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Review 综述

溃疡性结肠炎的菌群紊乱与中药调控研究进展

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摘　要：溃疡性结肠炎(ulcerative colitis, UC)是一种慢性非特异性炎症性疾病，发病机制复杂。近年研究表明，肠道菌群在其病程中起关键作用：乳杆菌、双歧杆菌等有益菌属可调节菌群平衡、修复黏膜屏障、缓解炎症；而埃希氏菌属等有害菌属过度增殖或分泌毒素，则会破坏黏膜完整性、诱发炎症，加速病情恶化。在此基础上，中药活性成分如黄芩多糖、白头翁皂苷、人参皂苷Rg1等中药活性成分可通过调节菌群结构、增强屏障功能及维护黏膜完整性，展现出治疗UC的潜力。本文综述肠道菌群对UC的调控机制及中药干预的最新研究进展，为临床治疗提供新策略与理论支撑。

关键词：溃疡性结肠炎；肠道菌群；嗜酸乳杆菌；长双歧杆菌；艰难拟梭菌；中药调控

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Research progress in gut microbiota dysregulation in ulcerative colitis and its regulation by traditional Chinese medicine

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Abstract: Ulcerative colitis (UC) is a chronic non-specific intestinal inflammatory disease with complex pathogenesis. Recent studies have identified a pivotal role of the gut microbiota in the etiology of the disease. Beneficial bacteria, such as *Lactobacillus* and *Bifidobacterium*, have been shown to regulate the balance of the gut microbiota, repair the mucosal barrier, and alleviate inflammation. In contrast, excessive proliferation or secretion of toxins by harmful bacteria, such as *Escherichia*, can damage the integrity of the mucosa, induce inflammation, and accelerate the progression of UC. The active ingredients of traditional Chinese medicine, such as *Scutellariae radix* polysaccharides, pulchinenosides, and ginsenoside Rg1, may offer a promising avenue for the treatment of UC by modulating the structure of the gut microbiota and enhancing the barrier function and mucosal integrity. The present article reviews the latest research progress in the regulation mechanism of the gut microbiota in UC and the traditional Chinese medicine intervention, with a view to providing new strategies and theoretical support for clinical treatment.

Keywords: ulcerative colitis; gut microbiota; *Lactobacillus acidophilus*; *Bifidobacterium longum*; *Clostridioides difficile*; regulation by traditional Chinese medicine

溃疡性结肠炎(ulcerative colitis, UC)是临床常见的慢性肠道疾病，主要病理表现为结肠和直肠黏膜的慢性非特异性炎症；其病变部位较为局限，主要累及大肠黏膜及黏膜下层，炎症分布呈持续性与弥漫性并存的典型特征[1]。病变多起始于直肠并向近端结肠逆行蔓延，甚至累及末端回肠；主要临床表现为左下腹痛(也可累及全腹)、腹泻及黏液脓血便，可伴有腹胀、食欲不振、恶心、呕吐等[2]。近年来，UC 的发病率呈显著上升趋势，青壮年高发的特征进一步加重了社会经济负担，而其病因尚未完全阐明[3]。UC 的发病机制复杂，是遗传、环境、肠道菌群与免疫紊乱四大因素交互作用的结果：遗传易感个体在环境因素触发下对肠道菌群产生异常免疫应答，导致黏膜屏障破坏与慢性持续炎症[4]；且病程常表现为缓解与复发交替的特点，给患者带来巨大的身心压力[5]。当前临床治疗仍以 5-氨基水杨酸、皮质类固醇、免疫抑制

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剂和生物制剂为主，但这些药物通常伴随较多不良反应，亟需优化治疗方案[6]。

肠道微生物群是已知最为复杂的微生物群落体系之一，由细菌、古菌、真菌及病毒等多种微生物共同构成，其中细菌在肠道菌群中占据核心地位[7]。正常人体肠道菌群以芽孢杆菌门(*Bacillota*)、拟杆菌门(*Bacteroidota*)、假单胞菌门(*Pseudomonadota*)和放线菌门(*Actinomycetota*)四大门类为主，芽孢杆菌门和拟杆菌门占主导地位，维持微生态稳定；而蓝细菌门(*Cyanobacteriota*)、疣微菌门(*Verrucomicrobiota*)及梭杆菌门(*Fusobacteriota*)则以低丰度存在，发挥辅助调节作用[8]。肠道菌群与宿主之间建立了相互依赖的关系，共同维系肠道生态环境的动态平衡。在 UC 的病理过程中，肠道菌群大致可分为有益菌群和有害菌群 2 类。有益菌群包括乳杆菌属(*Lactobacillus*)、双歧杆菌属(*Bifidobacterium*)及阿克曼氏菌属(*Akkermansia*)等，可通过参与黏膜屏障构建、强化肠道物理防护功能，以及调节宿主免疫应答、维持肠道微环境稳定等途径对 UC 发挥积极的调控作用[9]。与之相对的是有害菌群，如埃希氏菌属(*Escherichia*)、志贺氏菌属(*Shigella*)、肠球菌属(*Enterococcus*)等，这类菌群可借助释放促炎因子触发肠道局部炎症反应，破坏肠道黏膜完整性；同时扰乱肠道微生态平衡，干扰有益菌群的正常生理功能，加速 UC 的病理进程[10]。

众多研究证实[11]，肠道菌群与 UC 的发生发展密切相关。一方面，肠道菌群可通过代谢产物的动态变化影响 UC 的病理进程。这些代谢产物在肠道微环境中充当关键信号分子，能够调节肠道上皮细胞功能、免疫细胞活性及肠道神经信号传导，从而影响疾病进展[12]。另一方面，肠道菌群失衡可作为 UC 的潜在生物标志物，具体表现为：生物多样性降低，微生物丰富度下降，生态系统稳定性受损；有益菌群减少，肠道屏障完整性与免疫调节能力减弱；有害菌群异常增殖，屏障功能与免疫功能受损，炎症反应加剧[13]。通过检测肠道菌群的组成与结构变化有助于 UC 的早期诊断、严重程度评估及预后预测。鉴于肠道菌群对 UC 具有“保护-致病”的双重特性，靶向干预菌群有望成为突破 UC 治疗瓶颈的关键策略。除短链脂肪酸(short-chain fatty acids, SCFAs)和胆汁酸外，多中心代谢组学与蛋白质组学研究揭示氨基酸代谢同样是 UC 炎症放大过程中的关键代谢枢纽。Liu 等[14]通过多中心代谢组学与蛋白质组学分析发现，多个 UC 患者队列中血清精氨酸水平显著升高，且与 Mayo 评分(Mayo clinic endoscopic score)呈正相关；同时结肠组织中精氨酸代琥珀酸合成酶 1 (argininosuccinate synthetase 1, ASS1)表达上调。在此基础上，该研究进一步通过葡聚糖硫酸钠(dextran sulfate sodium, DSS)诱导的结肠炎小鼠模型验证了该通路的病理功能：外源性精氨酸补充或 ASS1 过表达均加重体重下降、疾病活动指数(disease activity index, DAI)升高及结肠缩短等病理改变，并伴随哺乳动物雷帕霉素靶蛋白(mammalian target of rapamycin, mTOR)信号通路活化；而抑制 ASS1 则可缓解上述炎症反应。上述证据提示，“精氨酸-ASS1-mTOR/诱导型一氧化氮合酶(inducible nitric oxide synthase, iNOS)轴”可能构成代谢紊乱与黏膜免疫之间的功能桥梁，为 UC 的代谢干预提供了新靶点与机制依据。

在此背景下，中药以整体调节与多靶点干预的独特优势，在调控肠道菌群治疗 UC 方面开辟了新路径，取得了一系列创新性研究成果。前沿研究表明，肠道菌群可通过多维生理途径深度介入 UC 发生发展的关键环节。具体而言，黄芩多糖 SP2-1、木犀草素等成分可促进双歧杆菌等有益菌增殖；白头翁皂苷与淫羊藿苷可调控 SCFAs 生成；β-熊果苷与壳聚糖可提升菌群 α 多样性；人参皂苷 Rg1 与沙棘多糖可抑制核因子 κB (nuclear factor kappa-B, NF-κB)通路，降低肿瘤坏死因子-α (tumor necrosis factor-alpha, TNF-α)、白细胞介素(interleukin, IL)-6 等促炎因

子水平。上述机制共同实现了肠道菌群结构优化与黏膜屏障功能强化，较传统药物具有不良反应少、作用持久等优势，为 UC 治疗提供了“菌群-宿主”协同调控的新策略与临床转化前景(图 1)。

