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基于多种化疗肠损伤发生机制的中医药防治进展

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摘要 肠损伤是临床应用化疗药物的常见不良反应，限制了化疗药的进一步应用，并给病人造成严重的身心负担。目前化疗肠损伤的发生机制比较复杂，中医药具有极好的防治作用。本文综述化疗引起肠道菌群失调、氧化应激、炎症反应、细胞凋亡、免疫损伤等造成肠损伤的相关机制，总结中医药防治的作用，将为防治化疗肠损伤的中药研发提供理论基础。

关键词 化疗；肠损伤；机制；中药；防治

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癌症负担的持续增长，构成了极大的公共卫生挑战[1]。化学疗法作为公认的三大疗法之一，在癌症治疗中占有重要的地位[2]。但作为非选择性药物，化疗药物在杀伤肿瘤细胞的同时对正常的组织、细胞也会造成影响[3]。由于肠道组织更新快，对细胞毒性药物敏感，因此肠道损伤是化疗最常见的副作用，其特征在于对肠黏膜的广泛损害，引发腹泻、出血、恶心、呕吐、腹痛、营养不良、感染以及与细菌易位相关的脓毒症等症状[4]。近年来中医药防治化疗肠损伤已成为研究热点，如中药有效成分、单味药及复方在防治化疗肠损伤方面具有显著疗效。本文就目前引起化疗肠损伤的潜在机制及中药治疗进行综述。

1 化疗药物引发肠损伤的机制

大多数化疗药物对免疫系统会有不同程度的抑制作用。在身体的免疫系统中，肠道被认为是体内最大的免疫器官，因为它与抗原接触的表面积最大，免疫细胞数量众多[5]。因此能引起肠损伤的化疗药物如抗代谢类药5-氟尿嘧啶（5-fluorouracil）、铂类抗癌药物顺铂（cisplatin）、天然化合物抗肿瘤药物伊利替康（irinotecan）、烷化剂环磷酰胺（cyclophosphamide）等会通过破坏肠道菌群平衡、氧化应激、炎症反应、细胞凋亡及免疫损伤等方式引起肠损伤，出现体质量减轻、肠道绒毛长度缩短、肠道通透性增加破坏肠道屏障的完整性等表现，导致腹泻或肠黏膜炎（表1）。

1.1 肠道微生物平衡失调 肠道微生物可以通过产生有益的代谢物和促进免疫调节来积极影响宿主的生理功能[6]。正常的肠道菌群能维持肠道的动态平衡，一旦肠道菌群失调，菌群之间的共生及拮抗关系就会被破坏，进而影响机体的营养、代谢、免疫能力[7-8]。研究发现，肠道菌群与肿瘤的发生、发展和转移有着密切的关系，而化

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疗能够改变肠道菌群组成，破坏肠道微生态平衡[9]。化疗导致的肠道菌群失调主要表现为肠道细菌丰富度的改变，益生菌被抑制，潜在致病菌过度增殖[10]。对健康小鼠腹腔注射5-氟尿嘧啶后，肠道内梭状芽孢杆菌、乳酸杆菌数量减少，而链球菌属、大肠杆菌数量增加[11]。接受5-氟尿嘧啶、顺铂和多西他赛联合化疗后的小鼠肠道内乳酸杆菌数量减少，而艰难梭菌和肠球菌的数量显著增加[12]。伊立替康能导致肠道微生物群落中有益菌（如双歧杆菌属）数量减少，有害菌（如大肠杆菌）数量增加[13]。环磷酰胺腹腔注射后小鼠肠道中有益菌乳酸菌、罗斯氏菌属和毛螺菌属的相对丰富度减少，而致病菌螺杆菌、消化球菌的相对丰富度显著增加[14]。顺铂通过破坏肠道微生物群稳态，使小鼠肠道中乳酸菌的相对丰度下降，阿克曼氏菌、大肠埃希菌、志贺菌的相对丰度增加来诱导肠道黏膜炎症[15]。

