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黄芩苷对胰腺外分泌疾病的防治潜力及机制研究进展

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摘 要:胰腺外分泌疾病主要包括急性胰腺炎、慢性胰腺炎和胰腺癌,发病率逐年上升,临床以对症治疗为主。近年来众多研究显示中医药在胰腺外分泌疾病的防治中具有潜在作用。黄芩苷作为中药黄芩的主要活性成分,有研究证实其在胰腺外分泌疾病中具有应用价值。黄芩苷可通过调节NF-κB、Nrf2/Keap1、TGF-β1/Smad和JNK等信号通路,发挥调控炎症反应、减轻氧化应激、抑制胰腺星状细胞活化及肿瘤细胞增殖、侵袭迁移、凋亡等作用。黄芩苷在胰腺外分泌疾病中展现出的干预特性,为相关疾病的临床转化提供了科学依据和创新思路。

关键词:黄芩苷;胰腺外分泌疾病;炎症反应;氧化应激;胰腺纤维化;细胞凋亡;肿瘤进展
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Research progress on the mechanisms of baicalin in preventing and treating pancreatic exocrine diseases

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Abstract: The incidence of pancreatic exocrine diseases including acute pancreatitis (AP), chronic pancreatitis (CP), and pancreatic cancer (PC) continues to rise and becomes a significant and growing global health burden. While current clinical management for pancreatic exocrine diseases remains largely supportive rather than curative, it is necessary to explore novel therapeutic strategies targeting the underlying complex pathophysiology. Traditional Chinese Medicine (TCM) has long been recognized for its multi-targets, holistic approach to complex diseases. Based on the TCM etiological understanding of exocrine diseases, formulas such as Dazhihu Decoction and Chaiqin Chengqi Decoction (with Huang Qin as an important ingredient) have shown good therapeutic effects in the clinical treatment of AP, CP, and PC. Baicalin, a major bioactive flavonoid derived from the root of *Scutellaria baicalensis* Georgi (Huang Qin), has emerged as a compound which possesses a broad spectrum of pharmacological properties including anti-inflammatory, antioxidant, anti-fibrotic, and anti-tumor activities. Many studies have shown baicalin plays an important therapeutic role in various preclinical models of gastrointestinal and metabolic disorders. This article systematically reviews the recent advances about the therapeutic potential and molecular mechanisms of baicalin against major pancreatic exocrine diseases, providing a foundation for its future clinical translation. In AP, the therapeutic effects of baicalin are mainly achieved through anti-inflammatory and antioxidant actions. Its anti-inflammatory effect is mainly manifested by inhibiting key signaling pathways, especially NF-κB, JAK2/STAT3, and MAPK/JNK, to further reduce the production of proinflammatory cytokines (eg., TNF-α, IL-6, IL-1β) in the pancreas. Simultaneously, baicalin exerts potent antioxidant effects by activating the Nrf2/Keap1 pathway, which enhances the activity of antioxidant enzymes (SOD, GSH-Px) and reduces oxidative stress markers. Additionally, baicalin regulates cell fate by influencing autophagy (via Akt/mTOR) and apoptosis (through Bcl-2/Bax and Caspase-3). It also exhibits systemic protection by mitigating AP-associated injury to distant organs such as the lungs, liver, and kidneys. In CP, baicalin targets the key processes of fibrosis and chronic inflammation. It inhibits acinar-to-ductal metaplasia (ADM) that is an early pathological event of CP, by downregulating the IL-6/STAT3 pathway. Its anti-fibrotic activity is achieved by suppressing the activation of pancreatic stellate cells (PSCs) through interfering with the TGF-β1/Smad and NF-κB signaling

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cascades, thereby reducing the deposition of extracellular matrix proteins such as collagen and fibronectin. In PC, baicalin exhibits antitumor properties at multiple levels. It not only inhibits cancer cell proliferation by inducing cell cycle arrest and promotes apoptosis via mechanisms involving the JNK/FoxO1/BIM axis and caspase activation, but also suppresses cell migration, invasion, and epithelial-mesenchymal transition (EMT) by attenuating TGF-β1/Smad signaling. In summary, baicalin exerts broad-spectrum beneficial effects against pancreatic exocrine diseases through interconnected mechanisms targeting inflammation, oxidative stress, fibrosis, and tumor progression. While preclinical evidence is compelling, its clinical translation requires rigorous evidence through well-designed clinical trials to prove its efficacy, optimal dosing, and safety in patients with pancreatic exocrine diseases.

Key words: baicalin; pancreatic exocrine disease; inflammatory response; oxidative stress; pancreatic fibrosis; apoptosis; tumor progression

胰腺作为人体重要的消化腺体,承担着复杂而精密的外分泌与内分泌功能。其中,胰腺外分泌功能主要通过分泌多种消化酶及碳酸氢盐,参与蛋白质、脂肪和碳水化合物等营养物质的消化与吸收。然而,由于其特殊的解剖结构和功能特性,胰腺极易受到多种内外因素的损伤,从而引发一系列胰腺外分泌功能障碍性疾病,包括急性胰腺炎(acute pancreatitis,AP)、慢性胰腺炎(chronic pancreatitis,CP)以及胰腺癌(pancreatic cancer,PC)等[1]。尤其是近年来,随着饮食结构改变和肥胖、代谢综合征等高危因素的普遍存在,胰腺外分泌相关疾病的发病率呈现逐年上升趋势,并逐渐成为全球范围内影响人群健康的重要公共卫生问题[2,3]。

目前,临床上对于胰腺外分泌疾病的治疗主要依赖于对症支持治疗、营养支持、胰酶相关制剂以及手术干预等措施[4-6]。中医药近年来在胰腺外分泌疾病治疗中展示出了良好的疗效,其多靶点、副作用小、疗效确切的特点被普遍认可。作为传统中药黄芩中的主要黄酮类活性成分,黄芩苷具有抗炎、抗氧化、抗纤维化、免疫调节、抗凋亡以及抗肿瘤等多重生物学效应[7]。研究表明,黄芩苷对非酒精性脂肪性肝病、病毒性肝炎、炎症性肠病、溃疡性结肠炎等多种消化系统疾病具有改善作用[8,9]。近期,黄芩苷在胰腺外分泌疾病中的防治作用也受到关注,因此本文围绕黄芩苷在AP、CP及PC中的防治作用机制进行综述,旨在为黄芩苷的后续深入研究与临床应用奠定坚实的理论基础。

1 黄芩苷

黄芩苷是从中药黄芩中分离得到的重要黄酮类活性成分,属于黄酮-7-O-葡萄糖苷化合物,分子式$C_{21}H_{18}O_{11}$(图1),相对分子质量446.37[10]。现代药理研究证实,黄芩苷口服后在小肠中经代谢转化实现有效吸收,达峰时间较短;其血药浓度通过肠肝循环得以维持,从而延长药效持续时间,同时黄芩苷主要经胆汁排泄,肾脏负担较小,具备成为临床治疗药物的良好基础[11]。多项研究表明,黄芩苷凭借其多靶点、多途径的药理特性,在治疗胰腺外分泌疾病中展现出潜在的研究与应用价值。黄芩苷可抑制胰腺炎中关键炎症因子的释放[12,13],减轻氧化应激[12]及细胞凋亡反应[14]等,有效缓解胰腺组织损伤。