本文就肠道菌群对 UC 的作用机制及中药调控肠道菌群治疗 UC 的研究进展进行概述，以期为运用靶向肠道菌群的 UC 治疗提供参考依据。

1 有益菌与溃疡性结肠炎

随着微生物组学技术取得突破性进展，肠道菌群研究已成为现代医学的前沿热点，其在 UC 发病机制中的枢纽作用日益明确。肠道菌群失调是 UC 复发或病情加重的关键驱动因素，精准调控肠道微生物群落结构以重建其动态平衡[15]，可显著改善 UC 患者临床症状并提升整体治疗效果。因此，众多学者投身于肠道菌群与 UC 相互作用机制的研究，并取得了一定进展。以益生菌干预疗法为例，通过定向补充有益菌群(包括益生菌、共生有益菌等)有效提升肠道内有益菌的数量与活性，构建强大的肠道生物防御屏障[16]。与此同时，有益菌通过竞争性抑制、产生抗菌物质等机制精准抑制有害菌群过度增殖，打破肠道微生态失衡的恶性循环；这种调节作用不仅有助于修复受损的肠道黏膜屏障、恢复其完整性，还能有效缓解炎症反应，减轻患者腹痛、腹泻、便血等临床症状[17]。此外，有益菌还可通过调节肠道免疫细胞降低肠道内病原菌与毒素侵袭的风险，为肠道黏膜提供全方位保护，进一步巩固治疗效果[18]。研究进一步证实，某些特定肠道菌群具备合成抗炎活性物质的能力，其中 SCFAs 的发现尤为突出[19]。这类由肠道菌群代谢膳食纤维产生的代谢产物，如乙酸、丙酸、丁酸等可通过多种途径发挥抗炎作用[20]。它们不仅可作为肠道上皮细胞的能量来源，促进黏膜细胞的增殖与修复，还能调节肠道免疫细胞活性，抑制促炎因子释放，进而缓解炎症反应，改善 UC 患者的肠道微环境与临床症状[21]。

当前应用最广泛的有益菌包括乳杆菌、双歧杆菌、芽孢杆菌、阿克曼氏菌等[22]。有益菌对酸和胆盐的耐受能力，以及其在胃肠道内的生存率与在肠道黏膜上的定植能力，构成了其在消化系统中发挥益生作用的关键基础。因此，

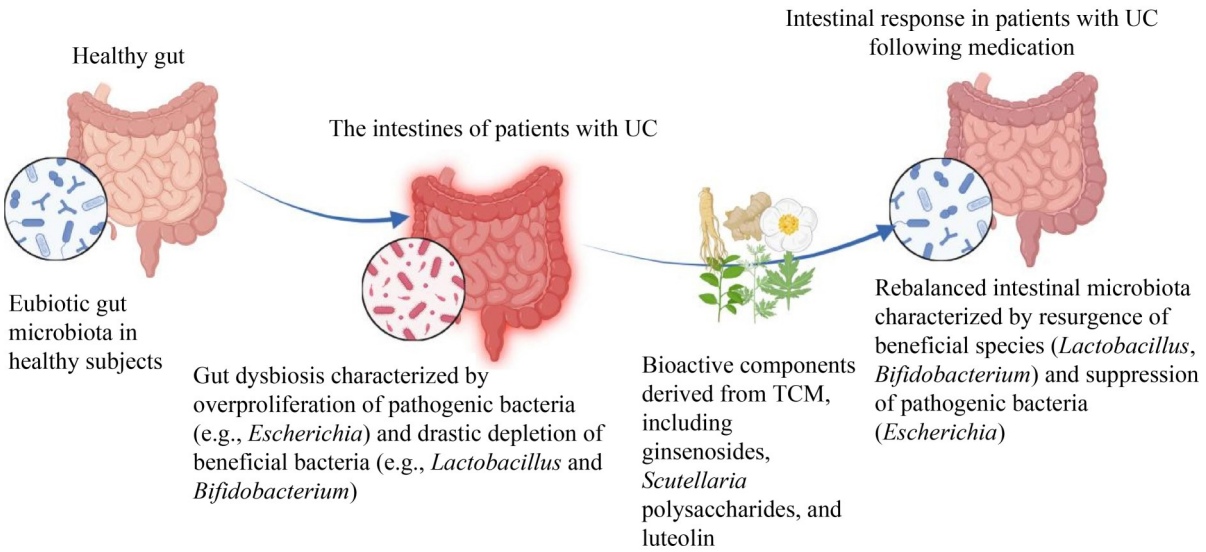

图1 肠道菌群对溃疡性结肠炎患者的作用机制

Figure 1 Role of gut microbiota in patients with ulcerative colitis. TCM: Traditional chinese medicine.

当摄入足量有益菌时可增强肠道屏障功能、纠正肠道菌群失衡、增强机体免疫[23]。众多研究已表明，有益菌具有显著的辅助治疗效果，可有效缓解 UC 患者腹泻、腹痛和便血等症状[24]，有助于病情缓解。目前，已发现多种有益菌可用于 UC 患者的治疗(表 1，图 2)。

1.1 乳杆菌属(*Lactobacillus*)

乳杆菌属是肠道菌群中的有益菌属，借助其拮抗作用抑制有害菌增殖，协同调控肠道菌群比例以恢复动态平衡。同时，乳杆菌通过分泌 SCFAs 等代谢产物，为肠道提供营养支持，增强肠道屏障功能，进一步维护肠道稳态[50]。在 UC 患者的肠道中，乳杆菌能够附着于肠黏膜，阻止病原微生物在肠道的定植，进而抑制致病菌的过度增殖，有助于维护肠道微生态的平衡[51-52]。

嗜酸乳杆菌(*Lactobacillus acidophilus*)是乳杆菌属的一种，目前在临床上应用广泛。它通过分泌乳酸抑制有害菌生长、调整肠道免疫平衡，有助于降低炎症反应，进而对 UC 患者症状的改善起到积极作用。Deng 等[25]研究证实，嗜

表1 肠道菌群在溃疡性结肠炎中的有益作用

Table 1 Beneficial role of gut microbiota in ulcerative colitis

Gut microbiota	Mechanism of action
Lactobacillus acidophilus	Regulates intestinal immune disorder, activates RapGap/PI3K-AKT/NF-κB signaling pathway, and regulates Treg cells and M_1 macrophages[25]
Lacticaseibacillus casei	ATCC 393 and its metabolites (tubocurarine chloride, 3,7-diaminoheptanoic acid, 3-amino-4-phenylbutyric acid) alleviate intestinal inflammation, dysbiosis, and barrier damage[26-27]
Lactobacillus johnsonii	Activates primary macrophages to become $CD206^+$ macrophages *via* the TLR1/2-STAT3 pathway and releases the anti-inflammatory cytokine IL-10[28]
Lacticaseibacillus rhamnosus	LGG alleviates colonic tissue damage and shortening, and reduces intestinal inflammation by inhibiting the TLR4/NF-κB/NLRP3 pathway; reshapes the gut microbiota and alters metabolic pathways in UC mice[29-32]
Bifidobacterium longum	Regulates intracellular signaling pathways to effectively reduce the expression levels of pro-inflammatory cytokines, enhance the intestinal epithelial barrier, and modulate inflammatory responses[33-35]
Bifidobacterium breve	Bif11 supplement inhibits harmful bacteria and expands beneficial bacteria to restore microecological balance[36]; M_1^* and M_2^* subspecies inhibit inflammatory cytokine release to maintain the intestinal epithelial barrier[37]; CBT BR3 alleviates intestinal inflammation by promoting goblet cell regeneration[38]; alleviates intestinal inflammation through exopolysaccharides[39]
Bifidobacterium animalis	*Bifidobacterium animalis* subsp. *lactis* A6 improves intestinal barrier integrity, reduces oxidative stress, and inhibits inflammatory responses by modulating cytokine levels in colon tissue[40]; *Bifidobacterium animalis* subsp. *lactis* BLa80 significantly increases the abundance of beneficial bacterial genera and reshapes the gut microbiota to alleviate UC[41]
Bifidobacterium longum subsp. *infantis*	B8762 downregulates pro-inflammatory cytokine levels, protects colonic structure, and alleviates inflammatory edema[42]; FJSYZ1M3 increases species richness, reduces harmful bacteria, and increases butyrate levels in the cecal contents of UC mice[43]; ATCC 15697 combined with xylooligosaccharides enhances colonic epithelial barrier integrity and protects against colonic injury[44]
Akkermansia muciniphila	Promotes the release of the anti-inflammatory cytokine IL-10, stimulates the immune system, and enhances intestinal barrier function[45-47]; inhibits the kynurenine pathway and activates the microbial tryptophan metabolism pathway to regulate tryptophan metabolism, activate the AhR signaling pathway, and alleviate colitis[48]
Parabacteroides distasonis	Strain F1-28 reduces intestinal mucosal damage, repairs intestinal barrier function, and exerts anti-inflammatory effects in UC mice[49]

M_1^* and M_2^* represent different subspecies of *Bifidobacterium breve*.

