Global Science Publishing

# 天然产物对酒精性肝损伤的保护作用研究进展

**崔新妍[1]，娄在祥[1*]，段文杰[2]，段光志[2]**
1．江南大学食品学院，江苏无锡
2．湖北仙之灵食品有限公司，湖北荆门

**摘要：**酒精性肝损伤是指由于长期或短期内大量饮酒引起的肝组织病变，逐渐会发展为脂肪肝、酒精性肝炎、纤维化、肝硬化和肝癌。近年来，天然产物因其靶点多、毒性低且副作用少的优点而受到越来越多的关注，一些天然产物及其活性成分被证明对酒精性肝损伤具有显著的保护作用。本文综述了酒精性肝损伤的主要发病机制，包括乙醇代谢、氧化应激、炎症反应、脂质代谢异常和肠道菌群失调等方面，以及天然产物对酒精性肝损伤的防护作用和机制，以期为天然产物的进一步开发和利用提供参考。

**关键词：**天然产物；酒精性肝损伤；发病机制；保护作用

# Research Progress on the Protective Effects of Natural Products against Alcoholic Liver Injury

**Xinyan Cui[1], Zaixiang Lou[1*], Wenjie Duan[2], Guangzhi Duan[2]**
1. School of Food Science and Technology, Jiangnan University, Wuxi, Jiangsu
2. Hubei Xianzhiling Foods Corporation, Jingmen, Hubei

**Abstract:** Alcoholic liver injury refers to liver tissue lesions caused by long-term or short-term heavy drinking, which can gradually develop into fatty liver, alcoholic hepatitis, fibrosis, cirrhosis, and liver cancer. In recent years, natural products have attracted increasing attention due to their multiple targets, low toxicity, and fewer side effects. Some natural products and their active components have been proven to have significant protective effects on alcoholic liver injury. This article reviews the main pathogenic mechanisms of alcoholic liver injury, including ethanol metabolism, oxidative stress, inflammatory response, lipid metabolism abnormalities, and intestinal flora disorders, as well as the protective effects and mechanisms of natural products on alcoholic liver injury, in order to provide references for the further development and utilization of natural products.

**Keywords:** Natural products; Alcoholic liver injury; Pathogenesis; Protective effects

* 第一作者简介：崔新妍（2001-），女，硕士研究生在读，研究方向为食品功能因子。
通信作者简介：娄在祥（1983-），男，博士，副教授，硕士研究生导师，主要从事食品功能因子和功能食品研究开发。

# 1 引言

酒精性肝损伤（Alcohol-induced liver injury, AILI）是指由于长期或短期内大量饮酒导致的肝组织病变[1]，酒精性肝病（Alcoholic liver disease, ALD）是一种由长期大量饮酒而引起的肝病，是慢性肝损伤的主要原因之一[2,3]。ALD的发病率呈上升趋势，给全球公共卫生和世界经济带来巨大负担。ALD在初始阶段表现为酒精性脂肪肝病（Alcoholic fatty liver disease, AFLD），逐渐发展为酒精性肝炎、纤维化和肝硬化，严重者会发生肝细胞死亡、肝功能衰竭和肝细胞癌[4,5]，在确诊为肝硬化的患者中，15%会发展为肝细胞癌[6]。自1990年以来，中国的酒精消费量一直在增加，酗酒者的比例从1982年的0.21%增加到2000年的14.8%，2013年，中国已成为全球第二大饮酒国家，ALD患病率从2000年的2.27%增加到2015年的8.74%[7,8]。ALD已成为一个不可忽视的安全问题，基于我国现在ALD发病率的不断增加和ALD的严重后果，当前迫切需要更多有效和安全的疗法来应对ALD。

如今，对肝脏的保护越来越受到人们的重视，保肝药物尤其是天然产物成为一种有利的治疗方法。天然化合物具有靶点多、毒性低且副作用少的优点，作为预防和治疗ALD的潜在药物受到越来越多的关注[9]，在促进人类健康和治疗疾病方面发挥着至关重要的作用。许多来源于天然产物中的活性成分如当归多糖[10]、黄芩苷[11]、紫甘薯花青素[12]等化合物，都被证明具有缓解AILI的效果。本文旨在总结AILI的发病机制和近年来天然产物在AILI保护中的研究进展，为天然产物的进一步开发和利用提供参考。

# 2 AILI的发病机制

虽然AILI的发病机制尚未完全阐明，但普遍认为AILI与乙醇代谢、肝脏氧化应激、炎症反应、中性粒细胞浸润、脂质代谢失调、肠道菌群失调和铁死亡等过程有关[13-15]。深入了解AILI的发病机制，有助于我们为研发新的治疗方法和药物提供理论依据。

## 2.1 乙醇代谢

当机体摄入乙醇后，少量乙醇会立即在胃中代谢，而大部分剩余的乙醇会被胃肠道吸收，吸收后的乙醇经过门静脉输送到肝脏[16]。当乙醇进入肝脏后主要通过三种代谢途径分解代谢成乙醛，分别是乙醇脱氢酶（ADH）系统、微粒体乙醇氧化系统（MEOS）和过氧化氢酶（CAT）系统[14,17]。

ADH系统先将乙醇氧化成乙醛，产生的乙醛被乙醛脱氢酶（ALDH）进一步氧化为乙酸盐，并且需要烟酰胺腺嘌呤二核苷酸（NAD+）、至少8种ADH同工酶和4种ALDH同工酶的共同参与[18]。MEOS系统主要由细胞色素P450 2E1（CYP2E1）酶构成，CYP2E1在乙醇诱导的氧化应激中发挥作用，也是乙醇氧化的次要途径[19]。在正常条件下，CYP2E1催化少量乙醇（约10%）氧化成乙醛，但在过度饮酒期间，会诱导微粒体系统，并增加CYP2E1蛋白表达。CYP2E1还可以催化乙醛氧化为乙酸盐，但在乙醇存在下反应会减弱。此外，CYP2E1的催化反应还会产生大量的活性氧（ROS）[18]。CAT是一种存在于肝细胞中的过氧化物酶，通过将过氧化氢转化为$H_2O$将乙醇代谢成乙醛参与乙醇代谢[20]。

## 2.2 氧化应激

在乙醇代谢过程中，可以通过激活黄嘌呤氧化酶、CYP2E1和还原型辅酶Ⅱ（NADPH）复合物产生ROS，其中CYP2E1在酒精诱导的肝脏氧化应激中起关键作用[21]。在ALD模型中，酒精摄入会增加肝脏中CYP2E1的表达[22]，肝细胞产生大量ROS，这些ROS需要被肝脏抗氧化防御系统去除，包括超氧化物歧化酶（SOD）、CAT、总抗氧化能力（T-AOC）和谷胱甘肽过氧化物酶（GSH-Px）、非酶抗氧化剂谷胱甘肽（GSH）、食物来源的维生素C和维生素E。然而，长期大量饮酒导致的胃肠道功能障碍减少了食物来源中抗氧化剂的吸收，另一方面体内大量抗氧化剂的消耗和ROS在肝脏中的积累，最终引起氧化应激和脂质过氧化[17]。