1.2 氧化应激 氧化应激已被证明参与多种疾病的发生发展[16]，细胞氧化性物质活性氧（reactive oxygen species，ROS），在各种生理过程中产生，并参与许多信号通路[17-18]。ROS的过度积累能导致氧化应激，破坏氧化还原信号传导并对生物分子造成损害[19]。顺铂能增加组织中ROS的产生[20]。伊立替康通过刺激ROS相关的JNK和p38-MAPK通路促进自噬依赖性细胞凋亡，随后导致黏膜炎和组织损伤[21]。脂质过氧化产物[如丙二醛（MDA）]，作为一种氧化应激生物标志物，是氧化攻击细胞膜的主要生化后果[22]。5-氟尿嘧啶和卡培他滨口服治疗后大鼠肠道组织的MDA，蛋白质羰基化和过氧化氢（H_2O_2）升高，抗氧化剂谷胱甘肽过氧化物酶（GPx）、超氧化物歧化酶（SOD）、过氧化氢酶（CAT）降低[23]。Nrf2/HO-1信号通路是关键的内源性抗氧化应激途径之一，5-氟尿嘧啶能够降低小鼠体内Nrf2和HO-1蛋白水平，抑制Nrf2/HO-1信号通路的激活[24]。

1.3 炎症反应 炎症在体内平衡和组织损伤中的各种作用是对抗疾病的关键[25]。肿瘤坏死因子（TNF-α）和白细胞介素（IL-1β）是重要的促炎细胞因子[26]。IL-1β和TNF-α通过促进白细胞迁移到炎症组织中来协同增强炎症，参与肠道损伤相关化疗诱导的隐窝细胞凋亡[27]。通过对化疗诱导的肠黏膜炎中促炎细胞因子的分析发现，5-氟尿嘧啶诱导的小肠黏膜炎中IL-1β水平升高，导致小鼠小肠绒毛和隐窝显示结构完整性丧失，绒毛长度和隐窝深度缩短[28]。顺铂能增加肠组织中TNF-α、IL-6和IL-1β的水平，导致肠绒毛长度和隐窝深度缩短[29]。同时促炎细胞因子能破坏紧密连接而参与肠道屏障功能障碍[30]。5-氟尿嘧啶显著提高小鼠血清中IL-1β和TNF-α表达，降低紧密连接蛋白（ZO-1和Occludin）的表达，使肠道通透性增加，进而破坏肠屏障功能[31]。伊立替康诱导肠道嗜中性粒细胞和嗜酸性粒细胞浸润的增加，诱导肠道炎症反应使肠道运动过度，导致排便频率增加引起腹泻[32]。研究发现TLR通路是多种信号转导通路的焦点和核心机制[33]。TLR-MyD88信号通路能诱导促炎细胞因子（如TNF-α、IL-6和IL-1β）的级联样释放，并引起不受控制的炎症反应[34]。在伊立替康诱导的小鼠模型中敲除TLR/MyD88途径抑制了胃肠道中IL-6、IL-1β和TNF-α的水平，降低肠毒性[35]。

1.4 细胞凋亡 细胞凋亡是一种程序性细胞死亡，其特征是细胞圆变、核碎裂和质膜起泡[36-37]。它在肠上皮细胞中自发发生，维持着肠道正常的形态和功能[38]。调节细胞凋亡的多条信号通路，参与化疗药物引起的细胞凋亡。如IL-6/STAT3信号通路能调节肠上皮细胞的增殖和存活[39]。5-氟尿嘧啶可以激活大鼠小肠隐窝上皮细胞（IEC-6细胞）中IL-6/STAT3通路的信号传导，使IEC-6细胞组的TNF-α、IL-1 β和IL-6水平显著增加，抑制IEC-6的活力，进而诱导IEC-6的凋亡，破坏空肠黏膜表面和绒毛结构的完整性[40]。p38 MAPK途径能调节人体组织中的细胞凋亡[41]。激活p38 MAPK信号通路促进5-氟尿嘧啶诱导的肠黏膜细胞凋亡[42]。IRE1α/JNK通路与细胞凋亡密切相关[43]。顺铂通过IRE1α/JNK轴介导的凋亡信号通路在体外和体内诱导急性肠损伤[44]。