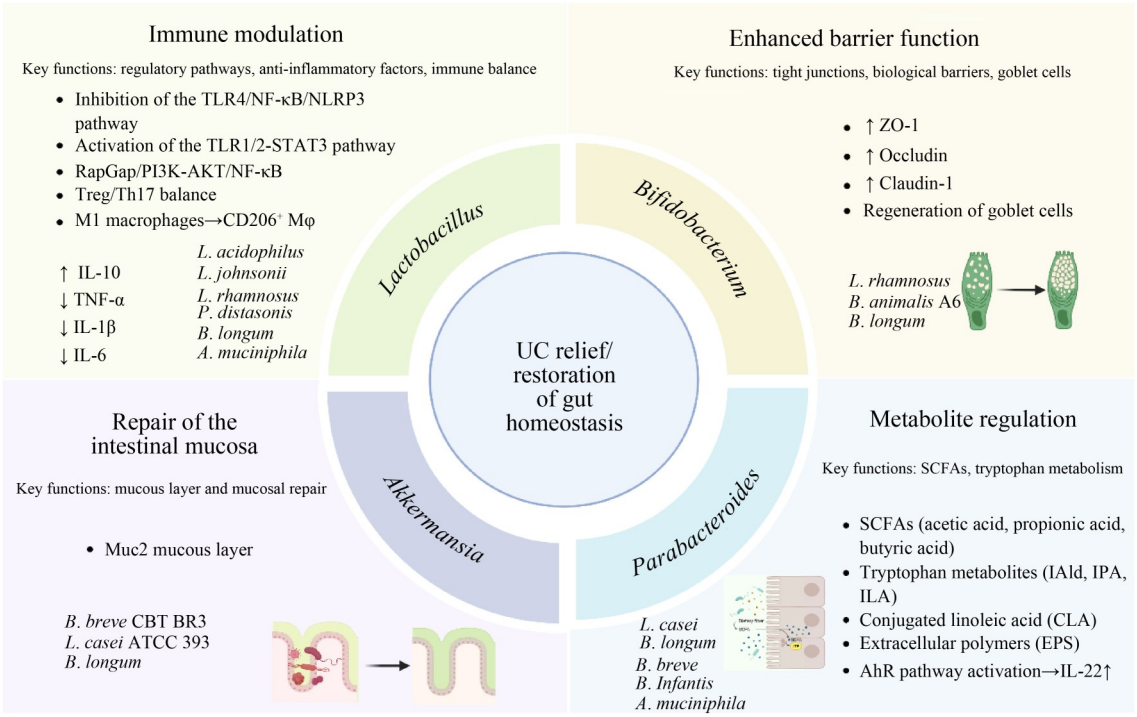

图2　有益菌缓解溃疡性结肠炎的机制网络图

Figure 2　Network diagram of the mechanisms by which beneficial bacteria alleviate ulcerative colitis.

酸乳杆菌能明显改善 UC 小鼠的病情，调节肠道免疫紊乱。嗜酸乳杆菌及其代谢产物熊去氧胆酸可通过激活 Rap GTP 酶激活蛋白(Rap GTPase-activating protein, RapGAP)/磷脂酰肌醇 3-激酶(phosphatidylinositol 3-kinase, PI3K)-蛋白激酶 B (protein kinase B, AKT)/核因子 κB (nuclear factor kappa-light-chain-enhancer of activated B cells, NF-κB) 信号通路 (RapGAP/PI3K-AKT/NF-κB signaling pathway)，并调节性 T (regulatory T, Treg)细胞和 M_1 巨噬细胞来治疗 UC。

干酪乳酪杆菌(*Lacticaseibacillus casei*)存在于肠道中，具有良好的益生菌特性。干酪乳酪杆菌菌株的多种特性对 UC 发挥积极作用[53]：其较强的胃肠道转运耐受性有利于适应肠道环境、实现定植并发挥保护屏障功能，预防 UC 发生；寡糖发酵能力有助于维持肠道环境稳定、加强肠上皮屏障；高黏附能力在肠道定植中占优势，可防止损伤、抑制致病菌黏附并调节免疫反应以缓解炎症。此外，干酪乳酪杆菌所产生的胞外聚合物 (extracellular polymeric substances, EPSs)、乙酸和共轭亚油酸(conjugated linoleic acid, CLA)等有益物质，在对抗病原菌、修复炎症损伤、提供能量、保护肠道黏膜屏障及调节免疫反应等方面发挥积极作用，与 UC 的缓解密切相关。Dou 等[26]研究发现，干酪乳酪杆菌 ATCC 393 及其代谢产物(如特定肽类、胞外多糖、有机酸等)可有效缓解 DSS 诱导的小鼠结肠炎。经胃内给药后，该菌及其代谢物能显著逆转小鼠体重下降，降低 DAI 评分，并提高存活率；同时还能改善小鼠血液及结肠组织中抗炎/促炎细胞因子的表达失衡。此外，干酪乳酪杆菌 ATCC 393 及其代谢产物可上调紧密连接蛋白的表达，减轻肠道黏膜损伤与免疫细胞浸润，从而修复 DSS 引起的肠道屏障功能障碍[27]。综上所述，干酪乳酪杆菌 ATCC 393 及其代谢产物可能通过减轻炎症反

应、调节肠道菌群失调及保护肠道屏障功能，进而改善 UC。

约翰逊氏乳杆菌(*Lactobacillus johnsonii*)可调节肠道免疫微环境、修复肠道屏障，具有潜在抗炎作用。Jia 等[28]研究发现，约翰逊氏乳杆菌作为一种潜在的抗炎细菌，可通过特异性增加肠道巨噬细胞的比例及抗炎因子白细胞介素-10 的分泌来缓解 UC；同时，体内和体外补充约翰逊氏乳杆菌可激活信号转导和转录激活因子 3 (signal transducer and activator of transcription 3, STAT3)增强 $CD206^+$巨噬细胞 IL-10 的活性；临床研究表明，约翰逊氏乳杆菌的丰度与 UC 结肠组织中甘露糖受体 C 型 1 (mannose receptor C-type 1, *MRC1*) 和 Toll 样受体 1/2 (Toll-like receptor 1/2, TLR1/2)的表达水平呈正相关；最终，约翰逊氏乳杆菌通过 TLR1/2-STAT3 通路将原生巨噬细胞激活为 $CD206^+$巨噬细胞，并释放 IL-10，从而缓解 UC 症状。综上所述，约翰逊氏乳杆菌有望作为治疗 UC 的免疫调节剂和抗炎治疗新靶点。

鼠李糖乳酪杆菌(*Lacticaseibacillus rhamnosus*)，曾用名：鼠李糖乳杆菌(*Lactobacillus rhamnosus*)是一种常见且重要的益生菌，在肠道环境中能够定植和繁殖，依附于肠上皮细胞，形成肠道黏膜生物屏障，增强紧密连接蛋白的表达，防止肠道上皮细胞凋亡，进而提升肠道黏膜屏障能力[54]。鼠李糖乳酪杆菌还可通过参与炎症相关信号通路的调节，抑制 Toll 样受体 4/核因子 κB (TLR4/NF-κB)信号通路，进而调节由 DSS 等诱导的炎症细胞因子表达水平，改善结肠炎症状[55]。鼠李糖乳酪杆菌作为益生菌，可通过竞争排斥作用抑制有害菌的增殖和附着，同时刺激有益菌的繁殖，调整肠道菌群平衡。例如，其可利用寡糖益生元进行发酵，产生 SCFAs 等代谢产物，维持肠道内环境稳定，加强上皮屏障，有助于预防和治疗 UC[56]。Tong 等[29]和 Zhang 等[30]研究发现，鼠李糖乳酪杆菌 GG (LGG)释放的细胞外囊泡(extracellular vesicles of *Lacticaseibacillus rhamnosus* GG, LGG-EVs)可有效缓解结肠组织损伤和结肠缩短，并通过抑制由 TLRs 激活、NF-κB 传递、寡聚化结构域样受体蛋白 3 (NLR family pyrin domain containing 3, NLRP3)启动形成 TLR4/NF-κB/NLRP3 信号通路，减轻结肠组织损伤和缩短炎症反应。LGG-EVs 具有抗炎作用，通过抑制 TLR4 信号通路下调髓样分化因子 88 (myeloid differentiation primary response 88, MyD88) 和 RelA 蛋白(transcription factor relA, RelA/p65)的表达，降低 DSS 诱导的 UC 小鼠促炎细胞因子：TNF-α、IL-1β、IL-6、IL-2 的水平[31]。核苷酸结合 NLRP3 作为肠道稳态的关键调节因子，可诱导 IL-1β 产生并激活 NF-κB 信号；而对 NLRP3 信号而言，Toll 样受体(Toll-like receptors, TLRs)能诱导线粒体 DNA 合成，三者形成的 TLRs/NF-κB/NLRP3 通路在 UC 发病机制中可能起关键作用[32]。上述研究进一步表明，鼠李糖乳酪杆菌可重塑 UC 小鼠肠道菌群，改变其代谢途径。