### 2.3 炎症反应

炎症是身体防止受伤、感染或暴露于脂多糖（LPS）等有害物质的复杂生理防御过程，这个过程涉及多种免疫防御细胞，如巨噬细胞和先天性淋巴细胞[23]。

当机体酒精摄入增加时，内源性一氧化氮（NO）的产生增加，丙二醛（MDA）含量增加，SOD活性下降，诱导氧化应激，氧化应激会破坏肠上皮细胞之间的紧密连接，降低紧密连接蛋白-1、紧密连接蛋白ZO-1和闭合蛋白Occludin的表达，最终破坏肠粘膜屏障。肠道机械屏障受到破坏会导致肠道通透性增加，促使肠道中一些病原菌、有害代谢产物和大量的LPS穿过肠粘膜屏障进入血液循环，通过门静脉进入肝脏，这些物质会直接损害肝细胞，还会与脂多糖受体结合形成二元复合物，该复合物随后与Kupffer巨噬细胞的膜表面的CD14受体结合，激活Kupffer巨噬细胞，进一步激活NF-κB，释放炎症因子TNF-α、IL-1β和IL-6导致细胞凋亡并并启动特定的细胞内信号级联反应，最终诱导急性AILI、酒精性肝炎和肝纤维化[24,25]。

### 2.4 脂质代谢异常

脂肪变性是ALD的初期表现，最近的研究表明脂肪变性与体内一些调节脂质代谢的因子有关。乙醇作用会抑制几种脂质代谢调节酶的活性[26]，包括AMP活化激酶（AMPK）、过氧化物酶体增殖物激活受体（PPAR）、类视黄醇X受体（RXR）、去乙酰化酶1（SIRT1）和5（SIRT5）等，而上调甾醇调节元件结合蛋白1（SREBP-1）、硬脂酰辅酶A去饱和酶1（SCD1）[27]表达。

AMPK是一种在控制脂肪代谢中起关键作用的酶[28]，在调节糖类、脂质和胆固醇代谢中发挥重要作用，AMPK可被其上游激酶CaMKK2激活[29]。在ALD的动物模型中，乙醇增多会上调microRNA-378b表达，从而抑制CaMKK2-AMPK信号传导[29]，AMPK的活性降低，脂肪酸氧化减少[28]，生成脂肪的基因SREBP-1水平表达增加[30]，脂肪酸合酶FAS相关蛋白质表达增加[31]，脂肪生成增加，从而导致酒精诱导的脂肪肝形成。

过氧化物酶体增殖物激活受体α（PPARα）也是肝脏脂质代谢的主要调节因子，肝脏中游离脂肪酸水平的增加会激活PPARα的表达，促进游离脂肪酸的β氧化，PPARα还可以通过诱导丙二酰辅酶A脱羧酶来抑制脂肪生成途径，从而促进脂肪酸生物合成前体丙二酰辅酶A的降解，而乙醇会降低PPARα蛋白水平，脂肪酸β氧化减少导致脂肪肝[26]。

### 2.5 肠道菌群失调

肠道菌群失调也与ALD相关，其影响菌群失调影响ALD的机制主要包括：胆汁酸代谢异常导致肠道细菌过度生长；微生物产物（如毒素）促进肝脏炎症和疾病；短链脂肪酸（Short-chain fatty acids, SCFAs）产生减少，进而加重肠道屏障功能损伤，导致肠道通透性，最终引发肝脏炎症；内毒素可以通过破坏肠道屏障进入肝脏，激活免疫细胞，加剧肝脏损伤[32]。

## 3 天然产物对AILI的保护作用

### 3.1 单一天然产物对AILI的保护作用

#### 3.1.1 葛根

葛根为豆科植物野葛（Pueraria lobate (Willd.) Ohwi）的干燥根，作为一种药食同源植物在中国已有悠久的历史，在古书《神农本草经》、《千金方》、《验方新编》、《食疗本草》、《证类本草》等中被记载有清热、消渴和解酒等功效[33,34]。

葛根提取物可以通过肝-肠-脑轴改善AILI，葛根提取物可以有效降低血清谷丙转氨酶（ALT）、谷草转氨酶（AST）、血清总胆固醇（TC）和甘油三酯（TG）水平以及炎症因子，减轻了肝脏炎症和醉酒状态，通过降低ADH1的基因表达水平和提高ALDH2的基因表达水平，抑制乙酰胆碱的产生并加快其分解，从而减轻了神经炎症、肝脏炎症和肠道屏障损伤。此外，葛根提取物改变了肠道菌群的组成，表现为变形菌门（Proteobacteria）和脱磺杆菌门（Desulfobacterota）减少，从而抑制了LPS的产生及其下游样TLR4/MyD88/NF-κB通路。葛根提取物还会增加拟杆菌属（Bacteroides）、瘤胃球菌属（Ruminococcus）和普雷沃氏菌属（Prevotella）的

数量，并增加短链脂肪酸SCFAs的浓度以保护肠道屏障[35]。一定剂量的野生葛根和栽培葛根对慢性酒精肝损伤小鼠均有护肝功效，相同剂量下野生葛根的保护效果更佳[36]。

### 3.1.2 灵芝

灵芝（Ganoderma lucidum）在传统中药中被广泛应用已有2000多年的历史。超过400种生物活性化合物，包括来自灵芝的多糖、三萜类化合物和糖肽，已广泛用于预防和治疗神经衰弱、癌症、关节炎和解毒[37]。

Guo等[38]在探究富含灵芝酸的灵芝乙醇提取物（Ganoderma lucidum ethanol extract, GLE）对AILI的保护作用中发现，GLE能够有效抑制酒精诱导的小鼠血清中TG、TC、低密度脂蛋白胆固醇（LDL-C）、ALT和AST的异常升高，改善肝脏氧化应激，调节肠道微生物群和肝脏代谢物的组成，以及调节与脂肪酸代谢、胆汁酸生物合、酒精代谢和炎症反应相关的关键基因的mRNA水平来改善AILI。灵芝的深层发酵产物也被证明能够减轻C57B/L小鼠的酒精诱导的脂肪型肝炎，通过抑制脂质积累和提高抗氧化能力，抑制肝脏炎症蛋白iNOS、COX2、NF-κB、TNF-α和IL-6的表达[39]。

灵芝孢子粉是灵芝在生长和成熟期排出的微小生殖孢子的粉末，保留了灵芝所有的遗传物质，表现出于抗炎、免疫调节、抗氧化、抗肿瘤、神经保护、改善肝损伤等多种生物学功能[40]。灵芝孢子粉可以降低血清中AST和ALT水平、减少IL-1β、IL-18和TNF-α炎症因子的水平、改善受损的肝细胞和调节肠道微生物群落多样性，且破壁灵芝孢子粉治愈小鼠AILI的疗效大于未破壁的[41]。

### 3.1.3 枸杞

枸杞（Lycium, wolfberry, goji）是茄科的一个属，已有2300多年的栽培历史，主要在宁夏和西北其他省份，中国最常见的枸杞品种是宁夏枸杞，已发现其果实含有一系列促进健康的成分，可作为出色的食用或药用资源[42]。