促凋亡基因Bax和抗凋亡标志物Bcl-2，在细胞凋亡过程中发挥着重要作用[45-46]。顺铂通过改变Bax和Bcl-2表达诱导细胞凋亡[47]。体外研究发现，顺铂可以上调IEC-6中Bax/Bcl-2比值，激活细胞色素C、裂解caspase-9、caspase-3、PARP和caspase-12来促进细胞凋亡[44]。5-氟尿嘧啶能上调小鼠回肠和结肠中p38、p-p38、p53、p-p53和Bax的表达水平，下调Bcl-2表达水平，显著增加

凋亡细胞数量[48]。伊立替康通过与拓扑异构酶I/DNA复合物相互作用防止单链断裂的再结合，从而引起双链DNA（dsDNA）断裂，最终导致DNA复制延迟并引发细胞凋亡[49]。

1.5　免疫损伤　环磷酰胺被广泛用作抗癌剂，可能引起多种副作用，如免疫抑制和肠道屏障损伤[50]。研究发现，在环磷酰胺诱导免疫缺陷小鼠中，TLRs/MyD88/NF-κB p65通路抑制，肠黏膜完整性相关基因（Occludin1、Claudin1和MUC-2）的表达下降，绒毛高度/隐窝深度（V/C）降低，肠道形态受损[51]。增加丙二醛（MDA）含量和二胺氧化酶（DAO）活性，破坏肠道免疫，加重肠损伤[52]。环磷酰胺通过破坏肠道微生物群组成，降低短链脂肪酸（SCFA）水平，减少$CD4^+$T细胞的数量及IL-17和IL-21的分泌，来降低肠道免疫力[53]。同时，减少小鼠免疫因子IL-4、IL-1β、TNF-α和IFN-γ的分泌，破坏肠道内乳酸杆菌、拟杆菌相对丰度[54]。

表1　化疗药引起肠损伤的机制

Tab.1　Mechanism of intestinal injury caused by chemotherapeutic agents

药物	机制	指标	文献
5-氟尿嘧啶	菌群改变	乳杆菌属、拟杆菌属和双歧杆菌属↓ 肠球菌属、葡萄球菌属↑	[11]
5-氟尿嘧啶、顺铂和多西他赛	菌群改变	乳酸杆菌↓ 艰难梭菌和肠球菌↑	[12]
5-氟尿嘧啶联合卡培他滨	氧化应激	MDA、H_2O_2↑ GPx、SOD、CAT、-SH↓	[23]
5-氟尿嘧啶	氧化应激	Nrf2/HO-1↓	[24]
5-氟尿嘧啶	炎症反应	IL-1β↑ 绒毛长度和隐窝深度↓	[28]
5-氟尿嘧啶	炎症反应	IL-1β、TNF-α↑ 肠道通透性↑	[31]
5-氟尿嘧啶	细胞凋亡	TNF-α，IL-1 β和IL-6↑ IL-6/STAT3↑	[40]
5-氟尿嘧啶	细胞凋亡	p38、p-p38、p53、p-p53、Bax↑ Bcl-2↓	[48]
5-氟尿嘧啶	细胞凋亡	p38 MAPK↑	[42]
伊立替康	菌群改变	双歧杆菌属↓ 大肠杆菌数量↑	[13]
伊立替康	氧化应激	JNK、p38-MAPK↑	[21]
伊立替康	炎症反应	嗜中性粒细胞和嗜酸性粒细胞↑	[32]
伊立替康	炎症反应	IL-6，IL-1β、TNF-α↓ TLR/MyD88↓	[35]
伊立替康	细胞凋亡	DNA复制延迟	[49]
顺铂	菌群改变	乳酸杆菌↓ 阿克曼氏菌、大肠埃希菌、志贺菌↑	[15]
顺铂	氧化应激	MDA↑ GSH、GPx、SOD↓	[55]
顺铂	炎症反应	TNF-α、IL-6、IL-1β↑ 肠绒毛长度和隐窝深度↓	[29]
顺铂	细胞凋亡	Bax↑ Bcl-2↓	[44]
环磷酰胺	免疫损伤	TLRs/MyD88/NF-κB p65↓	[51]
环磷酰胺	免疫损伤	MDA、DAO↑	[52]
环磷酰胺	免疫损伤	SCFA↓ $CD4^+$T↓及IL-17、IL-21↓	[53]