1.2 双歧杆菌属(*Bifidobacterium*)

双歧杆菌属作为肠道微生态体系中的核心菌群成员，在维系人体健康生态平衡中扮演着举足轻重的角色。其通过增强肠道防护功能、抑制有害细菌增殖及对抗病原微生物入侵，有助于稳固肠道微生态的菌群结构，维持其动态平衡[57]。双歧杆菌的代谢活动对优化肠道微环境具有显著贡献，其产生的 SCFAs (如乙酸、丙酸、丁酸以及少量乳酸)可有效降低肠道局部 pH 值，抑制有害菌群的生存，为有益菌的增殖提供适宜的生态环境；此外，酸性环境还能促进肠道蠕动加速排便，预防便秘并有助于净化肠道环境[58]。在营养代谢方面，双歧杆菌具备合成多种维生素(如维生素 B 族、维生素 K 等)的能力，这些维生素不仅是机体正常生理功能所必需的辅酶，还参与能量代谢、凝血功能等关键生理过程[59]。同时，双歧杆菌通过分泌有机酸降低肠道 pH 值，促进钙、铁、锌等矿物质的溶解，提高其生物利用度，为骨骼发育、血红

蛋白合成等提供充足的营养支持[60]。在免疫调节方面，双歧杆菌通过刺激免疫系统、调节辅助性 T 细胞(T helper cell, Th)的分化平衡，抑制促炎细胞因子(如 TNF-α、IL-6 等)的过度释放，促进抗炎细胞因子(如 IL-10)的分泌，继而维持肠道免疫系统的稳态，降低感染性疾病、过敏性疾病及自身免疫性疾病的发生风险[61-62]。因此，确保其菌群结构稳定与代谢功能活跃显得尤为关键。

长双歧杆菌(*Bifidobacterium longum*)是人体肠道中丰度最高的双歧杆菌之一，能够保护肠道上皮屏障和组织结构，平衡肠道菌群，与肠道健康密切相关。摄入长双歧杆菌能够改变肠道菌群的构成，而肠道菌群结构的改变又会对肠上皮细胞、黏液层、固有层免疫细胞以及机体的氧化应激状态产生影响[63]。长双歧杆菌通过平衡免疫系统、改善肠道屏障功能和增加乙酸盐的产生来抑制炎症。研究发现长双歧杆菌 YS108R 能产生丰富的胞外聚合物以调整肠道微生物群，抑制肠杆菌等致病菌的生长[33]。在 UC 中，长双歧杆菌可降低肠道中炎症细胞因子的表达，促进肠道黏膜的修复和再生，减少炎症对肠道黏膜的损伤。Sichetti 等[34]和 Lohrasbi 等[35]利用长双歧杆菌与巨噬细胞对肠上皮屏障功能进行模拟实验，研究发现长双歧杆菌组显著上调了 IL-10 的表达水平，而 IL-1β 和 IL-6 的表达水平分别下调了 70% 和 80%；进一步发现，经长双歧杆菌治疗的 UC 小鼠炎症状况得到缓解，肠道中 SCFAs 的含量也有所增加，表明长双歧杆菌能够调节细胞内信号通路，有效降低炎症因子的表达水平，减少 DSS 诱导的体外上皮屏障改变并缓解炎症反应。长双歧杆菌对 UC 具有显著的调节作用，能够改善肠道环境、减轻肠道炎症、有效抗氧化与清除自由基、增强免疫力并提供辅助治疗效果[64-65]。这些作用共同作用于肠道系统，有助于促进 UC 患者的康复。

短双歧杆菌(*Bifidobacterium breve*)是一种革兰氏阳性厌氧杆菌，广泛存在于人类母乳及婴儿和成人的胃肠道中，是肠道菌群的重要组成部分。其通过抑制病原菌增殖并促进益生菌定植，动态调控肠道菌群结构以重建肠道微生物的动态平衡，减少病原体对肠黏膜的损伤，同时增强肠道屏障功能。Singh 等[36]研究发现，与 DSS 诱导的 UC 小鼠相比，服用短双歧杆菌 Bif11 补充剂的小鼠肠道中假单胞菌门和拟杆菌门的相对丰度明显降低，其微生物群部分接近正常小鼠，说明短双歧杆菌有益地调节肠道菌群使其逐渐恢复动态平衡。此外，短双歧杆菌通过参与宿主的代谢互作，调节免疫系统，增强机体免疫力，为肠道健康提供全面支持，具有显著的益生功能。研究发现，短双歧杆菌亚种 M_1 和 M_2 通过产生 CLA、抑制炎症细胞因子、维持肠道上皮屏障和调节肠道菌群来缓解 UC[37]。Park 等[38]研究发现，短双歧杆菌 CBT BR3 经口给药后，有效改善了 DSS 和 2,4-二硝基苯磺酸(2,4-dinitrobenzenesulfonic acid, DNBS)诱导的结肠炎模型中的炎症症状，其增加了每个隐窝的杯状细胞数量及 *Notch*、*Spdef*、*Muc5* 和 *Il22* 的 mRNA 表达，同时增加了紧密连接蛋白 Occludin 和与丁酸代谢相关蛋白 Foxo3 在 DSS 和 DNBS 诱导的结肠炎模型中的 mRNA 表达；该菌株通过诱导体外芳香烃受体表达，缓解炎症引起的上皮细胞通透性增加并改善杯状细胞功能，说明短双歧杆菌 CBT BR3 可通过促进杯状细胞再生有效缓解肠道炎症。与双歧杆菌属其他菌种类似，短双歧杆菌也能利用 EPSs 减轻肠道炎症反应。研究显示，产生 EPSs 的短双歧杆菌菌株 H4-2 和 H9-3 可调节免疫和微生物屏障，修复 DSS 引起的小鼠肠道损伤，且 H4-2 的修复效果优于 H9-3，可能与 H4-2 的 EPSs 产量更高有关[39]。

动物双歧杆菌(*Bifidobacterium animalis*)是天然存在于结肠中的优势菌群之一，也是最早定植于人体肠道的微生物类群之一，有利于肠道免疫的形成，有益于调节肠道菌群平衡、促进

肠道正常发育、增强机体免疫力及提高抗病能力。研究发现，动物双歧杆菌亚种 A6 为增强肠道屏障的完整性，通过减少结肠损伤、恢复黏液层损失和提高紧密连接蛋白(包括 ZO-1、Occludin 和 Claudin-1)活性的方式，同时降低丙二醛(malondialdehyde, MDA)浓度并提高结肠组织中超氧化物歧化酶(superoxide dismutase, SOD)和谷胱甘肽(glutathione, GSH)的浓度，有效缓解氧化应激；此外还通过下调结肠组织中炎症因子(TNF-α、IL-1β 和 IL-6)的水平及上调抗炎因子 IL-10 的水平来抑制 DSS 诱导的炎症反应，说明动物双歧杆菌 A6 对 UC 具有抗炎作用[40]。通过 16S rRNA 基因测序发现，动物双歧杆菌亚种 BLa80 有效增加了 UC 小鼠微生物群落中的微生物丰度，显著增加了有益的龙包茨氏菌属(*Romboutsia*)和阿德勒氏菌属(*Adlercreutzia*)的菌株丰度，有效改变了 UC 小鼠的肠道菌群结构，说明动物双歧杆菌亚种 BLa80 可通过重塑肠道菌群来缓解 UC[41]。

长双歧杆菌婴儿亚种(*Bifidobacterium longum* subsp. *infantis*)属于革兰氏阳性厌氧菌，在维持肠道微生态稳态中发挥重要作用。长双歧杆菌婴儿亚种 B8762[42]通过下调促炎细胞因子水平，有效缓解结肠炎的临床症状，保护结肠结构，并减轻炎症水肿。Li 等[43]研究发现，长双歧杆菌婴儿亚种 FJSYZ1M3 可改善 UC 小鼠肠道菌群紊乱，显著增加肠道菌群的物种丰富度，在一定程度上降低了有害菌属的相对丰度，并增加盲肠内容物中丁酸的含量。此外，长双歧杆菌婴儿亚种 ATCC 15697[44]与木寡糖联合给药可增强结肠上皮屏障完整性，对 UC 所致结肠损伤起到保护作用。

1.3 阿克曼氏菌属(*Akkermansia*)