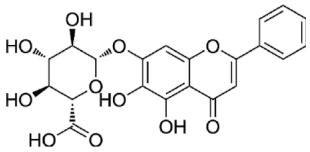

图1 黄芩苷结构式

Figure 1 Chemical structure of baicalin

2 黄芩苷在急性胰腺炎中的防治作用

急性胰腺炎主要表现为胰酶异常激活导致的胰腺自身消化、中性粒细胞浸润及微循环障碍,严重者可进展为胰腺坏死和多器官功能衰竭[15]。目前临床治疗仍以液体复苏、镇痛及器官支持为主[4]。近年来,以通里攻下法为主的中医药在AP治疗中展现出一定的临床价值,柴芩承气汤、清胰汤、大柴胡汤等因其对AP确切的疗效,而在临床广泛应用[16-18]。黄芩是以上方剂中共有的重要组成部分,黄芩苷作为黄芩的主要活性成分,通过抑制炎症反应、氧化应激,调控腺泡细胞凋亡与自噬以及对多器官的保护作用,显著缓解AP病情。黄芩苷在AP中的多靶点作用机制如图2所示。

2.1 抗炎作用

核因子κB(nuclear factor kappa B,NF-κB)在炎症免疫中发挥关键作用,其异常激活会导致炎性细胞因子过度释放,进而成为AP发病的重要机制[19]。

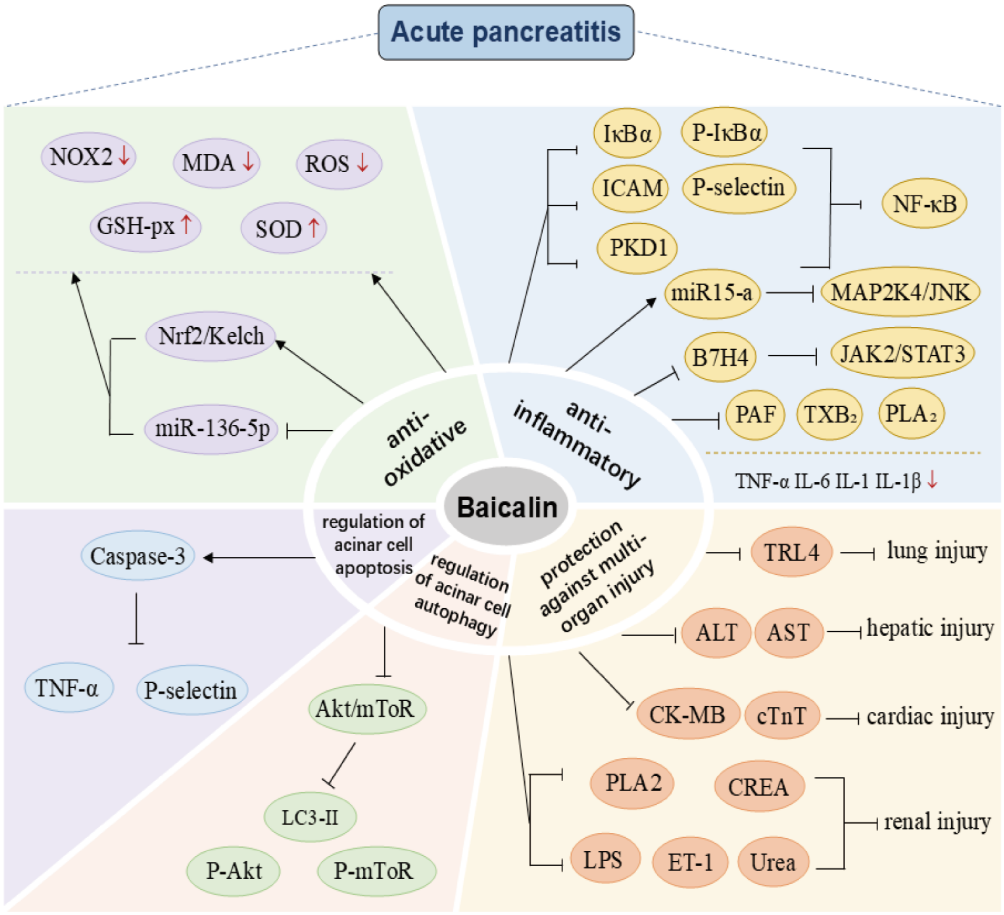

图2　黄芩苷在急性胰腺炎中的防治作用

Figure 2　Preventive and therapeutic effects of baicalin in acute pancreatitis

多项研究发现,黄芩苷可以通过调控NF-κB 在AP中发挥防治作用。Xue等[20]采用50 mg/kg黄芩苷干预雨蛙肽诱导的AP大鼠,发现其可有效抑制胰腺组织中NF-κB的激活和肿瘤坏死因子-α(tumor necrosis factor-α,TNF-α)的表达,减轻胰腺病理损伤。Zhao等[21]使用黄芩苷治疗牛磺胆酸诱导的重症急性胰腺炎(severe acute pancreatitis,SAP)大鼠,结果显示黄芩苷通过抑制胰腺组织核因子κB抑制蛋白α(inhibitor of kappa B alpha,IκBα)降解从而阻断NF-κB活化,降低TNF-α、白细胞介素6(interleukin-6,IL-6)等炎症因子的分泌以及细胞间黏附分子-1(intercellular adhesion molecule-1,ICAM-1)和P-选择素(P-selectin)的表达,减少中性粒细胞的浸润,缓解胰腺炎症和组织损伤。高甘油三酯血症急性胰腺炎(HTG-AP)表现出胰腺坏死等SAP的改变,Yang等[22]复制HTG-AP小鼠模型,发现黄芩苷显著降低胰腺组织中B7H4的过度表达,并通过抑制Janus激酶2(Janus kinase 2,JAK2)和信号转导和转录激活因子3(signal transducer and activator of transcription 3,STAT3)的磷酸化,阻断下游IL-6、TNF-α、IL-1β等炎症因子的释放,减轻胰腺的炎性损伤。Qian等[12]发现黄芩苷不仅下调血清中TNF-α、IL-6、白细胞介素1(interleukin-1,IL-1)等炎症因子水平,同时上调外周血中的群分化抗原3(cluster of differentiation 3,CD3)水平和γδT细胞百分比,并抑制胰腺组织中NF-κB蛋白及其下游蛋白激酶D1(protein kinase D1,PKD1)蛋白表达,从而减轻SAP大鼠的炎症反应。为了进一步探究黄芩苷抗胰腺炎症损伤的机制,周彬等[23]采用人正常胰腺导管上皮细胞(HPDE6-C7)给予脂多糖(lipopolysaccharide,LPS)诱导细胞损伤模型,观察10、20、40 μmol/L黄芩苷干预后对细胞的保护作用,发现黄芩苷可降低磷酸化IκBα(p-IκBα)/IκBα 蛋白水平,调控NF-κB信号通路,缓解胰腺导管上皮细胞的损伤。

