李涛, 姜敏, 孙铭璐, 等. 炎症性肠病的病理分型、发病机制与膳食干预策略研究进展 [J]. 食品工业科技, 2026, 47(12): 485−496. doi: 10.13386/j.issn1002-0306.2025060077
LI Tao, JIANG Min, SUN Minglu, et al. Advances in Pathological Classification, Pathogenesis, and Dietary Intervention Strategies for Inflammatory Bowel Disease[J]. Science and Technology of Food Industry, 2026, 47(12): 485−496. (in Chinese with English abstract). doi: 10.13386/j.issn1002-0306.2025060077

· 专题综述 ·

炎症性肠病的病理分型、发病机制与膳食干预策略研究进展

李　涛[1,2], 姜　敏[1,3], 孙铭璐[1,3], 纪文华[1,2], 董红敬[1,2], 王　晓[1,2,*]
（1.齐鲁工业大学（山东省科学院）, 山东省分析测试中心, 天然产物分离提取共性技术创新与应用山东省工程研究中心, 山东济南 250014;
2.齐鲁工业大学（山东省科学院）药学院, 山东省高等学校天然药物活性成分研究重点实验室, 山东济南 250014;
3.山东中医药大学药学院, 山东济南 250355）

摘　要: 炎症性肠病（Inflammatory bowel diseases，IBD）是一类以慢性肠道炎症为特征的复杂疾病，其全球发病率呈持续上升趋势。IBD 的发病机制主要涉及遗传易感性、肠道菌群失调、免疫系统异常及环境因素（如饮食结构）的多因素交互作用。尽管现有药物治疗取得一定进展，但临床缓解和预防复发仍存在严重挑战。膳食干预策略因其良好的安全性和调节肠道微生态的独特优势，在 IBD 治疗中展现出重要潜力。近年来研究表明，膳食干预通过调节肠道菌群结构、促进短链脂肪酸生成、增强上皮屏障功能及平衡 Th17/Treg 免疫应答等多途径缓解 IBD，兼具多靶向性等优势，为 IBD 防治策略的创新提供了重要方向。因此，本文系统综述了 IBD 主要病理分型及发病机制，并重点探讨了膳食功能性寡糖、多糖和益生菌及粪菌移植等干预方法对 IBD 的调节作用及其机制，为 IBD 的防治提供新的理论依据和治疗思路。

关键词: 炎症性肠病, 发病机制, 肠道菌群, 功能性糖, 益生菌, 粪菌移植
中图分类号: TS201.4　　**文献标识码:** A　　**文章编号:** 1002−0306(2026)12−0485−12
DOI: 10.13386/j.issn1002-0306.2025060077
本文网刊:

Advances in Pathological Classification, Pathogenesis, and Dietary Intervention Strategies for Inflammatory Bowel Disease

LI Tao[1,2], JIANG Min[1,3], SUN Minglu[1,3], JI Wenhua[1,2], DONG Hongjing[1,2], WANG Xiao[1,2,*]
（1.Shandong Engineering Research Center for Innovation and Application of General Technology for Separation of Natural Products, Shandong Analysis and Test Center, Qilu University of Technology (Shandong Academy of Sciences), Jinan 250014, China;
2.Key Laboratory for Natural Active Pharmaceutical Constituents Research in Universities of Shandong Province, School of Pharmaceutical Sciences, Qilu University of Technology (Shandong Academy of Sciences), Jinan 250014, China;
3.School of Pharmaceutical Sciences, Shandong University of Traditional Chinese Medicine, Jinan 250355, China）

Abstract: Inflammatory bowel diseases (IBD) are complex disorders characterized by chronic intestinal inflammation, exhibiting a steadily rising global incidence. The pathogenesis of IBD involves multifactorial interactions among genetic susceptibility, gut microbiota dysbiosis, immune dysregulation, and environmental factors (notably dietary patterns). While

收稿日期: 2025−06−09
基金项目: “十四五”国家重点研发计划（2023YFC3503805）; 财政部和农业农村部: 国家现代农业产业技术体系资助（CARS-21）; 泰山学者工程（tsqnz20231230）。
作者简介: 李涛（1992−）, 男, 博士, 助理研究员, 研究方向: 药食同源功能食品与健康, E-mail: litaosd@qlu.edu.cn。
*** 通信作者:** 王晓（1971−）, 男, 博士, 研究员, 研究方向: 药食同源资源开发与利用, E-mail: wangx@sdas.org。

current pharmacological therapies have advanced, significant challenges persist in achieving sustained clinical remission and preventing relapse. The dietary intervention strategies hold considerable therapeutic potential for IBD management due to their favorable safety profile and unique capacity to modulate the gut microbiome. Recent studies demonstrated that dietary interventions could alleviate IBD through multiple mechanisms, including restructuring the gut microbiota, promoting the production of short-chain fatty acids, enhancing epithelial barrier function, and balancing the immune responses of Th17/Treg. These strategies exhibit multi-target efficacy and offer a promising direction for innovating preventive and therapeutic approaches against IBD. Therefore, this review systematically summarizes the principal pathological subtypes and pathogenic mechanisms of IBD, with a specific focus on the regulatory effects and underlying mechanisms of dietary interventions, including functional oligosaccharides, polysaccharides, probiotics, and fecal microbiota transplantation. The findings will offer the novel theoretical insights and therapeutic approaches for IBD prevention and clinical management.