Guo等[43]在普通基础饲料中添加枸杞喂养小鼠14天，通过一次灌胃12mL/kg体重的50%乙醇溶液建立膳食枸杞对ALD小鼠保护作用模型，揭示了枸杞、肠道微生物群和肝脏稳态之间的联系。研究发现，枸杞可以降低血清中ALT、AST、促炎细胞因子水平以及肝组织中的脂多糖含量，维持上皮屏障的完整性，增加盲肠内容物中丁酸的水平。此外，通过粪便粪菌移植（Fecal microbiota transplantation, FMT）实验发现Goji和FMT-Goji都可以增加肝脏中的GSH含量，调节视黄酰β-葡萄糖醛酸、香草酸，并增加参与GSH代谢的L-谷氨酸和焦谷氨酸的水平，选择性地富集产丁酸肠道微生物嗜黏蛋白阿克曼菌（Akkermansia）和瘤胃菌（Ruminococcaceae）。

与枸杞汁相比，经副干酪乳杆菌E10、植物乳植杆菌M和鼠李糖乳酸乳杆菌LGG发酵后的枸杞汁表现出更好的预防急性AILI的活性效果，其中，副干酪乳杆菌E10发酵枸杞汁表现出更强的抗AILI能力比起植物乳植杆菌M和鼠李糖乳酸乳杆菌LGG发酵枸杞汁。这三种乳酸菌发酵枸杞汁都可以通过减轻结肠炎症反应来维持肠道稳态和肠道屏障功能，通过重组微生物群和改变微生物代谢来改善酒精诱导的肠道微生物群失调[44]。

### 3.1.4 枳椇

北枳椇（Hovenia dulcis Thunb., HDT）和枳椇（Hovenia acerba Lindl., HAT）都属于鼠李科枳椇属的植物，具有较强的抗氧化活性[45]，网络药理学分析结果表明，山奈酚、豆甾醇和柚皮素是枳椇中的主要生物活性化合物，调节氧化应激、炎症、肠道衍生产物和细胞凋亡是枳椇对ALD保护作用的潜在机制[46]。

Lan等[47]在探究HDT提取物对急性酒精中毒小鼠的作用效果中发现，HDT提取物还可以通过激活酒精代谢酶ADH和ALDH的活性，加速了乙醇代谢，行为学方面表现为小鼠醉酒率减少，酒精耐受时间延长和清醒时间缩短。此外，HDT提取物通过调节肠道菌群平衡和调节苯丙氨酸、酪氨酸

和色氨酸的生物合成途径，减轻乙醇消耗引起的氧化应激。

在细胞水平上，HAT花梗和种子提取物可以显著缓解酒精诱导的肝损伤和减轻氧化应激，抑制L02细胞凋亡[48]。在动物水平上，HAT花梗和种子提取物可以调节胆汁和脂质代谢失调，降低总胆红素（TBIL）和TG水平[46]，通过Nrf2/HO-1氧化应激途径调节蛋白质和基因的表达，HAT种子提取物因酚类化合物更多、抗氧化性更好会比HAT花梗提取物表现出更好的护肝效果[48]。

## 3.2 天然产物活性成分对AILI的保护作用

### 3.2.1 多糖类

天然多糖在中药中分布广泛，大多数多糖都具有清除自由基的能力，可以减少氧化应激期间抗氧化剂的消耗，并抑制脂质、酶和核酸的分解氧化，减少酒精代谢过程中产生的ROS，抑制脂质过氧化从而有效减少肝组织损伤[49]，茯苓多糖[50]、五味子酸性多糖[51]、肉苁蓉多糖[52]和铁皮石斛多糖[53]等多糖类化合物都表现出护肝效果。

枸杞多糖（Lycium barbarum polysaccharides, LBPs）是从枸杞中提取的一种粗多糖，枸杞多糖能够有效抑制酒精摄入引起的氧化应激反应，降低丙二醛水平和活性氧的产生，同时恢复抗氧化酶的活性，减轻AILI[54-56]。Wang等[55]在探究LBPs在对酒精诱导的L-02肝细胞损伤的保护能力的研究中发现，LBPs通过促进L-02细胞中Nrf2的核转位，下调促凋亡蛋白Bax和上调抗凋亡蛋白Bcl-2，抑制细胞色素C、caspase-3和caspase-9的活化，减少了肝细胞的凋亡。在动物水平上，Li等[56]通过建立小鼠AFLD模型，研究了LBPs对小鼠AFLD的预防和治疗效果，研究发现LBPs通过增加AMPKα2 mRNA的表达和减少SREBP-1c、CYP2E1、TLR4和Myd88mRNA的表达来调节与肝损伤相关的代谢。此外，LBPs的潜在保肝作用也可能归因于糖醛酸，包括多糖中的葡萄糖醛酸和半乳糖醛酸。

### 3.2.2 多酚类

#### 3.2.2.1 类黄酮

类黄酮化合物是一种广泛分布在植物界的多酚类化合物，包括黄酮、黄酮醇、黄烷-3-醇（儿茶素）、原花青素、黄烷酮和异黄酮，具有抗炎、抗氧化、保肝、抗病毒和抗癌等多种药理活性[57]。

近年来，葛根异黄酮作为葛根的主要活性成分，因其对AILI的潜在保护作用而备受关注[58,59]。研究表明，葛根素能够通过抑制MMP8的活性或表达，减轻肝脏的炎症反应，减少炎症因子的释放，并改善脂质代谢，从而减轻AILI的病理程度[60]。Li等[61]在通过网络药理学与动物实验结合的方法探讨葛根中活性成分缓解ALD中铁过载的机制中发现，葛根素和染料木素可以减轻AILI和改善氧化应激、抑制p-ERK1/2的表达、下调乙醇激活的MAPK/ERK信号通路、增加SMAD1/5/9和铁调素的表达和抑制十二指肠DMT1和FPN1的表达，最终导致肠道铁吸收减少，从而缓解酒精诱导的铁过载。

槲皮素是已在多种蔬菜、谷物和水果中发现的一种黄酮醇类化合物，具有抗氧化、抗炎、抗菌、抗病毒、降血压和降血糖等效果[62]。Liu等[63]在研究中指出，槲皮素一方面可以通过激活Nrf2/HO-1并诱导抗氧化HO-1的表达，还原的TNF-α和ROS降低了NF-κB的活性，并进一步下调了NLRP3炎性小体的启动和激活，导致下游促炎细胞因子IL-1β和IL-18的分泌受到抑制，从而缓解急性AILI；另一方面，槲皮素可以提高抗炎细胞因子IL-10的水平，重新调节促炎和抗炎之间的平衡。此外，槲皮素也被证明可以在体内和体外减轻乙醇诱导的溶酶体功能障碍，通过协调激活溶酶体介导的自噬和减少外泌体产生，进一步减轻乙醇诱导的肝损伤[64]。