阿克曼氏菌属是人类肠道中一种重要的共生菌属，在维护健康免疫系统中扮演着至关重要的角色。嗜黏蛋白阿克曼氏菌(*Akkermansia muciniphila*)是该属的代表菌种，于 2004 年从健康成人的粪便样本中被成功分离鉴定。因其参与调节宿主屏障功能和免疫反应，在代谢类疾病、癌症和免疫治疗等方面具有独特功效，受到广泛关注[45]。研究表明，在 UC 患者的粪便或肠道样本中，嗜黏蛋白阿克曼氏菌的丰度通常有所下降；在 DSS 诱导的 UC 小鼠模型中，灌胃给予嗜黏蛋白阿克曼氏菌能够有效缓解小鼠的黏膜炎症、维护肠道屏障的完整性，并降低肠道内炎症因子的水平，从而对 UC 产生积极的改善效果[46]。Ottman 等[47]报道，嗜黏蛋白阿克曼氏菌可促进抗炎细胞因子 IL-10 的释放，增强免疫系统功能，对 UC 发挥有益作用并增强屏障功能。Qu 等[66]研究发现，与 GMrepo 数据库中的健康人相比，UC 患者体内的嗜黏蛋白阿克曼氏菌含量有所减少；口服嗜黏蛋白阿克曼氏菌菌株 BAA-835 显著改善了 DSS 诱导的急性结肠炎症状，表明嗜黏蛋白阿克曼氏菌在 UC 治疗中起着至关重要的作用。Gu 等[48]针对嗜黏蛋白阿克曼氏菌在色氨酸(tryptophan, Trp)代谢方面的作用研究发现，嗜黏蛋白阿克曼氏菌及其外膜蛋白 Amuc_1100 增加了犬尿氨酸(L-kynurenine, Kyn)水平，降低了 2-吡啶甲酸(picolinic acid, PIC)水平和 PIC/Kyn 比率，显著恢复了粪便微生物群介导的 Trp 代谢富集，尤其显著逆转了吲哚乙酸(indole-3-acetic acid, IAA)水平的降低；其通过抑制 Kyn 途径(kynurenine pathway, KP)并激活微生物 Trp 代谢途径以调节 Trp 代谢，且该作用独立于结肠组织；嗜黏蛋白阿克曼氏菌及其外膜蛋白上调了芳香烃受体(aryl hydrocarbon receptor, AhR)靶向基因，包括细胞色素 P450 1A1 (cytochrome P450 family 1 subfamily A member 1, *CYP1A1*)、IL-10 和 IL-22，表明嗜黏蛋白阿克曼氏菌可通过调节 Trp 代谢激活 AhR 信号通路，从而减轻结肠炎症。

1.4 副拟杆菌属(*Parabacteroides*)

迪氏副拟杆菌(*Parabacteroides distasonis*)是副拟杆菌属的模式代表菌种，为人体核心菌群之一，通常定植于人和动物肠道中，通过抗炎、免疫调节、微生物调节及肠道屏障修复等多重

机制发挥益生菌作用。Sun 等[67]长期致力于迪氏副拟杆菌的免疫调节机制研究，首次揭示了肠道共生菌迪氏副拟杆菌通过调节免疫稳态缓解炎症性关节炎的作用机制，相关成果已于 2023 年发表于 *Gut* 上；该研究证明了迪氏副拟杆菌在调节 Th17/Treg 平衡和抗炎方面的核心作用，为理解其在 UC 等炎症性疾病中的潜在治疗价值提供了重要依据。Ma 等[49]研究发现，经迪氏副拟杆菌 F1-28 灌胃处理后可有效缓解 UC 小鼠的体重下降、减少结肠缩短、降低出血率，并改善粪便稠度，表明迪氏副拟杆菌 F1-28 可减少 UC 小鼠肠黏膜损伤，修复其肠屏障功能，发挥抗炎作用。

此外，周伟团队[68]关于脆弱拟杆菌(*Bacteroides fragilis*)缓解肾纤维化的研究拓展了对“肠道-肾脏轴”的认识，为理解肠道菌群通过代谢物调控远端器官病变提供了新视角，也为肠道菌群在 UC 等肠道局部炎症疾病中的作用研究提供了方法学借鉴。

2 有害菌与溃疡性结肠炎

UC 的发病进程与肠道菌群失调密切相关，其核心致病作用体现为致病菌过度增殖与有益菌锐减的失衡格局。例如，UC 患者肠道中假单胞菌门(如埃希氏菌属、肠杆菌属等)相对丰度显著升高，而芽孢杆菌门[如柔嫩梭菌(*Clostridium leptum*)、双歧杆菌等]及拟杆菌门等关键有益菌群数量显著降低，这种菌群结构紊乱将直接改变肠道代谢环境，这使得营养物质吸收效率下降、代谢产物组成失衡，诱导肠道黏膜屏障功能受损，引发持续性的黏膜免疫与炎症级联反应，加剧 UC 病情恶化[69]。

2.1 埃希氏菌属(*Escherichia*)

肠道菌群结构失衡所引发的代谢紊乱与黏膜屏障破坏，不仅为致病菌的侵袭性增殖提供了病理基础，更通过其分泌活性物质与宿主免疫系统的异常作用直接推动局部炎症反应的级联放大。其中，以埃希氏菌属为代表的致病菌群体在失衡微环境中过度扩增，其致病效应通过“毒素直接损伤+免疫激活”双路径协同发挥，既加剧肠黏膜屏障的物理性破坏，又持续诱导黏膜免疫系统处于高反应状态，造成炎症反应的恶性循环，最终导致 UC 患者病情呈不可逆性进展[70]。相关研究指出，大肠埃希氏菌(*Escherichia coli*)异常扩增可能释放毒素，同时激活宿主细胞免疫反应，这 2 种机制共同作用加剧了肠道炎症；UC 患者结肠隐窝上皮过度增殖，细胞末端分化进程受阻，成熟上皮尤其是黏液分泌型杯状细胞数量下降，进而造成黏液层变薄；黏液屏障缺损使大肠埃希氏菌等致病菌更易穿透黏液层侵袭肠黏膜，进一步加重 UC 黏膜损伤[71]。

2.2 拟梭菌属(*Clostridioides*)

艰难拟梭菌(*Clostridioides difficile*)作为一种革兰氏阳性、严格厌氧且具芽孢形成能力的条件致病菌，在肠道菌群稳态失衡(如抗生素暴露、宿主免疫功能抑制或饮食结构紊乱等诱因)下，其休眠芽孢可萌发并大量增殖，通过分泌细胞毒素 A (*Clostridioides difficile* toxin A, TcdA)和毒素 B (*Clostridioides difficile* toxin B, TcdB)直接破坏肠道上皮细胞紧密连接与微绒毛结构[72]，诱发黏膜屏障溃破、炎症因子风暴及水电解质代谢紊乱[73]，最终导致假膜性结肠炎、中毒性巨结肠等危及生命的肠道感染综合征[74]。研究表明，艰难拟梭菌感染对 UC 患者病情进展及预后存在显著负面影响，其可激活 UC 患者体内的 TLR4/NF-κB 信号通路，导致 TNF-α、IL-6 等促炎因子过度表达，加重结肠黏膜的炎症损伤[75]。合并艰难拟梭菌感染的 UC 患者肠道菌群多样性显著降低，拟杆菌属、变形杆菌属等致病菌丰度升高；而双歧杆菌属、副拟杆菌属及乳酸杆菌属等有益菌丰度明显降低[76]。这种菌群失调进一步损伤肠道屏障功能，加速病情恶化。

肠道菌群失调可导致细菌代谢产物的改变。研究发现，UC 患者及肠道炎症动物模型体内产

丁酸菌如丁酸梭菌(*Clostridium butyricum*)、普氏栖粪杆菌(*Faecalibacterium prausnitzii*)等数量显著减少，导致 SCFAs 含量显著降低[77]。这一变化通过双重机制破坏肠道稳态：一方面，SCFAs 水平下降会抑制 Treg 细胞的分化和扩增，削弱免疫耐受功能[78]；另一方面，上皮细胞增殖受阻，继而影响肠道屏障完整性[79]。

2.3 梭杆菌属(*Fusobacterium*)

在 UC 相关致病菌群的研究中，可变梭杆菌(*Fusobacterium varium*)作为一种革兰氏阴性、严格厌氧的梭杆菌属细菌，近年来被发现与 UC 的难治性及反复发作密切相关。由于肠道菌群失衡，黏液层变薄、肠上皮屏障功能减弱以及局部免疫微环境紊乱，为可变梭杆菌营造了适宜的定植环境[80]。该菌借助其特有的黏附因子和毒力因子直接参与了 UC 炎症的加重与组织损伤过程。