Key words: inflammatory bowel disease; pathogenesis; gut microbiota; functional sugars; probiotics; fecal microbiota transplantation

炎症性肠病(Inflammatory bowel diseases, IBD)是一种以慢性复发性肠道炎症为特征的全球性疾病,主要包括溃疡性结肠炎(Ulcerative colitis, UC)和克罗恩病(Crohn's disease, CD)两种临床亚型[1]。该病以反复发作的腹泻、腹痛、便血等消化道症状为主要临床表现,常伴有关节炎、生长发育迟滞等肠外表现,严重影响患者生活质量。根据疾病演变规律,IBD 分为 4 个流行病学阶段:疾病出现、发病加速、患病恶化和患病平衡[2]。目前,西方国家正处于患病恶化阶段,预计到 2030 年患病率将上升至 1%,而发展中国家正处于疾病出现阶段[3]。流行病学研究表明,在南美洲、非洲和亚洲等发展中地区 IBD 的发病率不断增加,预计到 2035 年,中国的发病病例将达到 41901 例,死亡 6568 人[4]。目前临床尚缺乏对 IBD 根治性治疗方案,亟需深入探索其发病机制以寻找新的治疗靶点。

IBD 的发病机制涉及环境因素、免疫紊乱、肠道菌群失调和遗传易感性等多因素复杂交互作用[5](如图 1 所示)。研究表明,宿主-微生物互作失衡是 IBD 发病的核心环节[6]。正常情况下,肠道菌群不仅参与营养代谢,还在免疫调节中发挥关键作用;而菌群失衡可导致病原体过度增殖,进而激活异常免疫反应,推动 IBD 的发生发展[7]。完整的肠道上皮屏障是维持肠道稳态的重要保障,可有效阻隔病原体和促炎物质的渗透[8]。然而,当菌群失调导致屏障功能受损时,脂多糖(LPS)和肽聚糖(PG)等细菌成分进入循环系统,触发持续的炎症级联反应[9]。在健康状态下,树突状细胞通过持续监测肠道菌群来维持对共生菌的免疫耐受;而在 IBD 患者中,屏障功能破坏导致共生菌侵入固有层,诱导促炎细胞因子释放,并通过免疫细胞的异常募集和增殖扩大炎症反应[10]。目前临床治疗主要依赖氨基水杨酸制剂、糖皮质激素、免疫抑制剂等传统药物,以及抗肿瘤坏死因子(Tumor necrosis factor, TNF)单抗、白细胞介素(Interleukin, IL)抑制剂等生物制剂和 JAK 抑制剂、S1P 受体调节剂等新型小分子药物。然而,这些治疗方案存在应答率低(仅约 50%)、继发性失效和严重不良反应(如感染、胰腺炎和恶性肿瘤等)的局限性[11−13]。手术治疗虽可缓解症状,但存在肠穿孔、大出血等风险[14]。因此,开发更安全、高效且经济的新型治疗策略已成为当前 IBD 研究领域的迫切需求。

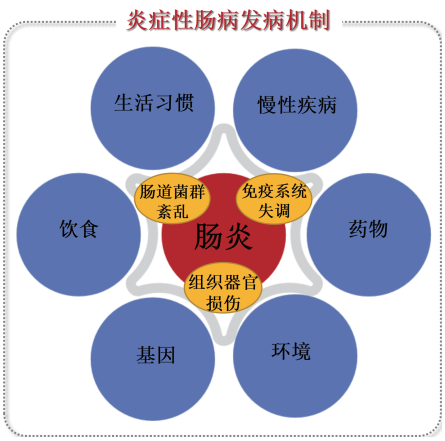


图 1 炎症性肠病的发病机制

Fig.1 Pathogenesis of inflammatory bowel disease

饮食是影响肠道菌群组成、肠道屏障和宿主免疫的关键因素之一,可作为改善疾病的重要潜在治疗手段[15]。由于其高效、安全、来源广泛,饮食干预已成为改善 IBD 的重要策略。流行病学研究证实,以高脂、高糖和低纤维为特征的西方饮食模式可显著改变肠道菌群结构,表现为产短链脂肪酸(SCFAs)菌群减少而条件致病菌(如螺杆菌属)富集,从而增加 IBD 发病风险[16]。Pereira 等[17] 也证实了低膳食纤维饮食会促进粘蛋白降解细菌的增殖,降低肠道屏障功能,导致 IL-10 缺陷小鼠罹患 IBD。近年来,功能性寡糖/多糖、益生菌及粪菌移植(FMT)等新型饮食干预策略在 IBD 治疗中具有巨大潜力。本文系统梳理了 IBD 的疾病分类和发病机制,并重点阐述了基于饮食调控的治疗策略,以期为 IBD 的精准营养干预提供理论依据。

1 炎症性肠病主要病理分型

1.1 溃疡性结肠炎

UC 作为一种特发于结肠的慢性炎症性疾病,其核心病理特征表现为结肠上皮细胞损伤及粘膜屏障功能破坏[5],其中最常见的症状是腹泻和黏液脓血

便[18]。UC 的发病机制涉及复杂的免疫调节网络失衡，其中 Th17/Treg 细胞平衡失调、PPAR-γ 信号通路异常以及 TLRs 表达改变等关键环节共同构成了疾病发生的分子基础。在免疫调节方面，UC 的特征性改变是 Th17 细胞过度活化与 Treg 细胞功能缺陷导致的免疫耐受失衡[19]。这种失衡不仅直接参与肠道炎症反应，还与 Th2 型免疫应答异常（表现为 IL-5 和 IL-13 过度分泌）共同构成了 UC 的免疫学基础。在分子机制层面，Jiang 等[20] 首次证实 UC 患者结肠细胞中 PPAR-γ 表达显著下调，该转录因子作为 NF-κB 信号通路的负调控因子，其表达缺失导致炎症反应失控[21]。值得注意的是，UC 患者肠道上皮和固有层中 TLR2 和 TLR4 表达水平异常升高[22]，虽然其因果关系尚未完全阐明，但模式识别受体在 UC 发病中可能发挥重要作用。