#### 3.2.2.2 芪类

白藜芦醇（Resveratrol，RSV）是一种天然存在的多酚，具有多种生物活性，包括抗氧化[65]、抗炎[66]、抗衰老[67]和保护心血管[68]等，已在许多体外模型（如肝细胞模型）和体内啮齿动物肝损伤模型中被证明对肝损伤有保护作用[69]。RSV可

能通过多种途径调节AILI，白藜芦醇可以调节抗氧化酶，改善氧化应激，降低caspase-3表达水平，减弱CYP2E1活性和蛋白质水平，减轻在转录水平介导的氧化应激、细胞凋亡和炎症来缓解ALD[70]。在AFLD大鼠模型中，RSV通过抑制肝脏中HIF-1α和线粒体ROS的产生来发挥其保肝作用，但还需要更多的研究来确定RSV调节肝脏中HIF-1α表达和线粒体ROS产生的详细机制[71]。

#### 3.2.2.3 酚酸类

绿原酸（Chlorogenic acid, CGA）是一种由奎宁酸和咖啡酸通过酯键缩合形成的酚酸，在咖啡、茶和一些水果和蔬菜等中都存在[72,73]。CGA可以降低细胞和线粒体内ROS水平，改善氧化应激，减弱肝细胞中DNA损伤和炎症反应诱导的信号通路p38/MAPK激活，从而抑制了肝脏脂肪变性、肝细胞凋亡和肝纤维化[72]。CGA可以显著减轻乙醇诱导的ALD小鼠肝损伤可能机制是肠-肝轴稳态的调节，通过对小鼠粪便肠道菌群16SrRNA基因测序发现，CGA可以增加有益菌群Muribaculaceae，拟杆菌属（Bacteroides），拟普雷沃氏菌属（Alloprevotella）和副拟杆菌属（Parabacteroides）的相对丰度，并降低机会性致病菌Eubacterium_no菌datum, Eubacterium_ruminantium和Anaerotruncus的相对丰度，从而保护ALD小鼠肠道屏障的完整性并减轻了AILI[73]。

#### 3.2.2.4 鞣酸类

没食子酸（Gallic acid, GA）是鞣酸（也称单宁酸）的水解产物之一[74]，广泛存在于石榴、葡萄、坚果、绿茶等植物中[75]。没食子酸能有效恢复乙醇诱导下L02肝细胞的细胞活性，并减少ALT、AST和LDH的释放；在分子水平上，没食子酸能够激活信号分子Nrf2表达来减少肝细胞坏死，表现为特定的坏死信号分子受体相互作用蛋白1（RIP1）和RIP3的表达降低以及高迁移率族蛋白B1（high mobility group box protein 1, HMGB1）的释放[75]。对氧磷酶（Paraoxonase, PON）和芳香酯酶是两种存在于肝脏中的酶，酒精诱导的肝损伤会导致这两种酶活性降低，而GA处理能够部分恢复由乙醇引起的PON活性下降，特别是在100mg/kg剂量时对PON活性的恢复效果最为显著。此外，50mg/kg的GA治疗恢复了由于乙醇暴露导致的芳香酯酶活性的损失[76]。

### 3.2.3 萜类

萜类化合物是所有生物体中的存在最多样化的一类天然化合物，已发现超过6000种萜类化合物，因此萜类化合物是一类主要的天然化合物[77]，因其广泛的药理作用，萜类化合物也被认为是药物发现的丰富候选化合物库[78]。

山楂酸（maslinic acid, MA）是一种五环三萜类化合物，广泛存在于多种油橄榄、枇杷叶、红枣、桉树和山楂等天然植物中[79,80]，具有抗氧化[81]、抗癌[82]、抗炎[83]、降血糖[84]等多种生物活性。MA可以通过保持GSH含量和GSH-Px活性，减少ROS、NO和炎性细胞因子的产生，并抑制LPS/TLR4、CYP2E1、COX-2、iNOS、NF-κB和MAPK表达来减轻酒精诱导的肝脏氧化和炎症损伤[85,86]。此外，山楂酸可以调节肠道菌群的平衡，扭转酒精摄入后有害细菌丰度的增加以及有益细菌丰度的减少[86]。

人参皂苷是人参属所独有的的主要活性成分，根据苷元结构不同可分为人参二醇型、人参三醇型、齐墩果酸型和奥克梯型四种[87,88]，具有抗氧化、抗炎和抗癌活性等多种生物效应。人参皂苷Rg1可以抑制炎症产生的多种途径，包括抑制CYP2E1的表达和ROS的产生，以及抑制线粒体损伤、肝细胞凋亡、NLRP3炎性小体激活和炎性细胞因子的产生，在酒精性肝炎中具有保肝作用[89]。人参皂苷Rb1[90]、Rc[91]、Rk2[92]、Rk3[93]、F2[94]也被证明对AILI具有保护效果。

### 3.2.4 生物碱类

生物碱是自然界中普遍存在的一种重要的次生代谢物，主要分布高等植物中，具有抗菌、抗炎、抗高血压、抗氧化、抗抑郁和保肝等多种生物活性[95]。

小檗碱（Berberine, BBR）是一种可以从黄连和黄芩等常见中草药中提取的异喹啉衍生物生物碱，具有显著的护肝效果[96]。BBR可以改善AFLD小鼠肝损伤和脂质代谢异常，其作用机制可能与BBR可以激活AMPK/SIRT1通路有关；通过抑制AFLD小鼠和酒精诱导的AML-12细胞中脂质代谢基因SREBP1C、SREBP2、FASN和HMGCR的表达，可以减轻肝损伤和脂肪变性，并发挥脂质调节作用[96]。Li等[97]在通过建立小鼠慢加急性酒精摄入模型、NIAAA模型和类G-MDSC细胞体外模型探讨BBR对与肠道微生物群-免疫系统轴相关的ALD治疗作用的潜在机制中发现，BBR通过介导IL-6/STAT3信号通路维持类G-MDSC细胞群的增加和功能，并且通过调节菌群落特别是通过增强嗜黏蛋白阿克曼菌丰度减弱AILI。

### 3.2.5 其他活性成分

除了上述多糖类、多酚类、萜类和生物碱类天然产物被证明对AILI有保护作用，其他天然产物如蛋白质肽类[98]、酚苷类[99]、木脂素类[100]、有机硫类[101]、类胡萝卜素类[102]、香豆素类[103]等化合物也具有改善AILI的效果。

牡蛎肽是一种通过现代生物技术将牡蛎中的蛋白质酶解成小分子肽而得到的产物，营养价值高，已在动物水平上被证明对ALD有保护作用[104,105]。与模型组相比，牡蛎肽实验组可以显著降低AST、ALT、谷氨酰转移酶（GGT）、ROS、MDA和TG水平，增加SOD活性和GSH浓度，通过上调氧化应激相关基因Nrf2、HO-1和NQO1的mRNA表达，下调炎症相关基因NF-κB、TNF-α和IL-6的mRNA表达和降低炎症因子IL-1β、TNF-α和IL-6水平来发挥对肝脏的保护作用[105]。