可变梭杆菌具有较强的黏膜黏附与侵袭能力。研究显示，它可利用自身表达的 *Fusobacterium varium* autotransporter protein (Fap2)蛋白及外膜蛋白，特异性识别肠上皮细胞表面过表达的半乳糖-β-1,3-*N*-乙酰半乳糖胺[galactose-β-1,3-*N*-acetylgalactosamine (Gal-GalNAc)，即 T 抗原]结构，从而突破黏液屏障，在隐窝区域实现定植；一旦成功定植，可变梭杆菌会分泌丁酸(但不同于产丁酸菌的有益代谢，其丁酸的生成通常伴随其他毒性代谢产物)及内毒素(lipopolysaccharide, LPS)，协同激活肠上皮细胞及固有层巨噬细胞表面的 Toll 样受体(TLR2/4)，触发下游 MyD88 依赖的 NF-κB 信号通路，诱导 IL-1β、IL-6、TNF-α 及 IL-8 等促炎因子大量释放[81-82]。这种持续性的免疫激活不仅会加重黏膜水肿和中性粒细胞浸润，还可通过上调基质金属蛋白酶(matrix metalloproteinases, MMPs)的表达，进一步破坏隐窝结构与细胞外基质的完整性。临床证据表明，可变梭杆菌在 UC 患者黏膜活检样本中的检出率明显高于健康对照组，尤其是在活动期 UC 及激素难治性 UC 患者中，其丰度与 Mayo 评分呈正相关[83]。机制研究进一步揭示，可变梭杆菌感染可诱导肠上皮细胞凋亡及紧密连接蛋白(如 Occludin、Claudin-1)表达下调，使肠道通透性显著升高，促使更多细菌抗原易位至黏膜下层，形成“菌群易位-免疫激活-屏障受损”的恶性循环[84]。此外，该菌的存在还与 UC 患者肠道菌群中双歧杆菌属、乳酸杆菌属等有益菌的持续减少密切相关，共同推动病情向慢性、迁延性方向发展。

具核梭杆菌(*Fusobacterium nucleatum*)是一种革兰氏阴性、严格厌氧的口腔共生菌，肠道菌群失衡时可异位定植于结肠黏膜，在 UC 的致病网络中发挥关键作用。与可变梭杆菌相似，具核梭杆菌在 UC 患者肠道黏膜中的丰度显著高于健康人群，其富集程度与疾病活动性及激素抵抗密切相关[85-86]。具核梭杆菌的致病机制呈现出“黏附侵袭-免疫激活-协同致病”的多维度特征，通过直接破坏肠上皮屏障、诱导免疫微环境紊乱及重塑菌群代谢生态位，共同推动 UC 的慢性进展与复发。具核梭杆菌致病始于其黏附侵袭及对屏障的破坏。该菌表面表达的关键毒力因子黏附素 A (*Fusobacterium* adhesin A, FadA)可特异性结合肠上皮细胞中过表达的 E-钙黏着蛋白(epithelial cadherin, E-cadherin)，启动内化过程并穿透上皮屏障[87]。FadA 与 E-cadherin 结合不仅能诱导上皮细胞骨架重排及紧密连接蛋白(ZO-1、Occludin)表达下调，还可激活 β-连环蛋白(beta-catenin, β-catenin)信号通路，促进上皮细胞异常增殖与间质转化，进一步削弱黏膜屏障的完整性[88]。此外，具核梭杆菌分泌的外膜囊泡(outer membrane vesicles, OMVs)携带 LPS 及脂蛋白(lipoprotein)，可直接作用于肠上皮细胞与固有层免疫细胞，诱导活性氧(reactive oxygen species, ROS)爆发及细胞凋亡，加剧黏膜损伤[89]。

同时，免疫激活与炎症放大是具核梭杆菌加重 UC 的核心机制。该菌通过其 LPS 及 Fap2 蛋白等分子模式，激活肠上皮细胞及巨噬细胞

表面的 TLR2/TLR4，触发 MyD88 依赖性 NF-κB 信号通路及 NLRP3 炎症小体的活化，诱导 IL-1β、IL-6、TNF-α 及 IL-17 等促炎因子大量释放[90-91]。研究表明，具核梭杆菌可诱导髓源性抑制细胞(myeloid-derived suppressor cells, MDSCs)及 Th17 细胞向炎症部位迁移，形成以中性粒细胞浸润为特征的炎症微环境，同时抑制 Treg 细胞的扩增，导致 Th17/Treg 比例失衡，从而使肠道免疫系统长期处于持续激活状态[92]。这种免疫偏离状态不仅加重结肠黏膜的炎性浸润，还通过反馈机制进一步促进具核梭杆菌的定植与扩增。在 UC 的菌群网络中，具核梭杆菌通过协同致病与代谢重塑发挥放大效应的重要作用。具核梭杆菌具备形成多菌种生物膜的能力，可介导其他致病菌(如大肠埃希氏菌)的共同定植与协同增殖[93]。在代谢层面，具核梭杆菌通过调控铁代谢及改变 SCFAs 的利用方式重塑肠道代谢环境，削弱产丁酸菌(如普氏栖粪杆菌)的竞争优势，使丁酸水平进一步下降，加剧 Treg 分化障碍与屏障功能缺陷[94]。临床研究证实，UC 患者黏膜中具核梭杆菌的丰度与粪钙卫蛋白水平、内镜下 Mayo 评分及疾病复发率呈显著正相关，提示该菌可作为评估 UC 活动性及预后的潜在生物标志物[95]。

2.4 弯曲杆菌属(*Campylobacter*)

简明弯曲杆菌(*Campylobacter concisus*)属于口腔来源的条件致病菌，在 UC 患者肠道中异常定植，为理解“口-肠轴”在 UC 发病机制中的作用提供了新的视角。作为一种革兰氏阴性、微需氧细菌，简明弯曲杆菌在正常肠道环境中难以大量存活，而 UC 患者黏膜炎症所致的局部氧张力改变及黏液层破坏为其创造了定植条件。该菌存在显著的菌株水平异质性：源自 UC 患者的菌株通常携带完整的毒力基因簇，而健康对照来源的菌株则多表现为无毒力表型，这一特征说明菌株分型可能比菌种鉴定更具临床意义。

简明弯曲杆菌的致病机制体现为多种毒素的联合攻击，可同时分泌细胞膨胀致死毒素(cytolethal distending toxin, CDT)、zonula occludens 毒素(zonula occludens toxin, Zot)及溶血素共调节蛋白(hemolysin-co-regulated protein, Hcp)等多种毒力因子，形成组合式屏障损伤效应；此外，该菌可分泌 *Campylobacter concisus* secreted protein 1 (Csep1)效应蛋白，重编程巨噬细胞进入以趋化因子为主导的特殊活化状态趋化型 M1 极化状态(M1-chemokine-dominant polarization state, M1-chem)，进而增强对共生菌群的炎症应答[96]。与此同时，简明弯曲杆菌感染可下调紧密连接蛋白(Occludin、tricellulin)表达，并激活 NF-κB、STAT 及 NLRP3 炎症小体等多条信号通路，诱导 IL-1β、IL-8 等促炎因子释放[97-98]。该菌感染与宿主免疫系统之间形成正反馈放大环：感染诱导肠上皮细胞分泌 IL-8 招募中性粒细胞，后者释放的活性氧和蛋白酶进一步损伤上皮连接；黏膜下巨噬细胞极化为 M_1 型，分泌 TNF-α 和 IL-1β，通过抑制紧密连接蛋白表达和激活肌球蛋白轻链激酶通路进一步削弱屏障功能。这种由细菌、上皮细胞与免疫系统三者交互作用所形成的循环放大效应，与前述梭杆菌属的致病方式存在相似之处。由于简明弯曲杆菌起源于口腔，说明口腔菌群有可能是 UC 肠道炎症的来源之一。此外，该菌可通过上调干扰素-γ (interferon-gamma, IFN-γ)致敏肠上皮细胞中免疫检查点分子程序性死亡受体 1 配体 1 (programmed cell death 1 ligand 1, PD-L1)的表达[99]，以及诱导 COX-2 和 miR-221 等肿瘤相关分子的产生[100]，在 UC 背景下增加结直肠癌的发病风险。