1.2　克罗恩病

CD 是一种具有终生复发倾向的透壁性炎症性疾病，其病变可累及从口腔至肛门的整个消化道，以回肠末端和结肠最为常见[23]。与 UC 不同，CD 的特征性病理改变包括非连续性透壁炎症、瘘管形成及肠梗阻等严重并发症[24]。尽管发病率持续攀升，但 CD 的病因和发病机制仍未完全阐明，目前认为其本质是遗传易感性、环境因素和免疫紊乱共同作用导致的自身免疫性疾病。在免疫学机制方面，CD 主要表现为 Th1/Th17 型免疫应答的异常激活。Th17/Treg 和 Th1/Treg 稳态失衡被认为是驱动 CD 的关键因素[25]。研究表明，CD 患者肠黏膜中存在大量 Th17 细胞浸润，同时伴有 Th1 型细胞因子（如 IFN-γ 和 TNF-α）的过度分泌[26]。这种免疫失衡的核心环节是 IL-12 刺激 Th1 细胞分化，进而通过 IFN-γ/TNF-α 轴导致肠道组织炎性损伤[1]。在临床治疗领域，TNF-α 拮抗剂（如英夫利西单抗）虽被证实对 CD 具有显著疗效，但其高昂的治疗费用、潜在的免疫抑制副作用以及对结核、肝炎等特殊人群的应用限制，凸显了开发新型治疗策略的紧迫性。

2　炎症性肠病发病机制

2.1　环境因素

越来越多的证据表明，环境因素在 IBD 的发生发展中起着关键作用[27]。从饮用水成分、饮食结构到化学污染物和物理刺激、多种环境暴露因素均可通过破坏肠道屏障、扰乱菌群稳态或激活炎症信号通路，进而促进 IBD 的发生。在饮用水方面，Zhou 等[28] 研究发现长期接触锰、汞、硒、四氧化硫、氯和硝酸盐氮等化学物质可显著增加 IBD 风险，而锌和氟则可能具有保护作用。饮食因素同样影响显著，过量摄入高糖饮料（如 30% 蔗糖或 20% 果糖溶液）可导致肠道菌群失衡，并加剧高脂饮食或应激诱导的结肠炎[29−30]。此外，食品污染物如脱氧雪腐镰刀菌烯醇可通过激活 JAK2/STAT3 信号通路加重 DSS 诱导的结肠炎[31]，而长期摄入食品添加剂二氧化钛纳米颗粒则可能破坏肠道菌群并诱发结肠炎症[32]。除化学因素外，物理刺激如冷水暴露也可损害肠道屏障功能，增加通透性并降低菌群多样性，进而诱发 IBD[33]。农业化学品的暴露同样值得关注，例如除草剂戊炔草胺可通过干扰芳烃受体信号传导，抑制 T 细胞和树突状细胞的 NF-κB 通路，从而促进肠道炎症[34]。此外，临床流行病学研究表明，抗生素的累积使用，尤其是 40 岁以上人群，可显著增加 IBD 发病风险[35]。综上，环境因素通过多途径、多机制参与 IBD 的发病过程。因此，明确关键环境暴露因素的剂量-效应关系及其分子机制是阐明 IBD 发病机制和寻找治疗靶点的重要途径。

2.2　肠道免疫

IBD 作为一种复杂的自身免疫性疾病，与先天性和适应性免疫系统的异常激活密切相关。多种免疫细胞（包括巨噬细胞、嗜酸性粒细胞、中性粒细胞及先天性淋巴细胞等）的数量变化、功能异常及其相互作用，共同构成了 IBD 复杂的免疫病理学基础[36]。在巨噬细胞调控方面，研究发现中脑星形胶质细胞源性神经营养因子可通过抑制炎性巨噬细胞中 C/EBP 同源蛋白-碱性亮氨酸拉链 ATF 样转录因子 2 信号通路，同时下调 Th17 细胞介导的免疫反应，从而显著改善结肠炎症状[37]。单核细胞趋化蛋白-1 诱导蛋白 1 的缺失会增强巨噬细胞迁移能力并促进 M1 型极化，这种异常分化通过抑制 Atf3-Ap1s2 信号轴，最终加剧肠道炎症反应[38]。嗜酸性粒细胞在急性结肠炎期间受 IL-33 和 IFN-γ 诱导大量聚集，通过过度激活 CD4+T 细胞而加重炎症进程[39]。中性粒细胞则通过产生大量活性氧簇（如 NO）促进炎症发展，其过度浸润导致的脂滴积累和 FOXO3a 表达缺失是驱动结肠炎的重要机制[40−41]。在先天性淋巴细胞方面，NCR-ILC3s 通过分泌粒细胞-巨噬细胞集落刺激因子激活中性粒细胞，从而促进 IBD 发展[42]；而 NCR+ILC3s 则通过增加 IL-22 分泌及维持 NCR−ILC3s/NCR+ILC3s 平衡发挥保护作用[43]。综上研究揭示了 IBD 发病过程中复杂的免疫调控网络，不同免疫细胞亚群通过特定的信号通路和细胞因子网络相互影响，共同决定疾病的发生发展。