此外，Zhen等[24]通过体内外实验深入研究了黄芩苷对AP的治疗作用。在体内实验中采用雨蛙素诱导AP小鼠模型，给予20 mg/kg黄芩苷干预，发现黄芩苷可上调胰腺组织miR-15a水平、抑制肺腺癌转移相关转录子1(metastasis-associated lung adenocarcinoma transcript 1，MALAT1)，进而抑制细胞分裂周期蛋白42(cell division cycle 42，CDC42)/有丝分裂原活化蛋白激酶激酶激酶1(mitogen-activated protein kinase kinase kinase 1，MAP3K1)，阻断丝裂原活化蛋白激酶激酶4(mitogen-activated protein kinase kinase 4，MAP2K4)介导的c-Jun氨基末端激酶(JNK)信号通路，降低血清中TNF-α、IL-6和IL-1β水平，最终减轻胰腺炎症损伤。进一步的离体实验验证，在雨蛙素诱导的大鼠胰腺腺泡细胞(AR42J)AP模型中，黄芩苷通过上调miR-15a，直接抑制 MAP2K4/JNK通路，减少炎症因子释放。Tian等[25]使用黄芩苷治疗SAP大鼠时发现，黄芩苷可控制血浆内毒素水平，降低血清TNF-α含量，抑制炎症反应。Zhang等[26]研究表明，黄芩苷可降低血液中IL-1β、血小板活化因子(platelet-activating factor，PAF)、血栓素B_2(thromboxane B_2，TXB_2)、磷脂酶A_2(phospholipase A_2，PLA_2)等炎症介质的含量，降低血液黏度，改善胰腺微循环障碍，减轻SAP胰腺局部缺血与损伤。综上所述，黄芩苷通过多靶点协同机制调节AP核心炎症反应，主要包括抑制关键的炎症反应调控因子NF-κB及其相关信号通路活化、下调TNF-α、IL-6、IL-1β等炎症因子、干预JAK2/STAT3通路及MAP2K4/JNK信号轴，减少炎症介质分泌并减轻其诱发的胰腺微循环紊乱和腺泡损伤。这些研究结果为黄芩苷作为多靶向抗炎候选药物应用于AP治疗提供了重要理论依据。然而，目前尚缺乏直接证据表明黄芩苷能够抑制胰酶的异常激活，其在这方面的作用仍需进一步研究。

2.2 抗氧化作用

长期以来，氧化应激在AP中的作用被广泛关注。研究发现，AP发作后胰腺腺泡细胞内的氧化应激增加，造成活性氧(reactive oxygen species，ROS)释放及脂质过氧化反应，进一步诱导胰腺损伤[27]。黄芩苷具有显著的活性氧清除能力，可减轻胰腺组织的氧化损伤[7]。Qian等[12]通过实验证实，黄芩苷能提高大鼠胰腺组织中超氧化物歧化酶(superoxide dismutase，SOD)和谷胱甘肽过氧化物酶(glutathione peroxidase，GSH-Px)活性，降低丙二醛(malondialdehyde，MDA)水平，从而减轻SAP大鼠胰腺组织的氧化损伤。Yang等[22]使用20 mg/kg黄芩苷治疗HTG-AP小鼠后发现，黄芩苷通过调控核因子E2相关因子2(nuclear factor erythroid 2-related factor 2，Nrf2)/Kelch样ECH关联蛋白1(Kelch-like ECH-associated protein 1，Keap1)信号通路，降低胰腺组织中的ROS水平和NADPH氧化酶2(NADPH oxidase 2，NOX2)蛋白表达，增加超氧化物歧化酶2(superoxide dismutase 2，SOD2)蛋白表达来缓解氧化应激，控制HTG-AP的疾病进展。Zhao等[28]在体外实验中分别采用5、10、25、50、75 mmol/L的黄芩苷干预AR42J细胞急性胰腺炎模型后发现，黄芩苷通过下调AR42J细胞的miR-136-5p表达，增强GSH-Px和SOD1等抗氧化酶的活性，从而降低ROS和MDA水平，抑制氧化应激，改善胰腺腺泡细胞的存活率。

以上研究表明，黄芩苷可调控Nrf2/Keap1这一氧化应激的关键信号通路，抑制NOX2蛋白表达，增强SOD、GSH-Px等抗氧化酶活性，调控miR-136-5p/SOD1轴改善氧化还原平衡，降低脂质过氧化产物MDA等对胰腺细胞的损伤作用，提示黄芩苷可通过多靶点机制调控氧化应激，在AP治疗中具有重要潜力。

2.3 调控腺泡细胞自噬及凋亡

在AP的病理过程中，胰腺细胞存在自噬紊乱，而精准调控自噬活性，可能成为控制AP病情进展的关键治疗策略[29]。林晶晶等[30]使用黄芩苷治疗牛磺胆酸钠构建的SAP大鼠，结果显示黄芩苷可抑制胰腺组织中磷酸化蛋白激酶B(phosphorylated protein kinase B，p-Akt)与磷酸化哺乳动物雷帕霉素靶蛋白(phosphorylated mechanistic target of rapamycin，p-mTOR)表达，降低LC3-II水平，表明黄芩苷通过调控Akt/mTOR信号通路来抑制细胞自噬过程，缓解胰腺细胞损伤，从而缓解SAP病情。此外，Zhang等[14]发现，黄芩苷可促进大鼠胰腺组织中半胱天冬酶-3(cysteinyl aspartate-specific proteinase-3，Caspase-3)表达，抑制TNF-α mRNA和P-selectin蛋白表达，诱导胰腺细胞凋亡，从而减轻SAP。以上研究表明，黄芩苷可通过抑制Akt/mTOR通路调控自噬、促进Caspase-3介导的凋亡，从而改善胰腺损伤。

2.4 多器官保护效应

黄芩苷不仅可以减轻AP时胰腺损伤，多项研究发现其还可减轻胰腺外器官损伤。Li等[31]发现黄

芩苷可降低血清淀粉酶、TNF-α和IL-6水平以及抑制胰腺和肺中Toll样受体4(Toll-like receptor 4,TLR4)表达,减轻AP大鼠胰腺和肺部损伤。Liu等[32]在牛磺胆酸钠诱导的小鼠SAP模型中发现,肠系膜淋巴液中组蛋白作为关键毒性介质诱导多器官功能障碍(multiple organ injury,MOI)发生。黄芩苷干预后,可通过与组蛋白结合中和其毒性,降低血清心肌酶(creatine kinase-MB,CK-MB)、心肌肌钙蛋白T(cardiac troponin T,cTnT)、丙氨酸氨基转移酶(alanine aminotransferase,ALT)、天冬氨酸氨基转移酶(aspartate aminotransferase,AST)及肾功能尿素(Urea)等指标,显著减轻心、肝、肾等器官的损伤。Tian等[25]使用黄芩苷治疗SAP大鼠时发现,黄芩苷可调节大鼠胰腺、肠黏膜、淋巴结和脾脏等的BCL2相关X蛋白(BCL2-associated X protein,Bax)蛋白表达,诱导炎症微环境中细胞凋亡,减轻炎症反应,促进多器官损伤的修复。