苯乙醇苷是一类酚苷类化合物，是肉苁蓉的主要成分之一，体内体外实验均证明其有护肝效果[106]。Qi等[107]使用利伯-德卡利（Lieber-Decarli）乙醇液体饲料建立小鼠NIAAA模型和假无菌小鼠进行FMT实验，研究肉苁蓉苯乙醇苷（Phenylethanol glycosides from C. tubulosa (Schenk) Wight, CPhGs）对ALD小鼠的肠道屏障和肠道微生物群的影响。长期乙醇液体饲料干预实验中发现，CPhGs高剂量组与模型组相比可以降低小血清中ALT、AST、TG、TC和炎症因子水平，还可能通过调节肠道黏液分泌量和肠道有益菌嗜黏蛋阿克曼（Akkermansia）潜在有害菌异杆菌（Allobaculum）的丰度和结构来保护肠道屏障肠道，降低内毒素脂多糖（LPS）、脂多糖结合蛋白（LBP）水平和肠道通透性指标二胺氧化酶（DAO）、D-乳酸（D-LA）水平[108]。将长期NIAAA模型小鼠用作粪菌供体进行的FMT实验进一步证实了CPhGs对肠道屏障损伤的改善作用。

## 4 结论

长期过量饮酒会导致ALD，从最初的脂肪变性，逐步会发展为酒精性肝炎、肝纤维化、肝硬化和肝细胞癌，严重危害人体健康。研究表明，氧化应激、炎症反应、脂质代谢异常、肠道菌群失衡等在ALD中扮演关键角色，为预防ALD提供了契机。近年来，天然产物因其靶点多、毒性低且副作用少等特点在促进人体健康中发挥重要作用，许多天然产物通过改善氧化应激、炎症反应、调节肠道菌群等手段来减轻酒精性肝损伤。基于这些途径，天然产物及其生物活性成分已被证明是预防和治疗ALD的理想候选者。未来，可以基于多组学分析（宏基因组、蛋白质组学和代谢组学）等方法对天然产物活性化合物进行机制研究，阐明它们对ALD的作用机制。

## 参考文献

[1] 曲航, 高鑫, 伊娟娟, 等. 食源性天然产物对酒精性肝损伤的防护作用研究进展[J]. 食品科学, 2020, 41(17): 283-290.

[2] Singal A K, Bataller R, Ahn J, et al. ACG Clinical Guideline: Alcoholic Liver Disease[J]. The American Journal of Gastroenterology, 2018, 113(2): 175-194.

[3] Sun Y, Dong Y, Cui X, et al. Effects of Marine Natural Products on Liver Diseases[J]. Marine Drugs, 2024, 22(7): 288.

[4] Yan J, Nie Y, Luo M, et al. Natural Compounds: A Potential Treatment for Alcoholic Liver Disease?[J]. Frontiers in Pharmacology, 2021, 12: 694475.

[5] Gao B, Bataller R. Alcoholic Liver Disease: Pathogenesis and New Therapeutic Targets[J]. Gastroenterology, 2011, 141(5): 1572.

[6] Yip W W, Burt A D. Alcoholic liver disease[J]. Seminars in Diagnostic Pathology, 2006, 23(3): 149-160.

[7] Manthey J, Shield K D, Rylett M, et al. Global alcohol exposure between 1990 and 2017 and forecasts until 2030: a modelling study[J]. The Lancet, 2019, 393(10190): 2493-2502.

[8] Wang W J, Xiao P, Xu H Q, et al. Growing burden of alcoholic liver disease in China: A review[J]. World Journal of Gastroenterology, 2019, 25(12): 1445.

[9] Ding R B, Tian K, huang L L, et al. Herbal medicines for the prevention of alcoholic liver disease: A review[J]. Journal of Ethnopharmacology, 2012, 144(3): 457-465.

[10] He Z, Guo T, Cui Z, et al. New understanding of Angelica sinensis polysaccharide improving fatty liver: The dual inhibition of lipid synthesis and CD36-mediated lipid uptake and the regulation of alcohol metabolism[J]. International Journal of Biological Macromolecules, 2022, 207: 813-825.

[11] Li P, Chen Y, Ke X, et al. Baicalin ameliorates alcohol-induced hepatic steatosis by suppressing SREBP1c elicited PNPLA3 competitive binding to ATGL[J]. Archives of Biochemistry and Biophysics, 2022, 722: 109236.

[12] Cai Z, Song L, Qian B, et al. Understanding the effect of anthocyanins extracted from purple sweet potatoes on alcohol-induced liver injury in mice[J]. Food Chemistry, 2018, 245: 463-470.

[13] Dogra A, Li F. Small-molecule chemical probes for the potential therapeutic targets in alcoholic liver diseases[J]. Liver Research, 2023, 7(3): 177-188.

[14] Kong L Z, Chandimali N, Han Y H, et al. Pathogenesis, Early Diagnosis, and Therapeutic Management of Alcoholic Liver Disease[J]. International Journal of Molecular Sciences, 2019, 20(11): 2712.

[15] Dunn W, Shah V H. Pathogenesis of Alcoholic Liver Disease[J]. Clinics in Liver Disease, 2016, 20(3): 445-456.

[16] Jiang Y, Zhang T, Kusumanchi P, et al. Alcohol Metabolizing Enzymes, Microsomal Ethanol Oxidizing System, Cytochrome P450 2E1, Catalase, and Aldehyde Dehydrogenase in Alcohol-Associated Liver Disease[J]. Biomedicines, 2020, 8(3): 50.

[17] Yang Y, Ji J, Di L, et al. Resource, chemical structure and activity of natural polysaccharides against alcoholic liver damages[J]. Carbohydrate Polymers, 2020, 241: 116355.

[18] Ceni E, Mello T, Galli A. Pathogenesis of alcoholic liver disease: Role of oxidative metabolism[J]. World Journal of Gastroenterology : WJG, 2014, 20(47): 17756.

[19] Lu Y, Cederbaum A I. CYP2E1 and oxidative liver injury by alcohol[J]. Free Radical Biology and Medicine, 2008, 44(5): 723-738.

[20] Zhao L, Mehmood A, Yuan D, et al. Protective Mechanism of Edible Food Plants against Alcoholic Liver Disease with Special Mention to Polyphenolic Compounds[J]. Nutrients, 2021, 13(5): 1612.

[21] Bardag-Gorce F, Li J, French B A, et al. The effect of ethanol-induced CYP2E1 on proteasome activity: the role of 4-hydroxynonenal[J]. Experimental and Molecular Pathology, 2005, 78(2): 109-115.

[22] Zhao N, Guo F F, Xie K Q, et al. Targeting Nrf-2 is a promising intervention approach for the prevention of ethanol-induced liver disease[J]. Cellular and Molecular Life Sciences: CMLS, 2018, 75(17): 3143.

[23] Sun S, Zhang J, Li H, et al. Anti-inflammatory activity of the water extract of Chloranthus serratus roots in LPS-stimulated RAW264.7 cells mediated by the Nrf2/HO-1, MAPK and NF-κB signaling pathways[J]. Journal of Ethnopharmacology, 2021, 271: 113880.