IBD 的免疫发病机制涉及复杂的抗原识别和细胞因子调控网络。肠道内的细菌、病毒或食物过敏原等潜在免疫原可通过模式识别受体（PRRs）系统激活先天免疫应答，继而触发 NF-κB 等关键炎症信号通路的活化，并通过促炎/抗炎细胞因子的动态平衡调控疾病进程。在抗原识别层面，巨噬细胞和树突状细胞等先天免疫细胞通过 Toll 样受体（TLRs）和核苷酸结合寡聚化结构域（NOD）等 PRRs 识别病原体相关分子模式。这种识别可激活 MyD88/IRAK/TRAF6/MEKK1 依赖的 NF-κB 信号通路，进而促进 IL-1β、IL-6、IL-8 和 TNF-α 等促炎因子及 ICAM-1 等粘附分子的表达[44]。其中，TLRs 不仅能识别 LPS 和肽聚

糖等病原体成分，还能刺激肠道分泌 IgA，增强黏膜免疫防御功能。在细胞因子调控方面，促炎因子（如 IL-1、IL-2、IL-8、TNF 等）通过招募和激活中性粒细胞、单核细胞等炎症细胞，促进其表面整合素表达和迁移能力，从而加剧炎症反应；而 IL-4、IL-10、IL-13 等抗炎因子则发挥重要的负向调控作用。临床研究表明，UC 患者病灶部位 IL-2 表达显著升高且与疾病严重程度呈负相关[45]，而 IL-8 和 IL-17 的表达水平则与结肠炎严重程度呈正相关[46]，凸显了细胞因子网络的失衡在 IBD 发病中的关键作用。肠道免疫系统通过 PRRs 介导的抗原识别和细胞因子网络的精细调控，在维持黏膜稳态和诱发炎症反应中扮演双重角色。

2.3 肠道菌群

肠道菌群失调已被证实是 IBD 产生的重要致病因素。IBD 患者的肠道微生态呈现特征性改变，主要表现为促炎微生物过度增殖而保护性菌群显著减少，这种失衡通过破坏黏膜屏障功能和扰乱免疫稳态等多重机制参与疾病进程。多项关键性研究为菌群失调与 IBD 的因果关系提供了直接证据。Sellon 等[47]通过无菌动物实验证实，*IL-10* 基因敲除小鼠在无菌环境下不发生结肠炎，而接受患病小鼠菌群移植后可诱发肠道炎症，这一发现确立了菌群在 IBD 发病中的必要性。临床观察表明，IBD 患者的肠道菌群特征性改变包括变形菌门、致病性大肠杆菌及某些真菌（如念珠菌属）的异常增多，而具有黏膜保护作用的嗜粘蛋白阿克曼氏菌等有益菌显著减少[48−49]。金黄色葡萄球菌、沙门氏菌、梭状芽孢杆菌等多种细菌可通过黏附于肠上皮细胞进而破坏肠上皮细胞参与 IBD 的发生发展过程[50−51]。更为重要的是，Kleessen 等[52]采用免疫荧光原位杂交技术，在 83% 的 UC 患者结肠黏膜中直接观察到细菌侵袭现象；Barnich 等[53]则从 CD 患者回肠中分离出具有侵袭特性的特殊菌株，该菌株不仅能黏附和侵入肠上皮，还可激活巨噬细胞分泌促炎因子 TNF-α 和 IFN-γ，从而加剧炎症反应。在机制研究方面，特定菌群通过调控免疫细胞分化影响疾病进程的分子机制逐渐被阐明。保护性菌群如双歧杆菌和乳酸杆菌能促进调节性 T 细胞（Treg）分化，维持免疫耐受[54]；而致病菌如分节丝状杆菌则可强烈激活 Th1、Th2 和 Th17 细胞反应，打破免疫平衡[55]。综上结果表明，肠道菌群失调影响机体 Th1/Th2/Th17/Treg 细胞的平衡，进一步促进 IBD 发生（如图 2 所示）。当前研究已充分证实肠道菌群失调在 IBD 发病中的核心地位，但仍存在若干关键问题有待解决：菌群改变与 IBD 的联结关系尚未阐明，特定菌群影响免疫系统的精确分子机制尚不明确，菌群调控在临床治疗上有效转化仍待挖掘。未来研究需要整合多组学技术、无菌动物模型和临床干预试验，深入解析关键功能菌群的作用靶点，为开发基于微生物组调控的精准治疗提供理论依据。

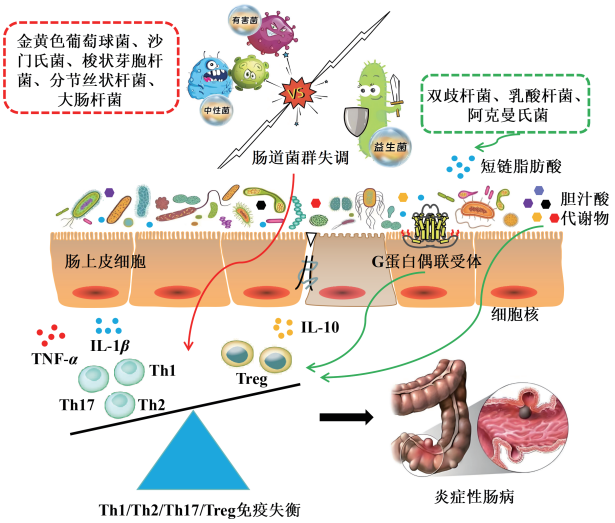


图 2 肠道菌群失调引起炎症性肠病的作用机制

Fig.2 Mechanism of inflammatory bowel disease caused by intestinal flora imbalance