Zhang等[33]在SAP模型中系统性研究了黄芩苷对多器官损伤的保护作用,他们发现黄芩苷不仅抑制SAP大鼠的肝肾NF-κB和P-Selectin表达,对SAP肝肾损伤有明显保护作用,还可通过调节B细胞淋巴瘤2(B cell lymphoma 2,Bcl-2)/Bax表达,诱导肝细胞凋亡,减轻肝脏病理损伤,降低血清ALT、AST水平,提高SAP大鼠存活率[34]。同时,研究还发现黄芩苷可抑制内毒素、PLA2、CREA、Bcl-2、TNF-α与ET-1等血浆毒性因子水平,降低肾脏损伤[35]。黄芩苷可控制炎症反应、抑制P-Selectin表达和诱导胸腺细胞凋亡,减轻胸腺病理损伤,降低大鼠死亡率[36]。在SAP相关脑损伤模型中,黄芩苷能显著抑制脑组织中NF-κB表达,缓解脑水肿与神经元损伤[37]。黄芩苷还对SAP并发的肠黏膜损伤有显著保护作用,其机制可能与抑制炎症介质和调控肠黏膜上皮细胞凋亡有关[38]。以上研究表明,黄芩苷在AP中不仅对胰腺具有保护作用,还可改善相关并发症,体现了黄芩苷作为多靶点治疗药物的潜在价值。

综上,大量临床前研究从抗炎、抗氧化、调控细胞自噬与凋亡以及多器官保护等多个角度,证实了黄芩苷在AP模型中的改善效果。但上述结论均基于基础研究得出,难以全面反映人类疾病的复杂病理过程。因此,尽管黄芩苷展现出多靶点作用优势,其在AP患者中的真实疗效、最优剂量及安全性仍有待高质量临床试验进一步验证。

3　黄芩苷在慢性胰腺炎中的防治作用

慢性胰腺炎是一种以胰腺炎症和纤维化为典型病理特征的综合征,可导致胰腺内外分泌功能受损[39]。病理上,CP主要表现为胰腺腺泡细胞萎缩、腺泡导管化生(acinar-to-ductal metaplasia,ADM)、炎症细胞浸润及胰腺星状细胞活化,进而引发细胞外基质过度沉积和胰腺纤维化[40]。目前临床治疗以缓解症状为主,如止痛、酶替代疗法等,但尚未有明确的药物可以有效逆转胰腺纤维化进程[5]。黄芩苷作为一种传统中药活性成分,其通过抑制ADM、缓解炎症反应,延缓胰腺纤维化进程等减轻CP进展,显示出潜在的干预价值。黄芩苷在CP中的防治作用机制具体如图3所示。

3.1　抑制ADM

ADM是CP进程中的早期病理学事件,其特点是腺泡细胞表型转变为导管样表型,目前认为ADM的形成在CP的病理进展中发挥一定作用[41]。魏圆圆[42]发现,雨蛙素诱导CP小鼠模型2周后,其腺泡细胞萎缩,呈管样表型,随着病程进展,ADM标志物细胞角蛋白19(cytokeratin 19,CK-19)的表达增加,ADM的形成受到IL-6/STAT3通路的调控。而黄芩苷能抑制胰腺组织IL-6/STAT3通路的激活,降低ADM标志物CK-19的表达,减少ADM的形成,减轻小鼠胰腺纤维化的程度。同时离体实验发现,雨蛙素刺激胰腺腺泡细胞系266-6细胞后,p-STAT3和CK-19表达增加,而采用黄芩苷干预可直接抑制以上蛋白的表达,这一结果与体内实验结论一致,再次验证了黄芩苷可能通过抑制 IL-6/STAT3通路的激活抑制ADM形成。

3.2　抗纤维化

胰腺纤维化作为CP最具特征的病理学改变,其发生发展的核心机制在于胰腺星状细胞(pancreatic stellate cell,PSC)的异常活化。活化的PSC通过促进细胞外基质过度沉积,在胰腺纤维化进程中发挥关键驱动作用[43]。因此,靶向调控胰腺星状细胞的活化已成为当前CP治疗策略的重要研究方向。转化生长因子-β1(transforming growth factor beta 1,TGF-β1)是诱导PSC活化的重要调控因子[43]。胡小兰[44]采用黄芩苷治疗二乙基二硫代氨基甲酸盐(DDC)诱导的大鼠CP模型时发现,黄芩苷可下调