[24] Luo C, Lin Q, Wen Y, et al. Protective effect of Acanthus ilicifolius extracts against acute alcoholic liver injury via suppressing TLR4/NF-κB signal pathway and modulating intestinal microbiota in mice[J]. Natural Product Research, 0(0): 1-7.

[25] Bai Y, Liu F, Zheng L, et al. “Yajieshaba” prevents acute alcoholic liver injury and repairs the intestinal mucosal barrier[J]. Journal of Ethnopharmacology, 2024, 318: 116921.

[26] Mello T, Polvani S, Galli A. Peroxisome Proliferator-Activated Receptor and Retinoic X Receptor in Alcoholic Liver Disease[J]. PPAR Research, 2009, 2009: 748174.

[27] Wang F, Tipoe G L, Yang C, et al. Lycium barbarum Polysaccharide Supplementation Improves Alcoholic Liver Injury in Female Mice by Inhibiting Stearoyl-CoA Desaturase 1[J]. Molecular Nutrition & Food Research, 2018, 62(13): 1800144.

[28] Tang C C, Huang H P, Lee Y J, et al. Hepatoprotective effect of mulberry water extracts on ethanol-induced liver injury via

anti-inflammation and inhibition of lipogenesis in C57BL/6J mice[J]. Food and Chemical Toxicology, 2013, 62: 786-796.

[29]Lu J, Zhang Y, Wang Y Z, et al. Caffeic acid dimethyl ether alleviates alcohol-induced hepatic steatosis via microRNA-378b-mediated CaMKK2-AMPK pathway[J]. Bioengineered, 2022, 13(4): 11123.

[30]You M, Matsumoto M, Pacold C M, et al. The role of AMP-activated protein kinase in the action of ethanol in the liver[J]. Gastroenterology, 2004, 127(6): 1798-1808.

[31]Madushani Herath K H I N, Cho J, Kim A, et al. Phenolic acid and flavonoid-rich fraction of Sasa quelpaertensis Nakai leaves prevent alcohol induced fatty liver through AMPK activation[J]. Journal of Ethnopharmacology, 2018, 224: 335-348.

[32]Zhao L, Wang S, Zhang N, et al. The Beneficial Effects of Natural Extracts and Bioactive Compounds on the Gut-Liver Axis: A Promising Intervention for Alcoholic Liver Disease[J]. Antioxidants, 2022, 11(6): 1211.

[33]邓小燕, 钟凌云, 朱卫丰, 等. 葛根炮制的历史沿革及其现代炮制机制研究进展[J]. 中华中医药杂志, 2020, 35(7): 3524-3526.

[34]曾文燊, 黄达荣, 谢斯威, 等. 葛根异黄酮组成、结构及功效机制研究进展[J]. 食品科学, 2023, 44(1): 353-361.

[35]Wu Q, Li P, Li X, et al. Pueraria Extract Ameliorates Alcoholic Liver Disease via the Liver–Gut–Brain Axis: Focus on Restoring the Intestinal Barrier and Inhibiting Alcohol Metabolism[J]. Journal of Agricultural and Food Chemistry, 2024, 72(44): 24449-24462.

[36]姚媛, 盖永强, 陈铁军, 等. 野生葛根与栽培葛根对慢性酒精中毒小鼠的护肝作用比较[J]. 食品科学, 2022, 43(23): 174-179.

[37]Xie C, Yan S, Zhang Z, et al. Mapping the metabolic signatures of fermentation broth, mycelium, fruiting body and spores powder from Ganoderma lucidum by untargeted metabolomics[J]. LWT, 2020, 129: 109494.

[38]Guo W L, Cao Y J, You S Z, et al. Ganoderic acids-rich ethanol extract from Ganoderma lucidum protects against alcoholic liver injury and modulates intestinal microbiota in mice with excessive alcohol intake[J]. Current Research in Food Science, 2022, 5: 515-530.

[39]Chung D J, Yang M Y, Li Y R, et al. Ganoderma lucidum repress injury of ethanol-induced steatohepatitis via anti-inflammation, anti-oxidation and reducing hepatic lipid in C57BL/6J mice[J]. Journal of Functional Foods, 2017, 33: 314-322.

[40]Zhang J, Cui X, Luo W, et al. The qualitative and quantitative analysis of Ganoderma lucidum spore powder chemical compounds as p38 MAPK inhibitors by the generation and verification of pharmacophore modelling[J]. LWT, 2024, 194: 115817.

[41]Leng Y, Wang F, Chen C, et al. Protective Effect of Ganoderma lucidum Spore Powder on Acute Liver Injury in Mice and its Regulation of Gut Microbiota[J]. Frontiers in Bioscience-Landmark, 2023, 28(2): 23.

[42]Yu J, Yan Y, Zhang L, et al. A comprehensive review of goji berry processing and utilization[J]. Food Science & Nutrition, 2023, 11(12): 7445-7457.

[43]Guo L, Guan Q, Duan W, et al. Dietary Goji Shapes the Gut Microbiota to Prevent the Liver Injury Induced by Acute Alcohol Intake[J]. Frontiers in Nutrition, 2022, 9: 929776.

[44]Duan W, Zhou L, Ren Y, et al. Lactic acid fermentation of goji berries (Lycium barbarum) prevents acute alcohol liver injury and modulates gut microbiota and metabolites in mice[J]. Food & Function, 2024, 15(3): 1612-1626.

[45] eng H, Deng Z, Chen X, et al. Major chemical constituents and antioxidant activities of different extracts from the peduncles of Hovenia acerba Lindl[J]. International Journal of Food Properties, 2018, 21(1): 2135-2155.

[46]Meng X, Tang G Y, Zhao C N, et al. Hepatoprotective effects of Hovenia dulcis seeds against alcoholic liver injury and related mechanisms investigated via network pharmacology[J]. World Journal of Gastroenterology, 2020, 26(24): 3432-3446.

[47]Lan H, Bai Z, Luo D, et al. Protective mechanisms of Hovenia dulcis Thunb extracts on acute alcoholism and liver injury[J]. Food Bioscience, 2024, 62: 105264.

[48]Cheng R fei, Sun M ke, Hu Q rui, et al. Hovenia acerba Lindl. peduncles and seeds extracts ameliorate alcoholic liver injury by activating the Nrf2/HO-1 signalling pathway in LO2 cells

and mice[J]. Food Bioscience, 2023, 51: 102224.

[49]Cao W, Wu J, Zhao X, et al. Structural elucidation of an active polysaccharide from Radix Puerariae lobatae and its protection against acute alcoholic liver disease[J]. Carbohydrate Polymers, 2024, 325: 121565.

[50]Zhou X, Wang J, Zhou S. Poria cocos polysaccharides improve alcoholic liver disease by interfering with ferroptosis through NRF2 regulation[J]. Aging (Albany NY), 2024, 16(7): 6147-6162.