注：激活↑；抑制↓。

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2 中药在化疗肠损伤中的防治作用

用于缓解化疗肠损伤的临床药物如昂丹司琼、洛哌丁胺、奥氮平等疗效单一、副作用较大且无法用于预防[56]。中药具有多靶点的优势，能起到预防和治疗化疗肠损伤的作用。中医学认为化疗属“药毒”之邪，易损伤脾胃，临床表现多恶心、呕吐、腹泻等，可归属于中医“泄泻”、“腹痛”等范畴[57]。脾胃乃气血生化之源[58]，为后天之本，《脾胃论》中称：“内伤脾胃，百病由生。”邪气损伤脾胃则纳运失司，气机升降失常。近年来从中药有效成分、单方药、复方入手，利用分子生物学机制解析中药药效，加大增强了中药治疗疾病的说服力，验证了中医药在治疗化疗肠损伤中的有效性，揭示其可作为化学药物所致肠道损伤的肠道保护和辅助治疗药物。这些药物主要通过调节肠道菌群、抗氧化、抗炎、抗凋亡及免疫调节等机制保护肠屏障，缓解化疗造成的肠损伤(表2)。

2.1 中药有效成分

2.1.1 多糖类 多糖作为中药的主要成分，通过抗炎、抗氧化、调节肠道菌群和机体免疫等方式，保护宿主细胞免受病原微生物的侵害，还可以通过与肠道微生物的相互作用改善肠道功能[59]。灵芝孢子多糖通过减少内毒素血症和上调紧密连接蛋白(包括ZO-1、E-cadherin、β-catenin和Occludin)增强肠道屏障功能[60]。冬虫夏草多糖能增加细胞自噬和凋亡抑制人结肠癌细胞系(HCT116)细胞的增殖[61]。鸡血藤具有很好的抗炎活性，可以降低促炎细胞因子TNF-α、一氧化氮合酶(iNOS)和环氧合酶2(COX-2)的表达[62]。此外，鸡血藤多糖能改善微生物群落多样性，调优势微生物群的相对丰度，并促进短链脂肪酸(SCFA)的产生，恢复环磷酰胺诱导的肠道微生物菌群失调[51]。蜂蜜多糖能防止小鼠的脾脏和胸腺指数以及体重降低，增加血清中IL-2、IL-6和TNF-α的水平来缓解环磷酰胺诱导的免疫抑制[52]。仙人掌多糖可有效增加环磷酰胺诱导的小鼠白细胞(WBC)计数指数，改善胸腺和脾脏指数，同时有效促进IL-4、IL-1β、TNF-α和IFN-γ的分泌[54]。

2.1.2 皂苷类 皂苷是多种植物药和中药的主要成分[63]。具有祛痰、抗炎、血管保护和抗菌等多种作用[64]。西洋参皂苷能抑制氧化应激，减少炎症和抑制细胞凋亡[65]。在顺铂诱导的肠道损伤中，西洋参皂苷能降低小肠中SOD和MDA等抗氧化酶活性，抑制促炎因子TNF-α、IL-1β的分泌以及下调NF-κB炎症通路，从而减轻肠道损伤[66]。同时西洋参皂苷能减少活化的半胱天冬酶家族蛋白标记的凋亡细胞，抑制肠细胞凋亡[66]。柴胡皂苷-A是一种三萜皂苷，具有抗炎、抗氧化、抗菌、免疫调节、抗肿瘤等作用[67]。柴胡皂苷-A通过增加摄食量及体重、减轻腹泻严重程度和死亡率改善肠黏膜炎[68]。组织病理学分析发现柴胡皂苷-A抑制促炎因子(TNF-α、COX-2、IL-1β和IL-6)的分泌和凋亡标志物(p-JNK、Casp-3)的水平，改善5-氟尿嘧啶诱导的炎性细胞浸润及肠绒毛萎缩[69]。人参皂苷Re通过抑制凋亡基因Bax以及半胱天冬酶家族成员caspase-3和caspase-9的过度表达减轻顺铂诱导的小鼠肠细胞凋亡[70]。