3 其他途径调节肠道菌群治疗溃疡性结肠炎

肠道菌群中除有益菌和共生菌对 UC 具有有益作用外，益生元、合生元及酵母均对 UC 具有一定的治疗效果。

国际益生菌和益生元科学协会(International

Scientific Association of Probiotics and Prebiotics, ISAPP)将益生元定义为经肠道微生物群选择性发酵、使宿主获得健康益处的基质。益生元是一类难以被人体消化吸收的膳食成分，其在肠道中对有益菌产生选择性刺激作用，有助于扩增有益菌群并激发其活性。在众多益生元中，菊粉、低聚糖(galacto-oligosaccharides, GOS)、低聚果糖(fructo-oligosaccharides, FOS)、乳果糖以及半乳糖和β-葡聚糖的衍生品最为普遍[101]。益生元已被证明可增强宿主免疫功能、降低感染率、增强结肠完整性并抑制过敏反应。然而，这并非益生元的直接作用，而是间接实现的[102]。大量研究表明，益生元可增强肠道菌群的代谢功能，有效减少炎症细胞因子(如IL-1α、IL-1β、IL-6、IL-12、TNF-α、IFN-γ)的产生，促进益生菌生长，并通过增加黏液层厚度和上皮细胞间紧密连接(tight junction, TJ)来改善肠道黏膜屏障，减少肠道中有害菌数量，为共生菌提供可代谢产生抗炎细胞因子的底物[103]。研究发现，乳果糖、低聚果糖和菊粉等益生元能够促进特定宿主微生物菌群的生长以增强肠道功能，这些难以消化的食物成分通过抑制TNF-α相关细胞因子的表达并提高IL-10水平发挥抗炎作用[104-105]。Li等[106]研究发现，对DSS诱导的UC小鼠口服菊粉后，盲肠腔中天然乳杆菌数量有所增加，同时结肠pH值降低；在DSS诱导的UC大鼠中，口服菊粉后黏膜炎症减轻，组织学损伤评分也有所降低；此外，与对照组相比，菊粉给药组UC大鼠表现出较低程度的黏膜损伤和较轻的隐窝损伤，表明菊粉对UC具有缓解作用。

在食品、药物和补充剂等产品中，益生菌与益生元的结合物被命名为“合生元”。它通过选择性促进有益菌群定植并激活其代谢过程，集益生菌和益生元的双重效益于一体，在宿主体内发挥积极作用，进而提高微生物膳食补充剂在胃肠道中的存活率及定植能力[107]。常用的合生元配方包括乳酸杆菌、双歧杆菌、低聚果糖、菊粉等。合生元能够通过预防和治疗2种途径降低DSS诱导的UC小鼠DAI评分[108]。同时，小鼠肠道内致病菌数量显著减少，免疫细胞、上皮细胞和肠道微生物群的功能得到调节，有助于维持肠道稳态，降低血清中IL-6和IL-8水平，有效缓解炎症反应[109]。研究显示，合生元具有缓解或改善UC的能力，并能显著提升患者肠道内有益菌数量，表明其对UC具有明显的改善效果[110-111]。

作为益生菌与益生元的复合制剂，合生元在肠道微生态系统中展现出显著的协同效应，不仅能重塑肠道菌群的动态平衡、有效抑制有害菌群异常增殖、缓解肠道炎症反应，还能为受损肠黏膜的修复创造适宜环境。与此同时，酵母在UC治疗领域的价值逐渐受到关注。其特定成分可深度参与免疫调节，减轻肠道免疫系统的过度应激反应，缓解肠道黏膜炎症[112]，并在强化肠道屏障功能方面展现出潜在价值，有效抵御有害物质侵袭，全面提升肠道免疫防御能力[113]。多项研究证实酵母在UC治疗中呈积极作用。Xu等[114]研究发现，布拉氏酵母菌(*Saccharomyces boulardii*)干预可有效改善结肠缩短和组织损伤，增加肠道紧密连接蛋白的表达，降低促炎细胞因子的释放，提升抗炎细胞因子的分泌，维持肠道微生物稳态，表明其可通过调节宿主免疫功能和维持肠道内环境稳定，显著减轻DSS诱导的小鼠疾病症状。同时，Sun等[115]针对酿酒酵母(*Saccharomyces cerevisiae*)的研究也表明，该菌种在DSS诱导的UC小鼠模型中表现出良好的抗炎活性，能够改善肠道组织学损伤、增强黏膜屏障功能、调节肠道免疫反应；进一步研究发现，酿酒酵母可重塑肠道微生物群落结构、提高代谢产物丰度，从而缓解UC病症，为治疗UC提供安全有效的新策略。

4 中药调控肠道菌群治疗溃疡性结肠炎的研究进展

近年来，中药在调节肠道菌群以治疗 UC 方面取得了显著进展。相关研究不仅揭示了肠道菌群在多种疾病发生发展中的关键作用，也突显了中药在调控肠道菌群、促进机体健康方面的独特优势。中药凭借其整体性和多靶点的作用特点，能够更有效地维持肠道微生物的动态平衡。依据中药成分对肠道菌群及其代谢产物的调控方式可将其归纳为以下 3 类：促进有益菌增殖、抑制有害菌定植、调节菌群代谢产物。

4.1 促进有益菌增殖的中药成分

该类中药成分主要通过作为益生元或直接促进有益菌生长，增加肠道中乳杆菌属、双歧杆菌属、阿克曼氏菌属、拟杆菌属等有益菌的丰度，优化肠道菌群结构。

在促进乳杆菌属增殖方面，黄芩多糖 SP2-1 可显著提升 UC 小鼠肠道内乳杆菌属、芽孢杆菌门、双歧杆菌属等有益菌数量[116]；壳聚糖可增加布劳特氏菌属(*Blautia*)和乳杆菌属等有益菌数量，减轻肠道菌群失调[117]；吴茱萸碱可特异性升高嗜酸乳杆菌丰度，增加乙酸盐含量，减少促炎细胞因子产生[118]。在双歧杆菌属的调控方面，沙棘多糖可促进双歧杆菌属和拟杆菌属的富集，增加 SCFAs 生成[119]；佛手柑多糖可促进双歧杆菌属、丁酸弧菌属、布劳特氏菌属和龙包茨氏菌属等有益菌增殖，生成乙酸和丁酸，增强紧密连接蛋白和黏蛋白表达[120]。针对拟杆菌属，人参皂苷 Rg1 虽未直接报道拟杆菌属的变化，但其对菌群整体结构的优化作用可为拟杆菌属的恢复提供有利生态位[121]；白头翁皂苷可促进鼠杆状菌属(*Muribaculum*)和梭菌纲(*Clostridia*) UCG-014 等有益菌繁殖，同时抑制特定致病性拟杆菌的生长[122]；佛手柑多糖也能增加拟杆菌门中有益菌的丰度[120]。在阿克曼氏菌属的调控方面，人参皂苷 Rg1 可显著增加嗜黏蛋白阿克曼氏菌的相对丰度，同时调节 Trp 代谢发挥抗炎作用[121]；淫羊藿苷可有效提高嗜黏蛋白阿克曼氏菌的数量和活跃度，减轻结肠组织损伤[123]。

4.2 抑制有害菌定植的中药成分

该类中药成分通过直接抗菌、竞争性排斥或调节肠道微环境等机制，减少 UC 相关致病菌(如假单胞菌门、埃希氏菌属、拟杆菌属中特定致病株等)在肠黏膜的定植与扩增。

在抑制假单胞菌门及埃希氏菌属方面，黄芩多糖 SP2-1 可抑制假单胞菌门和葡萄球菌属[116]；木犀草素可降低 DSS 诱导升高的假单胞菌门相对丰度，调节乳杆菌属/普雷沃氏菌属比值[124]；沙棘多糖可降低致病菌埃希氏菌属的丰度[119]。针对拟杆菌属中的特定致病株，白头翁皂苷可抑制有害拟杆菌属的生长[122]；淫羊藿苷可减少拟杆菌属(特定致病株)、幽门螺杆菌和苏黎世杆菌属的数量和活跃度[123]。β-熊果苷可通过增加产丁酸细菌的丰度促进肠道稳态，间接压缩有害菌的生存空间[125]。

4.3 调控菌群代谢产物的中药成分

该类中药成分主要通过影响肠道菌群的代谢功能，调节 SCFAs、Trp 代谢物等抗炎或促炎介质的生成，从而发挥治疗作用。

在 SCFAs 调控方面，佛手柑多糖可促进双歧杆菌属、丁酸弧菌属、布劳特氏菌属和龙包茨氏菌属等产短链脂肪酸菌群的增殖，生成乙酸和丁酸，降低肠道 pH 值以抑制有害菌繁殖，同时增强紧密连接蛋白和黏蛋白表达[120]；沙棘多糖可增加 SCFAs 生成，维持结肠内稳态，保护结肠屏障[119]；吴茱萸碱可升高乙酸盐含量，通过 SCFAs 介导的抗炎途径减少促炎细胞因子产生[118]；人参皂苷 Rg1 虽以调控色氨酸代谢为主，但其促进菌群重构也有助于改善 SCFAs 生成环境[121]。在 Trp 代谢物调控方面，人参皂苷 Rg1 可增加 Trp 代谢物吲哚-3-甲醛(indole-3-aldehyde, IAld)、吲哚-3-丙酸(indole-3-propionic acid, IPA)、吲哚-3-乳酸(indole-3-lactic acid, ILA)

等的表达水平，通过调节 Trp 代谢发挥肠道屏障保护和抗炎作用[121]；嗜黏蛋白阿克曼氏菌作为中药调控的靶向菌群，可通过调节 Trp 代谢激活 AhR 信号通路以减轻结肠炎症[126]，淫羊藿苷等成分可通过促进该菌增殖间接增强 Trp 代谢途径[123]。