肠道微生物代谢物作为宿主-菌群互作的关键介质，通过调节免疫平衡和维持肠道稳态在治疗 IBD 中发挥核心作用。IBD 患者特征性地表现为 SCFAs、胆汁酸和色氨酸代谢通路相关菌群（如粪杆菌属、瘤胃球菌属等）的显著减少，导致具有保护作用的代谢物水平下降而促炎代谢物相对增多，这种代谢失衡构成了 IBD 诱发的重要病理基础[56]。在保护性代谢物方面，SCFAs 特别是丁酸盐通过调控 Th17/Treg 细胞平衡发挥抗炎作用[57]。特定菌群联合体（如梭状芽孢杆菌、卵形拟杆菌等）产生的次级胆汁酸（熊去氧胆酸和石胆酸）能显著增强肠道屏障功能[58]。此外，色氨酸代谢产物吲哚-3-丙酸在 IBD 患者粪便中含量降低，该物质已被证实具有抑制肠道炎症和纤维化的潜力[59]。抗炎代谢物棕榈油酸在 IBD 患者中也呈现显著减少的趋势，其可通过改善菌群组成发挥保护作用[60]。在促炎机制方面，色氨酸衍生物臭素通过激活 p38 和 JNK 信号通路促进 TNF-α 表达，直接加剧肠道炎症[61]。脱氧胆酸则通过上调 IL-1β 表达、改变 T 细胞亚群比例及减少簇状细胞数量等多种途径加重肠黏膜损伤[58]。这些发现不仅揭示了微生物代谢物调控 IBD 的分子机制，更为重要的是确立了特定代谢物水平与疾病活动的相关性。因此，应深入解析代谢物的时空动态变化规律及其细胞特异性作用靶点，为开发基于代谢调控的 IBD 精准治疗提供新思路。

2.4 基因

全基因组关联研究已鉴定出 240 多个与 IBD 相关的易感基因位点，这些遗传变异主要涉及上皮屏障功能、自噬调控、内质网应激、免疫应答及微生物抗原处理等关键生物学途径[62]。尽管遗传因素对疾病表型的贡献度有限，但特定风险基因通过改变宿主-微生物互作和免疫稳态，在 IBD 发病中发挥着奠基性作用。在关键易感基因中，*NOD2* 基因突变因其显

著的风险效应备受关注。突变型 NOD2 蛋白丧失对胞壁酰二肽的识别能力，导致促炎细胞因子和 I 型干扰素异常分泌[63−64]。PTPN22 则通过双重机制发挥保护作用：一方面调控肠道菌群组成，另一方面抑制 NLRP3 炎症小体过度激活[65]。*CARD9* 基因缺陷会引发菌群失调和色氨酸代谢紊乱，其在中性粒细胞中的表达缺失还会导致线粒体功能障碍和活性氧累积，最终削弱抗真菌免疫[66−67]。研究发现，结肠炎相关 IRF1 肠道稳态反义调节因子通过维持宿主-共生菌稳态对 IBD 具有保护效应[68]，这为解析遗传风险位点的功能机制提供了新视角。然而，遗传基因对 IBD 的影响能力是有限的，其中 CD 约为 13.6%，UC 约为 7.5%[69]。因此，IBD 的遗传架构呈现高度复杂性，其发病机制本质上是遗传易感性、环境暴露和免疫调控网络动态互作的结果。

3　炎症性肠病膳食干预策略

3.1　功能性寡糖

功能性寡糖作为一类具有显著功能活性的膳食成分，其通过多重机制发挥治疗作用，包括调节肠道菌群组成、增强屏障功能以及调控免疫应答等（如表 1 所示），成为 IBD 营养干预研究的重要方向。功能性寡糖可通过 TLR4 等模式识别受体激活 NF-κB、MAPK 和 STAT 信号通路，进而调控免疫细胞增殖分化及炎性因子分泌[70]。同时，功能性寡糖也可通过调节 IBD 患者肠道菌群及其代谢产物，减少肠道炎症（如图 3 所示）。研究表明，低聚果糖（FOS）则通过降低 MPO 活性，减少 IFN-γ、IL-17 等促炎因子分泌发挥抗炎作用[71]，并能特异性抑制艰难梭菌等致病菌生长[72]。低聚半乳糖（GOS）可增加双歧杆菌等有益菌丰度，显著改善 IBD 患者排便症状[73]。2’-岩藻糖基乳糖（2’-FL）通过调节 NF-κB/MAPK 信号通路和次级胆汁酸代谢发挥治疗作用[74−75]。其他寡糖如甘露寡糖（MOS）和裙带菜寡糖（UPO）通过选择性促进益生菌增殖及直接调节巨噬细胞功能等多重机制改善结肠炎[76−77]；低聚乳果糖（LS）则通过抑制 Th17 活性和多种促炎因子表达促进黏膜修复[78]。壳寡糖（COS）的抗炎机制涉及抑制 NF-κB 通路活化、降低氧化应激和细胞凋亡以及改善肠道菌群等[79−81]。功能性寡糖以其多靶点、低毒性的特点，通过重塑“菌群-宿主”互作网络为 IBD 治疗开辟了新途径，其“食疗-微生态-免疫”三位一体的作用模式不仅丰富了 IBD 的治疗策略，更为开发精准营养干预方案提供了理论依据。然而，当前研究仍存在以下关键问题亟待解决：不同寡糖的最佳治疗剂量和疗程尚未明确；个体化治疗方案缺乏生物标志物指导；长期安全性和有效性需进一步验证。

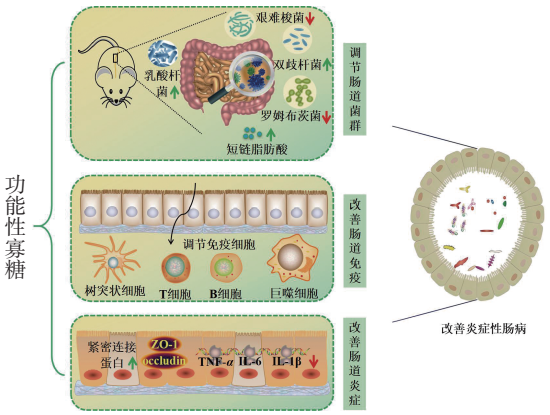


图 3　功能性寡糖调节炎症性肠病的作用机制

Fig.3　Mechanism of functional oligosaccharides in modulating inflammatory bowel disease