[51]Yuan R, Tao X, Liang S, et al. Protective effect of acidic polysaccharide from Schisandra chinensis on acute ethanol-induced liver injury through reducing CYP2E1-dependent oxidative stress[J]. Biomedicine & Pharmacotherapy, 2018, 99: 537-542.

[52]Wang H, Yan J, Wang K, et al. The gut-liver axis perspective: Exploring the protective potential of polysaccharides from Cistanche deserticola against alcoholic liver disease[J]. International Journal of Biological Macromolecules, 2024, 256: 128394.

[53]Nie G, Zhang Y, Zhou Z, et al. Dynamic evaluation of the protective effect of Dendrobium officinale polysaccharide on acute alcoholic liver injury mice in vitro and in vivo by NIR fluorescence imaging[J]. Analytical and Bioanalytical Chemistry, 2021, 413(23): 5715-5724.

[54]Yan Y, Wu W, Lu L, et al. Study on the synergistic protective effect of Lycium barbarum L. polysaccharides and zinc sulfate on chronic alcoholic liver injury in rats[J]. Food Science & Nutrition, 2019, 7(11): 3435.

[55]Wang H, Li Y, Liu J, et al. Hepatoprotective effect of crude polysaccharide isolated from Lycium barbarum L. against alcohol-induced oxidative damage involves Nrf2 signaling[J]. Food Science & Nutrition, 2020, 8(12): 6528-6538.

[56]Li D, Sun L, Yang Y, et al. Preventive and therapeutic effects of pigment and polysaccharides in Lycium barbarum on alcohol-induced fatty liver disease in mice[J]. CyTA - Journal of Food, 2018, 16(1): 938-949.

[57]Dhiman A, Nanda A, Ahmad S. A quest for staunch effects of flavonoids: Utopian protection against hepatic ailments[J]. Arabian Journal of Chemistry, 2016, 9: S1813-S1823.

[58]Liu Y S, Yuan M H, Zhang C Y, et al. Puerariae Lobatae radix flavonoids and puerarin alleviate alcoholic liver injury in zebrafish by regulating alcohol and lipid metabolism[J]. Biomedicine & Pharmacotherapy, 2021, 134: 111121.

[59]Chen X, Li R, Liang T, et al. Puerarin improves metabolic function leading to hepatoprotective effects in chronic alcohol-induced liver injury in rats[J]. Phytomedicine, 2013, 20(10): 849-852.

[60]Hu Y, Wang S, Wu L, et al. Puerarin inhibits inflammation and lipid accumulation in alcoholic liver disease through regulating MMP8[J]. Chinese Journal of Natural Medicines, 2023, 21(9): 670-681.

[61]Li X, Liu L, Wan M X, et al. Active Components of Pueraria lobata through the MAPK/ERK Signaling Pathway Alleviate Iron Overload in Alcoholic Liver Disease[J]. Chemistry & Biodiversity, 2024, 21(5): e202400005.

[62]Batiha G E S, Beshbishy A M, Ikram M, et al. The Pharmacological Activity, Biochemical Properties, and Pharmacokinetics of the Major Natural Polyphenolic Flavonoid: Quercetin[J]. Foods, 2020, 9(3): 374.

[63]Liu S, Tian L, Chai G, et al. Targeting heme oxygenase-1 by quercetin ameliorates alcohol-induced acute liver injury via inhibiting NLRP3 inflammasome activation[J]. Food & Function, 2018, 9(8): 4184-4193.

[64]Chen H, Liu J, Peng S, et al. Autophagy and exosomes coordinately mediate quercetin’s protective effects on alcoholic liver disease[J]. The Journal of Nutritional Biochemistry, 2023, 116: 109332.

[65]Yao Y, Yuan H, Chen C, et al. Study of the Antioxidant Capacity and Oxidation Products of Resveratrol in Soybean Oil[J]. Foods, 2024, 13(1): 29.

[66]Zhang B, Zhang Y, Liu X, et al. Distinctive anti-inflammatory effects of resveratrol, dihydroresveratrol, and 3-(4-hydroxyphenyl)-propionic acid on DSS-induced colitis in pseudo-germ-free mice[J]. Food Chemistry, 2023, 400: 133904.

[67]Chu S H, Yang D, Wang Y ping, et al. Effect of resveratrol on the repair of kidney and brain injuries and its regulation on klotho gene in d-galactose-induced aging mice[J]. Bioorganic & Medicinal Chemistry Letters, 2021, 40: 127913.

[68] Wang Q, Yu Q, Wu M. Antioxidant and neuroprotective actions of resveratrol in cerebrovascular diseases[J]. Frontiers in Pharmacology, 2022, 13.

[69] McGill M R, Du K, Weemhoff J L, et al. Critical review of resveratrol in xenobiotic-induced hepatotoxicity[J]. Food and Chemical Toxicology, 2015, 86: 309-318.

[70] Peiyuan H, Zhiping H, Chengjun S, et al. Resveratrol Ameliorates Experimental Alcoholic Liver Disease by Modulating Oxidative Stress[J]. Evidence-Based Complementary and Alternative Medicine, 2017, 2017(1): 4287890.

[71] Ma Z, Zhang Y, Li Q, et al. Resveratrol improves alcoholic fatty liver disease by downregulating HIF-1α expression and mitochondrial ROS production[J]. PLOS ONE, 2017, 12(8): e0183426.

[72] Kim H, Pan J H, Kim S H, et al. Chlorogenic acid ameliorates alcohol-induced liver injuries through scavenging reactive oxygen species[J]. Biochimie, 2018, 150: 131-138.

[73] Zhu H, Jiang W, Liu C, et al. Ameliorative effects of chlorogenic acid on alcoholic liver injury in mice via gut microbiota informatics[J]. European Journal of Pharmacology, 2022, 928: 175096.

[74] Barrett A H, Farhadi N F, Smith T J. Slowing starch digestion and inhibiting digestive enzyme activity using plant flavanols/tannins— A review of efficacy and mechanisms[J]. LWT, 2018, 87: 394-399.

[75] Zhou Y, Jin H, Wu Y, et al. Gallic acid protects against ethanol-induced hepatocyte necroptosis via an NRF2-dependent mechanism[J]. Toxicology in Vitro, 2019, 57: 226-232.

[76] Kartkaya K, Oğlakçı A, Şentürk H, et al. Investigation of the possible protective role of gallic acid on paraoxanase and arylesterase activities in livers of rats with acute alcohol intoxication[J]. Cell Biochemistry and Function, 2013, 31(3): 208-213.

[77] Jahangeer M, Fatima R, Ashiq M, et al. Therapeutic and Biomedical Potentialities of Terpenoids – A Review[J]. Journal of Pure and Applied Microbiology, 2021, 15(2): 471-483.

[78] Yao P, Liu Y. Terpenoids: Natural Compounds for Non-Alcoholic Fatty Liver Disease (NAFLD) Therapy[J]. Molecules, 2023, 28(1): 272.

[79] 丁雯昕, 杜柏霖, 李娇, 等. 五环三萜类天然产物研究进展[J]. 药学学报, 2024, 59(5): 1163-1175.