综上所述，中药有效成分通过多途径调控肠道菌群治疗 UC (图 3)：在优化菌群结构方面，促进乳杆菌属、双歧杆菌属、拟杆菌属、阿克曼氏菌属等有益菌增殖；在抑制致病菌方面，抑制假单胞菌门、埃希氏菌属及特定致病性拟杆菌等有害菌定植，减轻炎症负荷；在调控代谢产物方面，促进 SCFAs 和 Trp 代谢物等抗炎介质的生成，修复肠道屏障功能(表 2)。上述 3 类作用相互影响，共同体现了中药多靶点干预的治疗特点。

5 总结与展望

肠道菌群与 UC 之间存在紧密且复杂的关联，在发病进程中扮演关键角色。正常情况下肠道菌群维持动态平衡，有益菌与有害菌相互制衡；UC 患者肠道内菌群出现显著失衡，有益菌数量锐减，有害菌如埃希氏菌属等过度增殖，破坏肠道黏膜屏障，使肠道易受炎症因子侵袭进而引发炎症反应；同时，菌群失衡会扰乱肠道免疫系统，导致免疫系统错误攻击肠道正常组织，诱发持续性炎症，而 UC 产生的炎症环境又会进一步改变菌群结构，形成恶性循环。从门层面看，拟杆菌门和假单胞菌门与促炎因子(IL-6、IL-17、TNF-α)呈正相关，且部分病原体

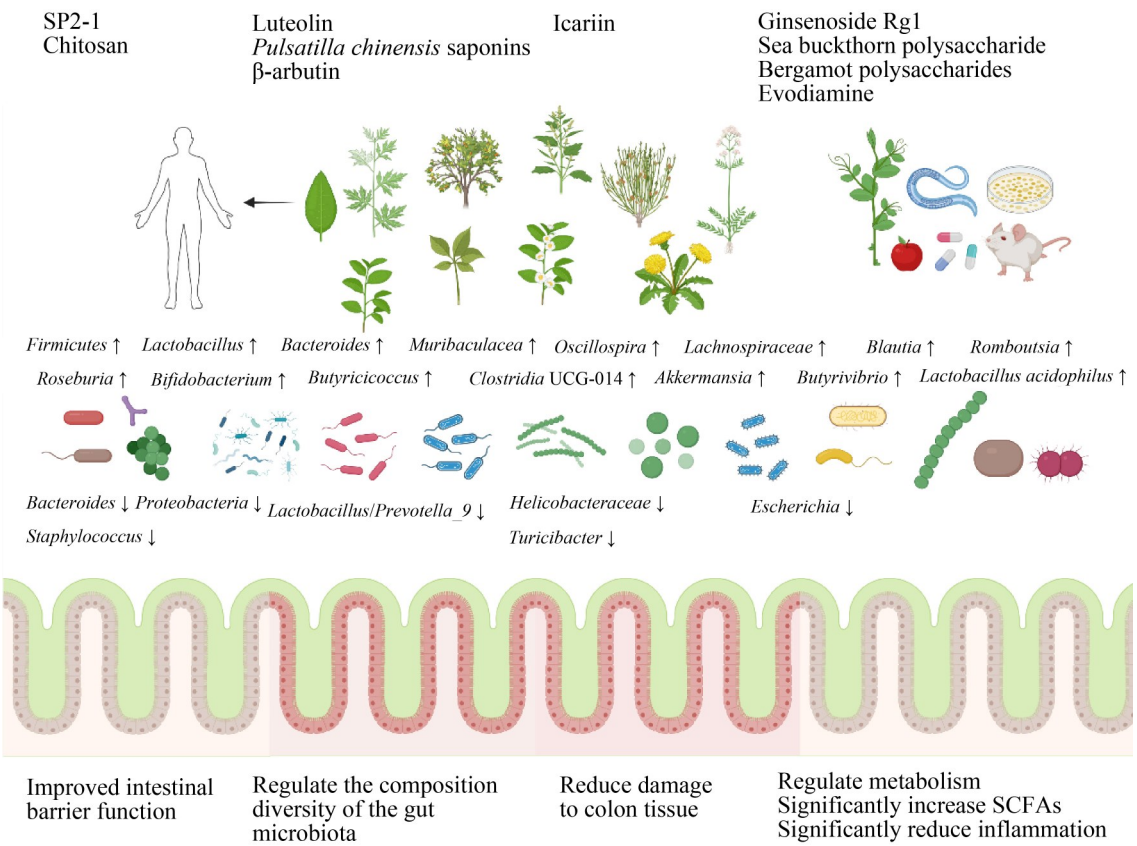

图3 中药调控肠道菌群治疗溃疡性结肠炎作用示意图

Figure 3 Schematic diagram of the effect of traditional Chinese medicine on regulating gut microbiota in the treatment of ulcerative colitis.

表2　中药有效成分对肠道菌群丰度的影响

Table 2　Effect of active ingredients in traditional Chinese medicine on the abundance of gut microbiota

TCM active ingredient	Decreased gut microbiota	Increased gut microbiota	Mechanism
Scutellaria baicalensis polysaccharide SP2-1	*Bacteroides*, *Pseudomonadota*, *Staphylococcus*	*Bacillota*, *Firmicutes*, *Bifidobacterium*, *Lactobacillus*, *Roseburia*	Inhibits pro-inflammatory cytokine production, enhances intestinal barrier function; increases beneficial bacteria abundance, optimizes gut microbiota composition to improve intestinal health[116]
Chitosan		*Blautia*, *Lactobacillus*	Enhances intestinal barrier function and improves gut microbiota dysbiosis[117]
Evodiamine		*Lactobacillus acidophilus*	Reduces pro-inflammatory cytokines, promotes goblet cell increase and antimicrobial peptide secretion, regulates *Bacillota*/*Bacteroidota* ratio, increases acetate levels[118]
Sea buckthorn polysaccharide	*Escherichia*	*Bifidobacterium*, *Bacteroides*	Enriches beneficial bacteria, increases short-chain fatty acids, maintains colonic homeostasis, protects colonic barrier and mucosal damage[119]
Bergamot polysaccharides		*Bifidobacterium*, *Butyrivibrio*, *Blautia*, *Roseburia*	Regulates gut microbiota and metabolism, produces short-chain fatty acids to reduce inflammation and enhance expression of tight junction proteins and mucins in the intestine[120]
Ginsenoside Rg1	*Odoribacter*	*Lactobacillus*, *Ileibacterium*, *Akkermansia muciniphila*	Regulates gut microbiota and tryptophan metabolism to exert intestinal barrier protection and anti-inflammatory effects[121]
Pulsatilla chinensis saponins	*Bacteroides*	*Muribaculum*, *Clostridia* UCG-014	Regulates the structure and diversity of gut microbiota[122]
Icariin	*Bacteroides*, *Helicobacteraceae*, *Turicibacter*	*Lactobacillus*, *Lachnospiraceae*, *Akkermansia muciniphila*	Improves colonic tissue damage[123]
Luteolin	Ratio of *Lactobacillus*/*Prevotella*, *Pseudomonadota*	*Roseburia*, *Clostridium butyricum*	Regulates the composition and structure of gut microbiota[124]
β-arbutin		Butyrate-producing bacteria	Reshapes gut microbiota structure, increases diversity and abundance of gut microbiota[125]

多属于假单胞菌门；芽孢杆菌门则与抗炎因子IL-10呈正相关，能促进肠上皮细胞增殖并增强屏障完整性。

目前，肠道菌群已成为中医药研究领域的热点，其与中医理论高度契合，是中药口服实现临床疗效的重要作用靶标。恢复肠道菌群稳态及肠道屏障功能，被视为UC有效治疗的新策略。诸多中药及其有效成分展现出通过调控肠道菌群治疗UC的潜力。例如，黄芪多糖具有抗炎等多重药理作用，可缓解小鼠结肠炎症状，抑制促炎细胞因子的生成，增强肠道屏障功能，同时促进有益菌增殖、调节肠道微生物群平衡；淫羊藿苷则能影响肠道菌群丰度，增加乳酸杆菌等多种有益菌数量，调控肠道菌群恢复动态平衡，进而影响肠道免疫应答、调节免疫平衡，为UC治疗提供多维度的新思路。

随着肠道菌群与中药研究的不断深入，中药在肠道菌群调控领域的应用潜力日益凸显，展现出广阔的疾病治疗前景。未来研究将聚焦于解析中药与肠道菌群相互调节的作用机制，为中药临床转化提供更具说服力的实验依据。伴随中药现代化与高质量发展进程，有望开发出更多机制明确、疗效显著的中药创新制剂，为患者提供更丰富的治疗选择。

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