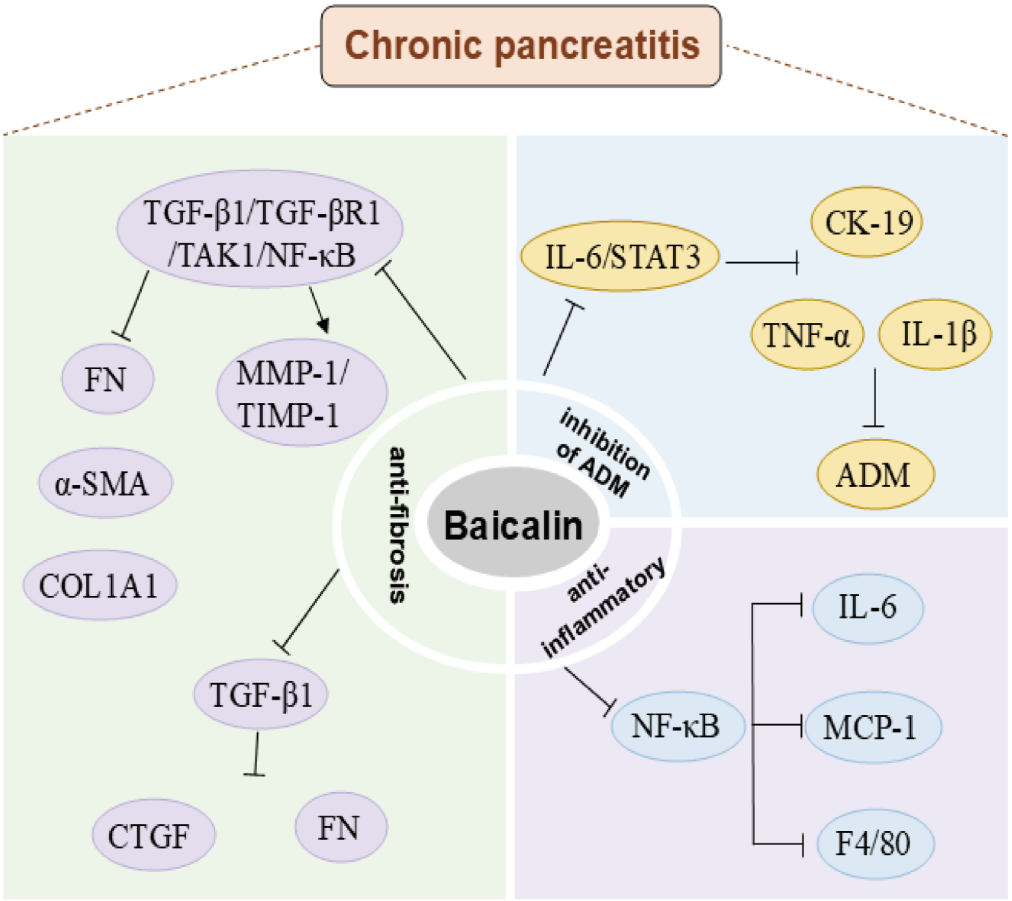

图3 黄芩苷在慢性胰腺炎中的防治作用

Figure 3 Preventive and therapeutic effects of baicalin in chronic pancreatitis

TGF-β1水平，抑制PSC活化，降低结缔组织生长因子(connective tissue growth factor，CTGF)和纤维连接蛋白(fibronectin，FN)的表达，改善胰腺组织纤维化程度。吴楠[13]采用TGF-β1诱导PSC活化，发现黄芩苷抑制NF-κB信号通路活性，降低α-平滑肌肌动蛋白(alpha-smooth muscle actin，α-SMA)和FN的表达，有效抑制PSC的活化。范建伟等[45]通过L-精氨酸诱导昆明小鼠CP模型，发现NF-κB信号通路活化通过影响基质金属蛋白酶-1(matrix metalloproteinase-1，MMP-1)/金属蛋白酶组织抑制剂-1(tissue inhibitor of metalloproteinases-1，TIMP-1)的相对平衡在胰腺纤维化中发挥重要作用。而黄芩苷通过抑制NF-κB信号通路的活化，调控MMP-1/TIMP-1的相对平衡，减少ECM沉积，改善胰腺纤维化。进一步通过体内外实验证实[46]，黄芩苷不仅能抑制雨蛙素诱发的小鼠胰腺纤维化，还可抑制原代分离的小鼠PSC中NF-κB的活化，降低TGF-βR1和p-TAK水平，调控TGF-β1/TGF-βR1/TAK1/NF-κB信号通路，抑制α-SMA和I型胶原蛋白α1链(collagen type I alpha 1 chain，COL1A1)的表达，从而阻断ECM的过度沉积及PSC活化。

3.3 抗炎作用

CP的病理进程与持续的炎症反应密切相关，其特征表现为免疫炎症细胞在胰腺组织的浸润、炎症因子的异常释放，形成炎症微环境，进一步激活胰腺星状细胞和促进细胞外基质沉积，反复发作的炎症反应是诱发胰腺组织损伤，最终导致胰腺纤维化不可逆进展的重要环节[43]。吴楠[13]发现，黄芩苷通过阻断NF-κB信号通路的活化，减少其下游炎症因子IL-6和单核细胞趋化蛋白-1(monocyte chemoattractant protein-1，MCP-1)的释放，改善炎症微环境。Fan等[46]进一步通过体内外实验证实，黄芩苷显著降低PSC分泌的MCP-1，抑制巨噬细胞向胰腺的迁移，从而缓解胰腺局部的炎症状态、减轻胰腺组织损伤。以上研究表明，黄芩苷在CP进展中具有显著的抗炎

作用，可通过抑制炎症细胞浸润及炎症因子的表达，有效降低胰腺组织中的炎症水平，从而改善CP的疾病进展。

现有研究初步揭示了黄芩苷通过抑制ADM、抗炎和抗纤维化等途径延缓CP进展的潜在机制，为其作为潜在抗纤维化药物提供了临床前依据。但CP是一种长期、复杂的慢性炎症性疾病，其人体病理环境远比动物和细胞模型复杂。黄芩苷作为单一单体成分，能否在临床中重现实验结果并转化为实际疗效，是未来研究面临的关键问题与挑战。

4　黄芩苷在胰腺癌中的防治作用

胰腺癌是消化系统肿瘤中恶性程度最高的肿瘤之一，具有起病隐匿、进展迅速、转移能力强和对常规放化疗抵抗性高等特点[47]。在病理上，PC表现为腺管结构紊乱，腺癌细胞高度异型增生，伴广泛纤维间质增生和神经血管侵犯，反映出其强侵袭性与治疗抵抗性[48]。目前，PC的治疗面临诸多挑战，包括早期诊断困难、化疗耐药性高以及肿瘤微环境的复杂性[49]。作为从黄芩中提取的主要活性成分，黄芩苷可抑制细胞增殖、诱导细胞凋亡及抑制细胞迁移与侵袭，显示出良好的抗肿瘤潜力。黄芩苷在PC中的防治作用机制具体如图4所示。

4.1　调控细胞增殖及凋亡

PC的快速进展与高细胞增殖率密切相关，因此，靶向抑制细胞增殖是当前抗PC治疗的重要策略之一[50]。魏昇等[51]分别用25、50、100和200 μmol/L的黄芩苷处理多种PC细胞系（PANC-1、MIAPaCa-2和BxPC-3）24、48、72 h后发现，黄芩苷对以上三种PC细胞的生长和增殖均具有抑制作用，且呈剂量和时间依赖性。而在另一种PC细胞SW1990，Huang等[52]分别用40、80、120和160 μmol/L的黄芩苷处理24、48、72 h后发现，黄芩苷可显著抑制SW1990细胞增殖，也具有明显的剂量与时间依赖性。此外，黄芩苷还可影响PC细胞的生长周期，可以抑制周期蛋白依赖性激酶2（cyclin-dependent kinase 2，CDK2）和周期蛋白E1（Cyclin E1）蛋白表达、上调p15水平，诱导细胞周期在G_1期阻滞，从而进一步影响细胞增殖。