[80] He Y, Wang Y, Yang K, et al. Maslinic Acid: A New Compound for the Treatment of Multiple Organ Diseases[J]. Molecules, 2022, 27(24): 8732.

[81] Cheng Y, Xia Q, Lu Z, et al. Maslinic acid attenuates UVB-induced oxidative damage in HFF-1 cells[J]. Journal of Cosmetic Dermatology, 2023, 22(8): 2352-2360.

[82] Lin X, Ozbey U, Sabitaliyevich U Y, et al. Maslinic acid as an effective anticancer agent[J]. CELLULAR AND MOLECULAR BIOLOGY, 2018, 64(10): 87-91.

[83] Huang L, Guan T, Qian Y, et al. Anti-inflammatory effects of maslinic acid, a natural triterpene, in cultured cortical astrocytes via suppression of nuclear factor-kappa B[J]. European Journal of Pharmacology, 2011, 672(1): 169-174.

[84] Gao H, Wu H. Maslinic acid activates renal AMPK/SIRT1 signaling pathway and protects against diabetic nephropathy in mice[J]. BMC Endocrine Disorders, 2022, 22(1): 25.

[85] Yan S lei, Yang H ting, Lee H lin, et al. Protective effects of maslinic acid against alcohol-induced acute liver injury in mice[J]. Food and Chemical Toxicology, 2014, 74: 149-155.

[86] Su J, Dai Y, Wu X, et al. Maslinic acid alleviates alcoholic liver injury in mice and regulates intestinal microbiota via the gut–liver axis[J]. Journal of the Science of Food and Agriculture, 2024, 104(13): 7928-7938.

[87] 李铭莹, 林霖, 王岩, 等. 人参皂苷抗肿瘤机制及其纳米药物递送系统的研究进展[J]. 中草药, 2024, 55(2): 688-696.

[88] Dana S M M A, Meghdadi M, Kakhki S K, et al. Anti-leukemia effects of ginsenoside monomer: A narrative review of pharmacodynamics study[J]. Current Therapeutic Research, 2024, 100: 100739.

[89] Yang C, He X, Zhao J, et al. Hepatoprotection by Ginsenoside Rg1 in alcoholic liver disease[J]. International Immunopharmacology, 2021, 92: 107327.

[90] Lai Y, Tan Q, Xv S, et al. Ginsenoside Rb1 Alleviates Alcohol-Induced Liver Injury by Inhibiting Steatosis, Oxidative Stress, and Inflammation[J]. FRONTIERS IN PHARMACOLOGY, 2021, 12: 616409.

[91] Pan Z, Guo J, Tang K, et al. Ginsenoside Rc Modulates SIRT6-NRF2 Interaction to Alleviate Alcoholic Liver Disease[J]. Journal

of Agricultural and Food Chemistry, 2022, 70(44): 14220-14234.

[92]Zou J, Yang R, Feng R, et al. Ginsenoside Rk2, a dehydroprotopanaxadiol saponin, alleviates alcoholic liver disease via regulating NLRP3 and NLRP6 inflammasome signaling pathways in mice[J]. Journal of Pharmaceutical Analysis, 2023, 13(9): 999-1012.

[93]Qu L, Zhu Y, Liu Y, et al. Protective effects of ginsenoside Rk3 against chronic alcohol-induced liver injury in mice through inhibition of inflammation, oxidative stress, and apoptosis[J]. Food and Chemical Toxicology, 2019, 126: 277-284.

[94]Kim M H, Kim H H, Jeong J M, et al. Ginsenoside F2 attenuates chronic-binge ethanol-induced liver injury by increasing regulatory T cells and decreasing Th17 cells[J]. Journal of Ginseng Research, 2020, 44(6): 815-822.

[95]Debnath B, Singh W S, Das M, et al. Role of plant alkaloids on human health: A review of biological activities[J]. Materials Today Chemistry, 2018, 9: 56-72.

[96]Zhu L, Xu J J, Li H D, et al. Berberine Ameliorates Abnormal Lipid Metabolism via the Adenosine Monophosphate–Activated Protein Kinase/Sirtuin 1 Pathway in Alcohol-Related Liver Disease[J]. Laboratory Investigation, 2023, 103(4): 100041.

[97]Li S, Wang N, Tan H Y, et al. Modulation of gut microbiota mediates berberine-induced expansion of immuno-suppressive cells to against alcoholic liver disease[J]. Clinical and Translational Medicine, 2020, 10(4): e112.

[98]Zhang F, Zhang J, Li Y. Corn oligopeptides protect against early alcoholic liver injury in rats[J]. Food and Chemical Toxicology, 2012, 50(6): 2149-2154.

[99]Tao Z, Zhang L, Wu T, et al. Echinacoside ameliorates alcohol-induced oxidative stress and hepatic steatosis by affecting SREBP1c/FASN pathway via PPAR α [J]. Food and Chemical Toxicology, 2021, 148: 111956.

[100]Li B, Li D, Wang Y, et al. Schisantherin A alleviated alcohol-induced liver injury by the regulation of alcohol metabolism and NF-kB pathway[J]. Experimental Animals, 2018, 67(4): 451-461.

[101]Chen L Y, Chen Q, Cheng Y F, et al. Diallyl trisulfide attenuates ethanol-induced hepatic steatosis by inhibiting oxidative stress and apoptosis[J]. Biomedicine & Pharmacotherapy, 2016, 79: 35-43.

[102]Zheng J, Tian X, Zhang W, et al. Protective Effects of Fucoxanthin against Alcoholic Liver Injury by Activation of Nrf2-Mediated Antioxidant Defense and Inhibition of TLR4-Mediated Inflammation[J]. Marine Drugs, 2019, 17(10): 552.

[103]Sun F, Xie M L, Zhu L J, et al. Inhibitory effect of osthole on alcohol-induced fatty liver in mice[J]. Digestive and Liver Disease, 2009, 41(2): 127-133.

[104]江新辉, 江敏, 江铭福, 等. 牡蛎肽对酒精性肝损伤与体力疲劳的影响[J]. 中国食品学报, 2024, 24(7): 201-207.

[105]Wang X, Yu H, Xing R, et al. Hepatoprotective Effect of Oyster Peptide on Alcohol-Induced Liver Disease in Mice[J]. International Journal of Molecular Sciences, 2022, 23(15): 8081.

[106]郭元亨, 曹丽丽, 赵兵, 等. 荒漠肉苁蓉苯乙醇苷对酒精诱导的慢性肝损伤的修复作用（英文）[J]. 食品科学, 2018, 39(13): 176-183.

[107]Qi Z, Liu J, Xu Y, et al. Protective effects of phenylethanol glycosides from Cistanche tubulosa against ALD through modulating gut microbiota homeostasis[J]. Journal of Ethnopharmacology, 2025, 337: 118925.

[108]亓照耀, 许源慧, 刘金存, 等. 肉苁蓉苯乙醇苷对ALD小鼠肠道黏膜屏障和肠道菌群的影响[J]. 中国实验方剂学杂志, 2024, 30(9): 65-73.

Copyright © 2025 by author(s) and Global Science Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access