3.2　功能性多糖

IBD 的肠道损伤机制中，吞噬细胞浸润导致的氧化应激与抗氧化系统失衡是关键环节。近年研究发现，多糖类物质通过独特的“抗氧化-免疫调节”双重作用机制，在 IBD 治疗中展现出显著的保护效应。在抗氧化方面，枸杞来源的阿拉伯半乳聚糖通过激活 Nrf2/HO-1 通路显著改善氧化应激指标（DAO、MDA）[82]，而石斛多糖则以剂量依赖方式提升 SOD、CAT 等抗氧化酶活性[83]。此外，多糖类物质能调节抗原呈递细胞和多种细胞因子，调节免疫系统动态平衡，保护结肠损伤（如图 4 所示）。沙棘多糖通过降低 TNF-α、IL-1β 等促炎因子水平减轻 IPEC-J2 细胞免受 LPS 诱导的炎症、凋亡和屏障功能障碍[84]；白术多糖通过调控 Th17/Treg 平衡和抑制 IL-6/STAT3 通路修复肠屏障[85]；茯苓多糖通过阻断 IL-33/ST2 信号通路减少炎症浸润[86]；冬虫夏草多糖（CSP）则通过下调 TLR4 表达和促进 IL-10 分泌发挥抗炎作用[87]。综上研究共同揭示了多糖通过调节“氧化-炎症-免疫”网络维持肠道稳态的分子机制。

多糖类物质通过“菌群-屏障-免疫”三位一体的

表 1　功能性寡糖改善炎症性肠病的作用靶点

Table 1　Target sites of functional oligosaccharides in improving inflammatory bowel disease

寡糖类型	模型	作用靶点	临床/动物模型效果	参考文献
低聚果糖	小鼠；大鼠	T淋巴细胞；致病菌	抑制促炎细胞因子分泌和致病菌生长	[71−72]
低聚半乳糖	人体	益生菌	改善IBD患者排便	[73]
2’-岩藻糖基乳糖	小鼠	NF-κB和MAPK通路；次级胆汁酸	调节结肠炎小鼠NF-κB和MAPK信号通路以及次级胆汁酸代谢	[74−75]
甘露寡糖和裙带菜寡糖	小鼠	巨噬细胞；肠道菌群	促进结肠炎小鼠肠道益生菌增殖及调节巨噬细胞极化	[76−77]
低聚乳果糖	大鼠	肠道菌群	抑制结肠炎大鼠促炎因子表达，增加双歧杆菌和乳酸杆菌的数量	[78]
壳寡糖	细胞；小鼠；大鼠	NF-κB和ERK1/2通路；肠道菌群	抑制NF-κB和ERK1/2通路，改善抗氧化能力、肠道屏障功能和肠道菌群	[79−81]

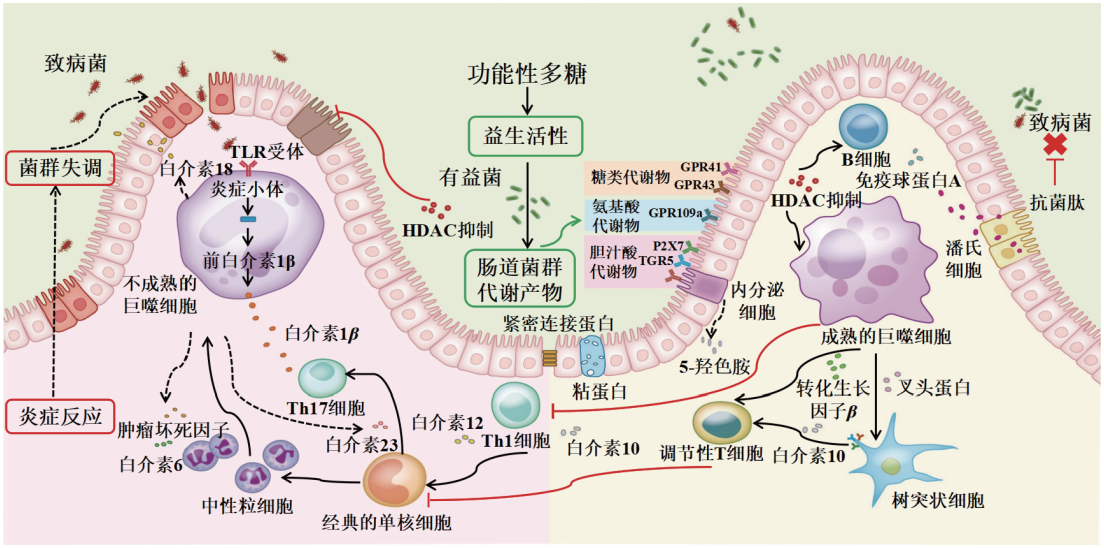


图 4　功能性多糖调节炎症性肠病的作用机制

Fig.4　Mechanism of functional polysaccharides in regulating inflammatory bowel disease