2.1.3 黄酮类 葛根素是一种从纯化的异黄酮成分，具有广泛的生物学活性，包括抗炎、抗肿瘤、抗凋亡和免疫调节[71]。JAK-STAT通路是参与肠黏膜炎促炎细胞因子反应的转录因子的主要通路[72]。葛根素抑制JAK的活化，从而抑制炎症，氧化反应，细胞凋亡和保护的肠道屏障功能，以改善5-氟尿嘧啶诱导的肠黏膜炎[73]。木犀草素是一种天然类黄酮，广泛存在于植物中，具有抗炎作用、抗氧化剂、抗肿瘤、神经保护等特性[74]。研究发现，木犀草素能降低ROS和非自由基的活性氧(LOOH)的水平并增加内源性抗氧化剂从而减轻伊立替康诱导的氧化应激，同时降低MPO酶活性，抑制TNF、IL-1β和IL-6以及增加IL-4、IL-10的分泌来减轻炎症反应，改善肠屏障[75]。具有抗炎活性的甜橙黄酮能够抑制顺铂诱导的促炎细胞内容物释放和炎症细胞死亡，减轻顺铂诱导的小鼠肠道损伤[76]。

2.1.4 酚类 姜黄素是来自草本植物姜黄根茎的一种疏水性多酚[77]。通过抑制NF-κB活化、氧化应激和内质网应激对伊立替康诱导的肠黏膜损伤起保护作用[78]。在体内，姜黄素能有效抑制NF-κB信号转导，改善伊立替康引起的裸鼠腹泻症状和肠黏膜结构异常[79]。在体外，姜黄素能改善细胞形态、抑制细胞凋亡、维持线粒体膜电位并降低由伊立替康诱导的ROS水平升高[79]。白藜芦醇是一种多酚类植物抗毒素，具有抗炎特

性，有效缓解肠道炎症[80-81]。对于环磷酰胺所致小鼠肠道屏障功能损伤，能通过增加益生菌的丰度来改善肠道菌群的多样性和肠道菌群结构，进而抵抗免疫抑制[82]。

2.2　单味药　多种中药在防治化疗肠损伤时具有良好的疗效。大黄具有抗菌、抗炎、抗纤维化和抗癌等作用[83]；大黄水提取物能显著降低5-氟尿嘧啶诱导大鼠肠道黏膜炎中MPO的活性，增加回肠黏膜厚度，缓解化疗引起的肠黏膜炎[84]。在环磷酰胺诱导的小鼠模型中，西洋参能上调绒毛VH/CD，杯状细胞数量，恢复肠道形态[85]。沉香具有镇痛、抗溃疡及促进胃肠运动的作用[86]。沉香提取物能降低NO浓度并增加谷胱甘肽（GSH）和超氧化物歧化酶（SOD）水平，显著降低IL-17和IL-33水平，并提高IL-10水平[87]。此外，沉香提取物上调核因子-E2相关因子2-抗氧化反应元件（Nrf2-ARE）通路的mRNA水平，并下调NF-κB通路的mRNA水平[87]。茯苓是一种著名的传统药用真菌，具有健脾的作用，临床上用于治疗脾虚相关的肠道疾病症状，如腹泻、消化不良、黏膜炎和体重减轻[88]。茯苓通过调节肠道微生物群减轻顺铂诱导的回肠和结肠损伤，减轻了体重损失并降低了血清中IL-2、IL-6的水平[89]。同时茯苓能减轻顺铂引起的肠道菌群失调，尤其是降低了变形菌、蓝细菌、瘤胃球菌科和螺杆菌科等病原菌的丰度，促进了韦荣球菌科和普雷沃菌科等益生菌的丰度[89]。鸦胆子油通过激活Nrf2/HO-1通路保护5-氟尿嘧啶诱导的小鼠肠黏膜损伤[90]。