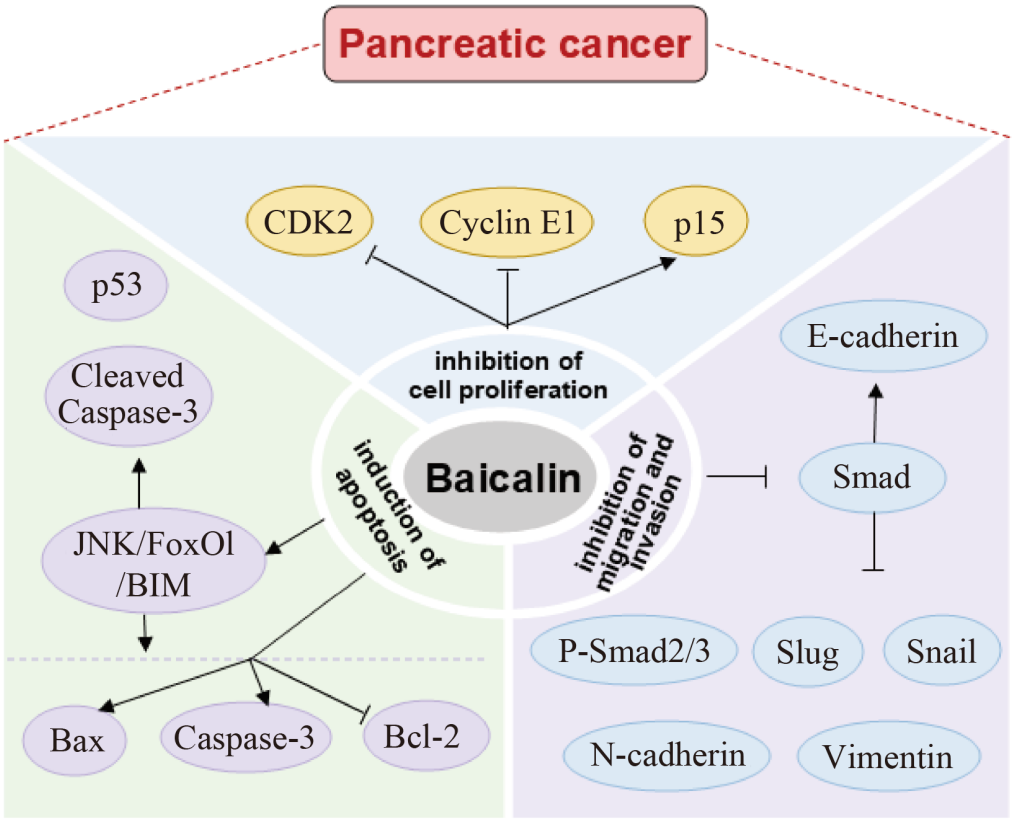

图4　黄芩苷在胰腺癌中的防治作用

Figure 4　Preventive and therapeutic effects of baicalin in pancreatic cancer

诱导细胞凋亡也是PC治疗的一个重要策略[50]。魏昇等[51]采用不同浓度的黄芩苷处理人PC细胞系PANC-1、MIAPaCa-2和BxPC-3，发现黄芩苷可上调促凋亡蛋白Bax、下调抗凋亡蛋白Bcl-2，并激活Caspase-3，诱导细胞凋亡。Huang等[52]研究发现，黄芩苷呈剂量依赖性诱导PC SW1990细胞凋亡，其作用机制与黄芩苷激活JNK/叉头框蛋白O1 (forkhead box protein O1，FoxO1)/BCL-2相互作用细胞死亡介导因子(BCL-2 interacting mediator of cell death，BIM)信号通路，降低Bcl-2蛋白水平，增加Bax、Cleaved Caspase-3和肿瘤蛋白p53蛋白水平，增加细胞内ROS水平有关。

4.2 抑制迁移与侵袭

PC的高度侵袭性是其临床恶性程度高、预后差的重要原因之一[50]。Zheng等[53]通过体外实验构建了TGF-β1诱导的PANC-1细胞上皮-间充质转化(epithelial-mesenchymal transition，EMT)模型，发现黄芩苷可显著抑制Smad2/3蛋白(mothers against decapentaplegic homolog 2/3)的磷酸化，阻断TGF-β1/Smad信号通路的激活，从而下调EMT关键转录因子Snail家族转录抑制因子1(Snail family transcriptional repressor 1，Snail)和Snail家族转录抑制因子2(Snail family transcriptional repressor 2，Slug)的表达，恢复上皮钙黏附蛋白(E-cadherin)等上皮标志物表达，抑制神经钙黏附蛋白(neuronal cadherin，N-cadherin)、波形蛋白(Vimentin)等间充质标志物的表达，最终有效抑制PC细胞的迁移与侵袭，且该作用呈明显的剂量依赖性。

大量体外研究表明，黄芩苷能有效抑制胰腺癌细胞的增殖、迁移与侵袭，并诱导其凋亡，显示出潜在的抗肿瘤活性，为其作为胰腺癌辅助治疗药物的开发提供了实验依据。然而，胰腺癌高度异质且肿瘤微环境复杂，现有研究多依赖有限的细胞系模型，难以全面模拟体内的真实病理过程。黄芩苷能否在临床中展现出稳定且显著的疗效，仍需更多高质量的转化研究加以验证。

5 结语

黄芩苷作为中药黄芩的核心活性成分，在胰腺外分泌疾病的防治中展现出广泛的药理作用。当前的研究表明，黄芩苷通过调节多个信号通路，发挥其多靶点的药理作用。具体机制包括：抗炎作用，在AP中，其主要通过抑制NF-κB、JAK2/STAT3、MAPK/JNK等炎症信号通路以快速减轻炎症反应；而在CP中，则更多表现为抑制炎性细胞浸润，下调IL-6、MCP-1等炎症介质，改善炎症微环境。前者侧重于急性信号通路的快速抑制，后者则强调炎症微环境和纤维化进程的调控；调节Nrf2/Keap1通路、miR-136/SOD1轴及NOX2表达，增强抗氧化酶活性，清除ROS，从而减轻胰腺组织氧化损伤；通过干预Akt/mTOR、自噬相关因子LC3及凋亡蛋白Caspase-3的表达，精准调控胰腺细胞的自噬与凋亡过程；抑制TGF-β1/Smad和IL-6/STAT3信号，抑制胰腺星状细胞活化，减少胶原沉积与ADM形成，延缓胰腺纤维化；此外，黄芩苷还可通过阻断Smad通路，激活JNK/FoxO1/BIM轴，抑制肿瘤细胞的增殖、侵袭并诱导凋亡。综上，黄芩苷在胰腺外分泌疾病中的特异性药理环节主要体现在：①抑制星状细胞活化及腺泡细胞损伤；②调控Nrf2与Smad信号，实现“氧化应激–纤维化”轴的平衡；③干预胰腺癌微环境并抑制EMT。上述机制提示，黄芩苷在胰腺外分泌疾病防治中具有相对的组织选择性调节优势，为其靶向研究与临床转化提供了理论依据。

尽管现有研究已初步证明了黄芩苷在胰腺外分泌疾病中的防治效果，为黄芩苷的潜在应用提供了有力证据，但目前的大量研究主要集中在体外或动物实验，这些发现能否直接转化为临床疗效尚属未知。多个含有黄芩的中药复方在临床上取得可靠的疗效，而作为黄芩主要成分的黄芩苷在临床中对胰腺外分泌疾病的疗效评价、安全性及具体机制仍然是值得进一步深入探讨的问题，需要通过大规模、随机对照的临床试验来验证其疗效和安全性。之前的研究发现传统制剂的黄芩苷生物利用度较低，这可能是影响其临床应用的原因之一。因此，新型制剂的研发成为提高黄芩苷临床应用前景的关键方向。随着纳米技术、脂质体制剂及其他药物载体的发展，黄芩苷的药物递送效率和靶向性有望得到显著提升，从而增强其临床治疗效果。

值得注意的是，胰腺囊性纤维化、胰腺外分泌功能不全等疾病同样属于胰腺外分泌疾病的重要类型，严重影响患者生活质量。然而，目前尚缺乏黄芩苷在这些疾病中作用的系统研究。未来应进一步探索黄芩苷在此类疾病中的潜在价值，以拓展其在胰腺外分泌疾病防治中的应用范围。此外，黄

芩苷在体内可水解为其主要代谢产物黄芩素(baicalein)。已有研究表明,黄芩素同样具有抗炎、抗氧化及抗肿瘤等多种药理作用[54],其作用机制与黄芩苷相似,并已有实验提示其在胰腺外分泌疾病中可能发挥相似的干预作用[55,56]。未来研究可进一步比较黄芩苷及黄芩素在胰腺外分泌疾病防治中的差异及协同效应,从而拓展药物开发与临床应用的可能性。综上所述,黄芩苷作为一种传统中药成分,已展现出在胰腺外分泌疾病治疗中的应用潜力。然而,当前研究仍处于探索阶段,未来的研究需进一步加强基础研究与临床试验的结合,优化药物制剂和使用方式,使其在胰腺外分泌疾病治疗中的优势得以充分发挥。

参考文献

[1] Mastracci TL, Apte M, Amundadottir LT, et al. Integrated physiology of the exocrine and endocrine compartments in pancreatic diseases: workshop proceedings. Diabetes, 2023, 72: 433–48.