调控网络，在 IBD 治疗中发挥核心作用。其作用机制主要涉及重塑肠道菌群结构、增强上皮屏障功能以及调控免疫稳态三个关键环节。在菌群调控方面，紫甘薯多糖可显著改善 UC 小鼠肠道菌群组成，主要调节拟杆菌等关键菌群[88]；金银花和菊花多糖则通过增加双歧杆菌等有益菌丰度，同时抑制大肠杆菌等致病菌增殖来恢复菌群平衡[89−90]。在屏障保护方面，竹荪多糖通过上调 claudin-1、occludin 等紧密连接蛋白表达，有效降低内毒素血症[91]；诺丽果、黄芩等来源的多糖同样具有增强肠道屏障完整性的作用[92−95]。美丽崖豆藤多糖不仅能改善肠绒毛形态[96]，还可促进 MUC2 等粘液蛋白表达，增强粘膜防御功能[97]。在免疫调节层面，巴戟天多糖具有增强免疫器官和免疫细胞的功能[98]；铁皮石斛多糖则通过抑制 NLRP3 炎性小体和 β-arrestin1 信号通路发挥抗炎作用[99]。多糖类物质通过重建“菌群-宿主”共生平衡为 IBD 治疗提供了新策略，其“生态-屏障-免疫”协同作用模式揭示了 IBD 治疗的新靶点。

多糖类物质通过肠道菌群发酵产生 SCFAs 等活性代谢物，构成其改善 IBD 的核心机制之一。这一“多糖-菌群-代谢物”转化过程不仅为结肠细胞提供能量，更通过多靶点调控肠道微环境稳态。研究表明，芦荟多糖可显著增加嗜黏蛋白阿克曼氏菌和经黏液真杆菌等产 SCFAs 菌群的丰度，同时降低与炎症相关的拟杆菌门比例，进而影响乙酸、丙酸等代谢产物水平及炎性细胞因子表达[100]。太子参多糖处理能提升 IBD 大鼠体内乙酸、丙酸和丁酸含量，通过 SCFAs 的免疫调节作用抑制肠道炎症[101]。紫甘薯碱溶性多糖则通过双重机制发挥作用，一方面改善菌群紊乱、提高 SCFAs 水平；另一方面下调 TLR4/NF-κB 信号通路表达，从而有效缓解溃疡性结肠炎[102]。这些发现共同揭示了多糖经菌群代谢调控“代谢-免疫”网络的分子基础。综上，多糖通过菌群代谢产生的 SCFAs 等活性物质，构建了连接膳食成分与宿主健康的桥梁，其“前药-转化-效应”的作用模式不仅拓展了 IBD 营养干预的认知边界，更为开发基于菌群代谢调控的精准治疗策略提供了新思路。

3.3　益生菌

益生菌作为一类具有明确健康效益的活微生物，通过抑制病原菌、调节免疫平衡、增强抗氧化防御和维护肠道屏障功能等多个层面（如图 5 所示），展现出独特的 IBD 治疗优势[103]，如乳酸杆菌、双歧杆菌和链球菌等。在免疫调节方面，罗伊氏乳杆菌、嗜酸乳杆菌等可通过降低促炎因子（TNF-α、IL-1β 等）和提升抗炎因子（IL-10）水平改善炎症状态[104]。瑞士乳杆菌 KLDS1.8701 产生的胞外多糖展现出显著的免疫调节活性[105]。在抗氧化方面，长双歧杆菌 CCFM681 通过产生共轭亚油酸增强 SOD、CAT 等抗氧化酶活性[106]，而乳酸菌胞外多糖则通过金属离子螯合等机制改善氧化应激[107]。值得注意的是，特定菌株如分节丝状杆菌和脆弱拟杆菌通过调控 Th17/Treg 平衡发挥保护作用[55,108]。肝螺杆菌胞外多糖则通过激活 TLR2/MSK/CREB 通路诱导巨噬细胞抗炎表型[109]，揭示了菌群-宿主互作的新机制。益生菌通过其独特的“活菌-代谢物-信号分子”多维作用体系，构建了连接微生物组与宿主健康的桥梁，

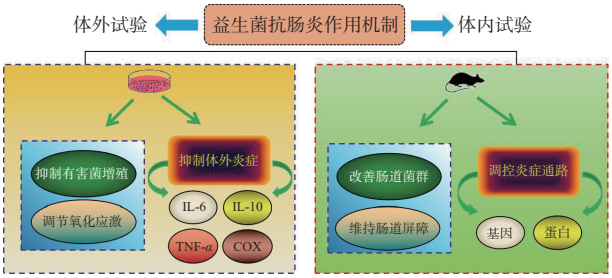


图 5　益生菌调节炎症性肠病的作用机制

Fig.5　Mechanism of probiotics in regulating inflammatory bowel disease

其多靶点、多层次的调控特性不仅为 IBD 治疗提供了新范式，更推动了微生物组精准干预理念的发展。

多菌株复合益生菌制剂凭借其协同增效作用，在 IBD 临床治疗中展现出显著的优势。以 VSL#3 为代表的混合益生菌通过多菌种协同调控“菌群-免疫”网络，为 IBD 治疗提供了新的选择。研究表明，含 8 株菌的 VSL#3 制剂（包含乳酸杆菌、双歧杆菌和链球菌）可有效缓解轻中度 IBD 患者症状[110]。两歧双歧杆菌 MIMBb75 单菌治疗使 47% 患者症状得到改善[111]，而五联益生菌制剂（含干酪乳杆菌等）治疗 6 周后显著改善 15.3% 患者的症状严重程度[112]。这些益生菌制剂通过增加乳杆菌、双歧杆菌等有益菌丰度和调节细胞因子平衡发挥作用。保护性菌群（如丁酸菌、螺旋菌）与抗炎因子 IL-10 呈正相关，而条件致病菌（普雷沃氏菌等）与促炎因子（TNF-α、IL-6 等）呈正相关。混合益生菌制剂通过“多菌协同-免疫调节-菌群重塑”的整合作用模式，为 IBD 的个性化治疗提供了新思路，其临床转化价值亟待通过更大规模的规范化研究进一步验证。