2.3　复方　中药复方防治化疗肠损伤方面起到很好的疗效，补中益气汤通过抑制炎性细胞因子上调来减少肠黏膜上皮细胞的凋亡和坏死，改善肠黏膜炎[91]。补中益气汤能改善5-氟尿嘧啶引起的小鼠体重减轻和腹泻，缓解肠黏膜上皮细胞绒毛高度缩短、隐窝破坏、细胞凋亡和坏死等肠道损伤，降低中性粒细胞浸润、亚硝酸盐水平和炎症因子（TNF-α和IL-1β）以及还原型谷胱甘肽水平[92]。敦煌平胃丸通过上调Occludin、ZO-1和分泌型免疫球蛋白A（sIgA）的表达，下调IL-6和TNF-α水平，改善小鼠腹泻程度，恢复小肠形态结构来缓解顺铂诱发小鼠肠道黏膜炎[93]。葛根芩连汤广泛用于治疗各种胃肠道疾病的腹泻和炎症症状[94]。在伊立替康诱导的腹泻小鼠中葛根芩连汤提取物通过激活Keap1/Nrf2通路抗氧化应激，并通过上调紧密连接蛋白（ZO-1、HO-1和occludin）的表达增强肠道屏障功能，降低结肠组织中的促炎细胞因子（IL-1β、COX-2、ICAM-1和TNF-α）水平[95]。补脾和胃汤通过抑制TLR-4/NF-κB信号通路的机制，抑制肠道中TLR-4、NF-κB和炎症因子（包括TNF-α、IL-1β和IL-6）的表达，减轻5-氟尿嘧啶诱导的大鼠肠黏膜损伤，降低腹泻评分，增加绒毛长度和体重[96]。大补脾汤通过减少大肠杆菌繁殖，降低细菌β-葡萄糖醛酸苷酶的产生，进而改善肠道菌群来缓解伊立替康诱导的小鼠腹泻[97]。当归补血汤与5-氟尿嘧啶共同给药能显著增加结直肠腺癌细胞系（HT-29细胞）的凋亡和细胞凋亡标志物的表达[98]。

表2　中药保护肠损伤的作用机制

Tab.2　Mechanism of intestinal injury protection by Chinese medicine

	中药	机制	指标	引用
有效成分	灵芝孢子多糖	保护肠屏障	ZO-1、E-cadherin、β-catenin、Occludin ↑	［60］
	冬虫夏草多糖	减轻免疫抑制 调节肠道菌群	$CD4^+$T细胞 ↑ (IL)-17、IL-21 ↑ (TGF)-β3、(Fox)p-3 ↑ TLR-2、-6、-9 ↑ TLR-4 ↓ SCFA ↑	［53］
	鸡血藤多糖	减轻免疫抑制 保护肠黏膜 调节肠道菌群	Occludin1、Claudin1、MUC-2 ↑ IL-2、IL-4、IL-10、TNF-α和IgG ↑ TLRs/MyD88/NF-κB p65 ↑ SCFA ↑	［51］
	蜂蜜多糖	减轻免疫抑制 抑制氧化应激	SOD、β-defensin ↑ MDA、DAO ↓ IL-2、IL-6和TNF-α p-ERK ↑ p-JNK和p-p38 ↓ 绒毛长度/隐窝深度比 ↑	［52］