[2] Wen Y, Luo Y, Huang Y, et al. Global, regional, and national pancreatitis burden and health inequality of pancreatitis from 1990 to 2019 with a prediction from 2020 to 2034. BMC Public Health, 2024, 24: 3329.

[3] Li T, Lin C, Wang W. Global, regional, and national burden of pancreatic cancer from 1990 to 2021, its attributable risk factors, and projections to 2050: a systematic analysis of the global burden of disease study 2021. BMC Cancer, 2025, 25: 189.

[4] Beij A, Verdonk RC, van Santvoort HC, et al. Acute pancreatitis: An update of evidence - based management and recent trends in treatment strategies. United European Gastroenterol J, 2025, 13: 97–106.

[5] Hines OJ, Pandol SJ. Management of chronic pancreatitis. BMJ, 2024, 384: e070920.

[6] Kolbeinsson HM, Chandana S, Wright GP, et al. Pancreatic cancer: a review of current treatment and novel therapies. J Invest Surg, 2023, 36: 2129884.

[7] 陆琦, 王婧斯, 都暖, 等. 黄芩苷药理作用及应用研究进展. 临床合理用药, 2025, 18: 176–81.
Lu Q, Wang J, Du N, et al. Pharmacological effects and applications of baicalin: A review. Clin Rational Drug Use, 2025, 18: 176–81.

[8] Ganguly R, Gupta A, Pandey AK. Role of baicalin as a potential therapeutic agent in hepatobiliary and gastrointestinal disorders: A review. World J Gastroenterol, 2022, 28: 3047–62.

[9] Wang X, Xie L, Long J, et al. Therapeutic effect of baicalin on inflammatory bowel disease: A review. J Ethnopharmacol, 2022, 283: 114749.

[10] 孙花丽, 门靖, 郭彩凤, 等. 黄芩苷的药理活性及其定性定量分析检测方法的研究进展. 化工与医药工程, 2023, 44: 57–63.
Sun H, Men J, Guo C, et al. Pharmacological activities of baicalin and its qualitative and quantitative analysis methods: A review. Chem Eng Pharm Eng, 2023, 44: 57–63.

[11] Huang T, Liu Y, Zhang C. Pharmacokinetics and bioavailability enhancement of baicalin: A review. Eur J Drug Metab Pharmacokinet, 2019, 44: 159–68.

[12] Qian Y, Chen Y, Wang L, et al. Effects of baicalin on inflammatory reaction, oxidative stress and PKDl and NF-κB protein expressions in rats with severe acute pancreatitis. Acta Cir Bras, 2018, 33: 556–64.

[13] 吴楠. NF-kB在胰腺星状细胞活化中的作用及黄芩苷对其干预机制研究[D]. 咸阳: 陕西中医药大学, 2017.
Wu N. The role of NF-κB in the activation of pancreatic stellate cells and the intervention mechanism of baicalin [D]. Xianyang: Shaanxi University of Chinese Medicine, 2017.

[14] Zhang X, Tian H, Zhang J, et al. Influence of baicalin on TNF-α mRNA, caspase-3 and P-selectin expression in pancreatic tissue of rats with severe acute pancreatitis. Indian J Gastroenterol, 2009, 28: 131–35.

[15] Mihoc T, Latcu SC, Secasan CC, et al. Pancreatic morphology, immunology, and the pathogenesis of acute pancreatitis. Biomedicines, 2024, 12: 2627.

[16] 李渊, 杨慧琴, 吴康盛. 清胰汤治疗重症急性胰腺炎临床研究. 河南中医, 2024, 44: 374–78.
Li Y, Yang H, Wu K. Clinical study on the treatment of severe acute pancreatitis with Qingyi Decoction. Henan Trad Chin Med, 2024, 44: 374–78.

[17] 张倩, 郝晓英, 张慧芳. 柴芩承气汤治疗急性胰腺炎(湿热壅滞证)患者的疗效观察. 中国中医急症, 2023, 32: 1042–45.
Zhang Q, Hao X, Zhang H. Observation on the efficacy of Chaiqin Chengqi Decoction in the treatment of acute pancreatitis (damp-heat obstructing syndrome). Chin J Acute Trad Chin Med, 2023, 32: 1042–45.

[18] 曾渊杰, 宋晓龙, 薛寅. 大柴胡汤加减辅助治疗急性胰腺炎(腑实热结证)的临床观察. 中国中医急症, 2025, 34: 491–94.
Zeng Y, Song X, Xue Y. Clinical observation on the auxiliary treatment of acute pancreatitis (excessive heat in the bowel syndrome) with modified Dazhihu Decoction. Chin J Acute Trad Chin Med, 2025, 34: 491–94.

[19] Jakkampudi A, Jangala R, Reddy BR, et al. NF-κB in acute pancreatitis: Mechanisms and therapeutic potential. Pancreatology, 2016, 16: 477–88.

[20] Xue D, Zhang W, Zhang Y, et al. Adjusting effects of baicalin for nuclear factor - κB and tumor necrosis factor-α on rats with caerulein - induced acute pancreatitis. Mediators Inflamm, 2006, 2006: 26295.

[21] Zhao H, Li H, Liu Z, et al. Baicalin inhibited nuclear factor κB (NF-κB) activation and attenuated sodium taurocholate of induced experimental pancreatitis in rats. Afr J Pharm Pharmacol, 2012, 6: 1176–85.

[22] Yang J, Han F, Wu G, et al. Dysregulated B7H4/JAK2/STAT3 pathway involves in hypertriglyceridemia acute pancreatitis and is attenuated by baicalin. Digest Dis Sci, 2023, 68: 478–86.

[23] 周彬, 魏志力, 刘文涛, 等. 黄芩苷对脂多糖诱导人正常胰腺导管上皮细胞(HPDE6-C7)损伤的影响. 吉林中医药, 2025, 45: 606–11.
Zhou B, Wei Z, Liu W, et al. Effect of baicalin on lipopolysaccharide-induced damage in human normal pancreatic ductal epithelial cells (HPDE6-C7). Jilin J Trad Chin Med, 2025, 45: 606–11.

[24] Zhen J, Chen W, Liu Y, et al. Baicalin protects against acute pancreatitis involving JNK signaling pathway via regulating miR-15a. Am J Chin Med, 2021, 49: 147–61.

[25] Tian H, Zhang X, Wu C, et al. Effects of baicalin and octreotide on the serum TNF-α level and apoptosis in multiple organs of rats with severe acute pancreatitis. Inflammation, 2009, 32: 191–201.

[26] Zhang X, Tian H, Wu C, et al. Effect of baicalin on inflammatory mediator levels and microcirculation disturbance in rats with severe acute pancreatitis. Pancreas, 2009, 38: 732–38.

