkanna tinctoria*[53]
32		Shikometabolins A	*Lithospermum erythrorhizon*[56]
33		Shikometabolins B	*Bacteroides fragillis*[55]

续表 1(Continued Tab. 1)

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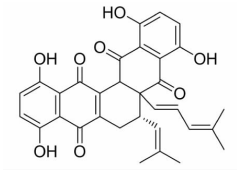
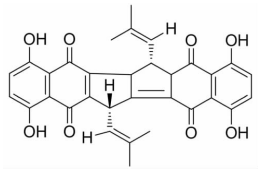
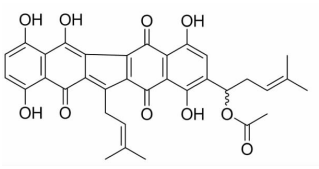
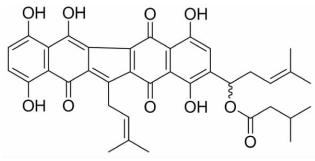
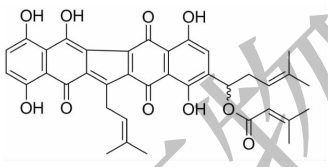
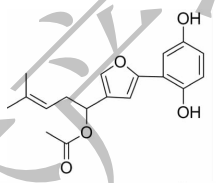
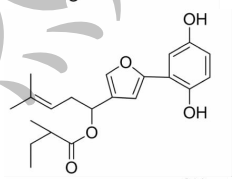
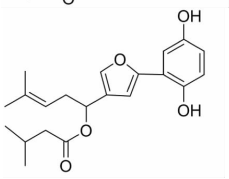
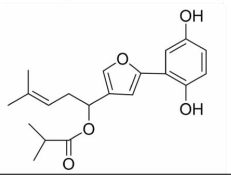
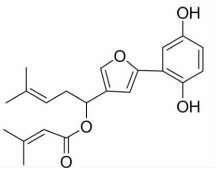
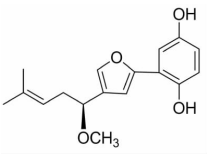
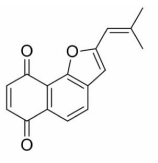
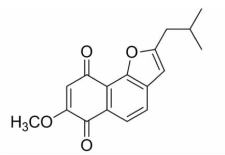
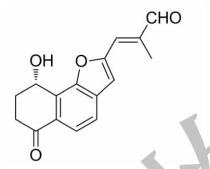
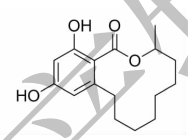
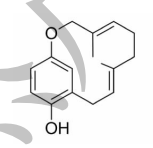
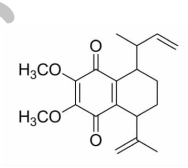
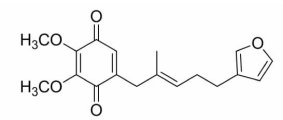
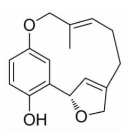
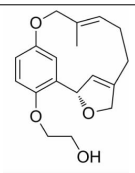
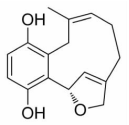
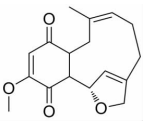
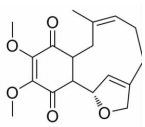
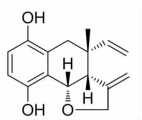
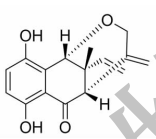
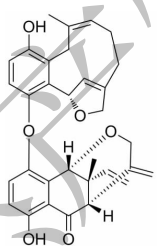
34		Shikometabolin C	*Bacteroides fragillis*[55]
35		Shikometabolin D	*Bacteroides fragillis*[55]
36		Shikometabolins E	*Lithospermum erythrorhizon*[56]
37		Shikometabolins F	*Lithospermum erythrorhizon*[56]
38		Shikometabolin G	*Onosma paniculatum*[65]
39		Shikonofuran A	*Lithospermum erythrorhizon*[60], *Arnebia euchroma*[67]
40		Shikonofuran B	*Lithospermum erythrorhizon*[60]
41		Shikonofuran C	*Lithospermum erythrorhizon*[60]
42		Shikonofuran D	*Lithospermum erythrorhizon*[60]

续表 1(Continued Tab. 1)

编号 No.	R	化合物 Compound	参考文献 Referrence
43		Shikonofuran E	*Lithospermum erythrorhizon*[60], *Arnebia euchroma*[67]
44		Shikonofuran J	*Lithospermum erythrorhizon*[63]
45		Naphthofuranin A	*Onosma paniculatum*[65]
46		Naphthofuranin B	*Onosma paniculatum*[65]
47		Naphthofuranin C	*Onosma paniculatum*[65]
48		Des-*O*-methyllasiodiplodin	*Arnebia euchroma*[66]
49		Arnebinol	*Arnebia euchroma*[66]
50		Arnebinone	*Arnebia euchroma*[66]
51		Arnebifuranone	*Arnebia euchroma*[67][69]
52		9,17-Epoxyarnebinol	*Arnebia euchroma*[67]

续表 1(Continued Tab. 1)

编号 No.	R	化合物 Compound	参考文献 Reference
53		3*E*,9*S*-10-O-(1,2-diolethane)-9,17-epoxyarnebino	*Arnebia euchroma*[67]
54		Arnebinol B	*Arnebia euchroma*[67]
55		Arnebinone B	*Arnebia euchroma*[67]
56		3*E*,9*S*-10-O-(1,2-diolethane)-9,17-epoxyarnebino	*Arnebia euchroma*[67]
57		Meroterpenoid 6	*Arnebia euchroma*[67]
58		Meroterpenoid 7	*Arnebia euchroma*[67]
59		Meroterpenoid 8	*Arnebia euchroma*[67]

5　讨论

药用紫草脂溶性化学成分研究主要集中于硬紫草、新疆紫草和滇紫草属植物,有关内蒙紫草的研究报道较少。主要成分紫草素类化合物在抗肿瘤、抑菌、抗炎、抗病毒和免疫调节方面展示了多种药理活性。其中紫草素及其衍生物的抗肿瘤活性报道最多,又以紫草素这一单体的研究最为透彻。然而,目前对于紫草素及其衍生物的研究仍然停留在实验室基础研究阶段,涉及初步药效学、药动学特性和安全性等成药性评价方面的研究报道较少。现行中国药典也明确规定:“药用紫草作为外用药,熬膏或用植物油浸泡涂擦”,紫草素及其衍生物能否作为体内制剂开发还有待继续深入研究。因此,继续深入开展对紫草素类成分的药理活性筛选及其药代动力学评价等方面的研究将具有重要意义。

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