续表2

	中药	机制	指标	引用
	仙人掌多糖	减轻免疫抑制 调节肠道菌群	WBC↑ IL-4、IL-1β、TNF-α和IFN-γ↑ 乳酸杆菌、拟杆菌和Akkermansia的相对丰度↑	［54］
	西洋参皂苷	抑制氧化应激 减少炎症 抑制细胞凋亡	DAO、SOD↑ MDA↓ TNF-α、IL-1β↓ NF-κB↓ 凋亡细胞↓ ZO-1、occludin↑	［66］
	柴胡皂苷-A	抑制氧化应激 减少炎症 抑制细胞凋亡	Nrf2、HO-1、SOD、GSH、GST和过氧化氢酶↑ MDA↓ TNF-α、COX-2、IL-1β和IL-6↓ p-JNK、caspase 3↓	［69］
	人参皂苷Re	抑制细胞凋亡	BAX、caspase 3 、caspase 9↓	［70］
	姜黄素	抑制氧化应激 减少炎症	P4HB、PRDX4↑ ROS↓ NF-κB↓	［79］
	葛根素	抑制氧化应激 减少炎症 抑制细胞凋亡	JAK↓	［73］
	木犀草素	抑制氧化应激 减少炎症	ROS、LOOH↓ MPO↓ TNF-α、IL-1β、IL-6↓ IL-4、IL-10↑	［75］
	甜橙黄酮	减少炎症	中性粒细胞↓	［76］
	白藜芦醇	保护肠屏障	ZO-1、claudin 1、occludin↑	［82］
单味药	大黄	减少炎症	MPO↓	［84］
	西洋参	保护肠道形态 调节肠道菌群	(VH)/(CD)↑ 梭状芽孢杆菌,双歧杆菌和棘皮动物门↑ Escherichia-Shigella和Peptocccaceae↓	［85］
	沉香	抑制氧化应激 减少炎症	NO↓ GSH、SOD↑ Nrf2-ARE↑ IL-17、IL-33↓ IL-10↑ NF-κB↓	［87］
	茯苓	减少炎症 调节肠道菌群	IL-2、IL-6↓ 变形菌、蓝细菌、瘤胃球菌科和螺杆菌科↓ 韦荣球菌科和普雷沃菌科↑	［89］
	鸦胆子	抑制氧化应激	Nrf2/HO-1↑	［90］
复方	补中益气汤	减少炎症	TNF-α和IL-1β↓	［92］
	敦煌平胃丸	保护肠道形态 减少炎症	Occludin、ZO-1和sIgA↑ IL-6和TNF-α↓	［93］
	葛根芩连汤	抑制氧化应激 减少炎症 保护肠屏障	Keap1/Nrf2↑ IL-1β、COX-2、ICAM-1、TNF-α↓ ZO-1、HO-1和occludin↑	［95］
	补脾和胃汤	减少炎症	TNF-α、IL-1β、IL-6↓ TLR-4/NF-κB↓	［96］
	大补脾汤	调节肠道菌群	大肠杆菌↓ 细菌β-葡萄糖醛酸苷酶↓	［97］
	当归补血汤	增强细胞毒性	HT-29凋亡↑	［98］

注:激活↑;抑制↓。

3　小结与展望

化疗肠损伤引起的腹泻、黏膜炎等临床症状，经常导致治疗停止和生活质量下降，是癌症治疗的主要障碍。目前，化疗肠损伤的发生机制比较复杂，防治上仍然存在不足之处。中医药防治化疗肠损伤的研究尚浅，其复杂的作用机理仍需进一步探索。本文综述了化疗肠损伤的作用机制及中医药治疗，加深了对中医药防治化疗肠损伤的认识，为防治化疗肠损伤，提供新的途径与思路。已有的研究预示了中医药在化疗肠损伤中具有广阔的应用前景，进一步开发中医药成为改善化疗肠损伤治疗的新方法值得深入研究。因此探究中药有效成分、单味药及中药复方治疗化疗肠损伤的机制具有重要意义。

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Progress in the prevention and treatment of traditional Chinese medicine based on the mechanism of intestinal injury of various chemotherapy

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ABSTRACT Intestinal injury is a common adverse reaction of clinical chemotherapy drugs, which limits the further application of chemotherapy drugs and causes serious physical and mental burden to patients. At present, the mechanism of chemotherapy-induced intestinal injury is complex, and traditional Chinese medicine has an excellent preventive effect. This article reviews the related mechanisms of intestinal flora imbalance, oxidative stress, inflammatory response, cell apoptosis, and immune damage caused by chemotherapy, and summarizes the role of traditional Chinese medicine in prevention and treatment of oxidative stress, inflammatory response, cell apoptosis , and immune damage.

KEYWORDS chemotherapy; intestinal injury; mechanism; traditional Chinese medicine; prevention and treatment