[27] Xia C, Chen H, Deng H, et al. Reactive oxygen species and oxidative stress in acute pancreatitis: Pathogenesis and new therapeutic interventions. World J Gastroenterol, 2024, 30: 4771–80.

[28] Zhao Z, Zhang Y, Sun Y, et al. Protective effects of baicalin on caerulein-induced AR42J pancreatic acinar cells by attenuating oxidative stress through miR-136-5p downregulation. Sci Prog, 2021, 104: 368504211026118.

[29] Zhang T, Gan Y, Zhu S. Association between autophagy and acute pancreatitis. Front Genet, 2023, 14: 998035.

[30] 林晶晶, 韩小乐, 李恒平, 等. 黄芩苷对急性胰腺炎大鼠胰腺细胞自噬及Akt/mTOR通路的影响. 中国中医急症, 2018, 27: 858–61+870.
Lin J, Han X, Li H, et al. Effect of baicalin on pancreatic cell autophagy and the Akt/mTOR signaling pathway in rats with acute pancreatitis. Chin J Acute Trad Chin Med, 2018, 27: 858–61+870.

[31] Li Z, Xia X, Zhang S, et al. Up-regulation of Toll-like receptor 4 was suppressed by emodin and baicalin in the setting of acute pancreatitis. Biomed Pharmacother, 2009, 63: 120–28.

[32] Liu S, Wang Q, Luo W, et al. Histones are critical toxic factors in gut lymph of severe acute pancreatitis: neutralization by baicalin and baicalein for protection. Phytomedicine, 2025, 139: 156474.

[33] Zhang X, Zhang J, Xu Q, et al. Influence of baicalin and octreotide on NF-κB and P-selectin expression in liver and kidney of rats with severe acute pancreatitis. Inflammation, 2009, 32: 1–11.

[34] Zhang X, Zhang J, Ren Z, et al. Study on protecting effects of baicalin and octreotide on hepatic injury in rats with severe acute pancreatitis. World J Gastroenterol, 2008, 14: 6551–59.

[35] Zhang X, Tian H, Lai Y, et al. Protective effects and mechanisms of baicalin and octreotide on renal injury of rats with severe acute pancreatitis. World J Gastroenterol, 2007, 13: 5079–89.

[36] Zhang X, Feng G, He J, et al. Baicalin protects thymus of rats with severe acute pancreatitis. Inflammation, 2010, 33: 157–65.

[37] Ou J, Zhang X, Wang C, et al. Study of dexamethasone, baicalin and octreotide on brain injury of rats with severe acute pancreatitis. Inflamm Res, 2012, 61: 265–75.

[38] Zhang X, Feng G, Weng W, et al. Protective effects of baicalin and octreotide on intestinal mucosa of rats with severe acute pancreatitis. Turk J Gastroenterol, 2009, 20: 108–15.

[39] Shimizu K, Ito T, Irisawa A, et al. Evidence-based clinical practice guidelines for chronic pancreatitis 2021. J Gastroenterol, 2022, 57: 709-24.

[40] Wang Z, Dong S, Zhou W. Pancreatic stellate cells: Key players in pancreatic health and diseases. Mol Med Rep, 2024, 30: 109.

[41] Marstrand-Daucé L, Lorenzo D, Chassac A, et al. Acinar-to-ductal metaplasia (ADM): on the road to pancreatic intraepithelial neoplasia (PanIN) and pancreatic cancer. Int J Mol Sci, 2023, 24: 9946.

[42] 魏圆圆. IL-6/STAT3信号通路参与胰腺腺泡细胞导管化生及黄芩苷的干预作用机制的研究[D]. 咸阳: 陕西中医药大学, 2021.
Wei Y. The role of IL-6/STAT3 signaling pathway in the ductal metaplasia of pancreatic acinar cells and the intervention mechanism of baicalin[D]. Xianyang: Shaanxi University of Chinese Medicine, 2021.

[43] Kong F, Pan Y, Wu D. Activation and regulation of

pancreatic stellate cells in chronic pancreatic fibrosis: A potential therapeutic approach for chronic pancreatitis. Biomedicines, 2024, 12: 108.

[44] 胡小兰. 黄芩苷对大鼠胰腺纤维化的保护作用[D]. 武汉: 湖北中医药大学, 2010.
Hu X. Protective effect of baicalin on pancreatic fibrosis in rats[D]. Wuhan: Hubei University of Chinese Medicine, 2010.

[45] 范建伟, 许小凡, 辛嘉萁, 等. 黄芩苷通过调控TGF-β1/TAK-NF-κB通路对胰腺纤维化的防治作用. 中国病理生理杂志, 2020, 36: 268–75.
Fan J, Xu X, Xin J, et al. Protective and therapeutic effects of baicalin on pancreatic fibrosis by regulating the TGF-β1/TAK-NF-κB signaling pathway. Chin J Pathophysiol, 2020, 36: 268–75.

[46] Fan J, Duan L, Wu N, et al. Baicalin ameliorates pancreatic fibrosis by inhibiting the activation of pancreatic stellate cells in mice with chronic pancreatitis. Front Pharmacol, 2021, 11: 607133.

[47] Stoop TF, Javed AA, Oba A, et al. Pancreatic cancer. Lancet, 2025, 405: 1182–202.

[48] McDonald OG. The biology of pancreatic cancer morphology. Pathology, 2022, 54: 236–47.

[49] Halbrook CJ, Lyssiotis CA, di Magliano MP, et al. Pancreatic cancer: Advances and challenges. Cell, 2023, 186: 1729–54.

[50] Duan H, Li L, He S. Advances and prospects in the treatment of pancreatic cancer. Int J Nanomed, 2023, 18: 3973–88.

[51] 魏昇, 任帅, 田迎, 等. 黄芩苷抑制胰腺癌细胞的恶性进展及相关机制研究. 现代肿瘤医学, 2024, 32: 4015–22.
Wei W, Ren S, Tian Y, et al. Inhibitory effects of baicalin on the malignant progression of pancreatic cancer cells and related mechanisms. Modern Oncol, 2024, 32: 4015–22.

[52] Huang Q, Zhang J, Peng J, et al. Effect of baicalin on proliferation and apoptosis in pancreatic cancer cells. Am J Transl Res, 2019, 11: 5645–54.

[53] Zheng L, Zhou Z, He Z. Baicalin inhibits TGF-β1-induced epithelial-to-mesenchymal transition and suppresses pancreatic cancer cell migration and invasion. Int J Clin Exp Pathol, 2016, 9: 1054–60.

[54] Munjal K, Goel Y, Gauttam VK, et al. Molecular targets and therapeutic potential of baicalein: a review. Drug Target Insights, 2024, 18: 30–46.

[55] Pu WL, Bai RY, Zhou K, et al. Baicalein attenuates pancreatic inflammatory injury through regulating MAPK, STAT 3 and NF-κB activation. Int Immunopharmacol, 2019, 72: 204–10.

[56] Li Z, Zou X, Zhu H, et al. Inhibitory effect of baicalein combined with gemcitabine in human pancreatic cancer cell lines. Oncol Lett, 2018, 15: 5459–64.