3.4　粪菌移植

FMT 作为一种创新的微生物组靶向治疗策略，通过重建肠道微生态平衡在 IBD 治疗领域展现出独特的价值，其核心机制是将健康供体的功能菌群移植至患者肠道，以纠正菌群失调并恢复肠道稳态。FMT 是 FDA 批准的一种治疗复发性艰难梭菌感染的药物，目前其在治疗肠易激综合征和 IBD方面受到广泛关注[113]。研究表明，FMT 可以调节与 IBD 相关的肠道营养不良，减少炎症并促进粘膜修复[114]。临床证据表明，FMT 对 IBD 具有显著的治疗效果，其中 UC 患者的临床缓解率达 22%，而 CD患者可达 61%[115]。Paramsothy 等[116] 的荟萃分析（纳入 53 项研究、661 例患者）表明，新鲜粪便移植的临床缓解率（40.9%）优于冷冻粪便（32.2%）。在儿科人群中，FMT 治疗后 64.7% 的患儿达到临床缓解[117]，证实了其在特殊人群中的安全性。一项安慰剂对照试验表明，FMT 可引起 UC 患者的临床缓解和内窥镜改善，并且与结果相关的不同微生物变化相关[118]。Tikunov 等[119] 研究表明，8 周的 FMT 治疗后 UC 中有 19 名（95%）患者达到临床缓解。由于患者原始微生物群的独特性，不同患者的缓解持续时间存在显著差异。FMT 治疗的成功取决于供体和受体之间肠道菌群的相互作用。未来 FMT 可能会被使用确定的微生物群落所取代。因此，FMT 为治疗菌群失调和修复肠道菌群异常提供了一种可行的替代方案。

3.5　其他天然产物

天然产物作为药物研发的重要源泉，在 IBD 治疗领域展现出广阔的应用前景。这类由生物体通过初级和次级代谢途径产生的化学物质（包括黄酮类、多酚类、生物碱、萜类、醌类、皂苷、活性肽以及细菌代谢产物如短链脂肪酸、次级胆汁酸、色氨酸代谢物和维生素等），约占现有小分子药物的 50% 以上，其治疗潜力已得到广泛认可[120−121]。研究表明，多种天然产物在治疗 IBD 方面具有显著作用，包括黄酮、多酚、生物碱、萜类化合物、醌类、皂苷、肽和细菌次生代谢物（SCFAs、次级胆汁酸、色氨酸、维生素等），它们通过恢复失衡的肠道菌群、增强肠道屏障完整性和调节免疫反应等机制发挥治疗作用[122]（如图 6 所示）。天然产物凭借其结构多样性和多靶点调控特性，为 IBD 治疗提供了极具开发价值的候选资源库。然而，目前许多天然产物的抗 IBD 活性的验证主要依赖于动物模型和细胞模型，缺乏足够的临床支持。因此，仍需更多的临床证据确定这些化合物的安全性和有效性。

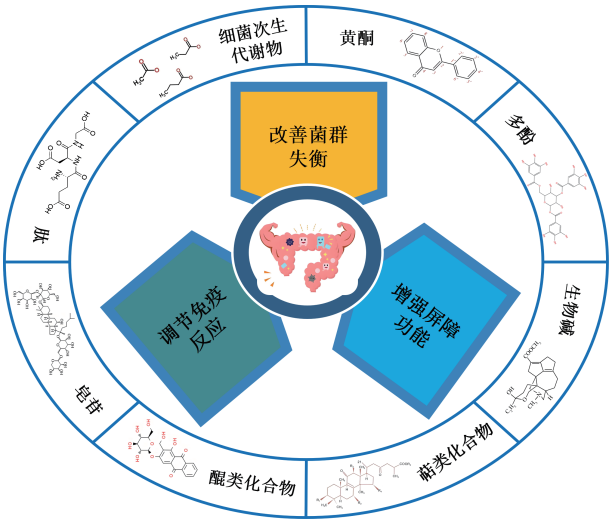


图 6　天然产物调节炎症性肠病的作用机制

Fig.6　Mechanism of natural products in modulating inflammatory bowel disease

4　结论和展望

炎症性肠病（IBD）主要包括克罗恩病（CD）和溃疡性结肠炎（UC）两种亚型，其发病机制涉及遗传易感性个体在环境因素作用下引发的肠道菌群失调及免疫调节异常等多因素相互作用。近年来，以功能性寡糖、多糖、益生菌及 FMT 为代表的微生态靶向干预策略，通过调控肠道菌群组成及其代谢活性、增强肠道屏障完整性以及恢复免疫稳态，在 IBD 治疗中展现出显著的临床潜力。与传统的药物干预和外科治疗相比，这些基于饮食微生态调节的干预方法具有成本效益显著、安全性良好且疗效确切的优势。多种饮食治疗模式的联合应用可能为 IBD 治疗提供更优化的临床方案。这些创新性干预策略不仅为 IBD 的防治提供了新思路，更有望显著改善患者的临床预后及生活质量。然而，当前以功能性寡糖、多糖、益生菌及 FMT 为代表的微生态干预研究仍面临诸多挑战。首先，功能性寡糖和多糖的结构-功能关系尚未完全阐明，其作用机制缺乏精准的分子靶点证据。其次，益生菌的菌株特异性、宿主个体差异及定植抗性限制了其临床疗效的稳定性。此外，粪菌移植

(FMT)的标准化、供体筛选及长期安全性仍需进一步验证。在临床转化方面,缺乏统一的疗效评价体系,且微生态药物的生产、保存及递送技术尚不成熟。未来需结合多组学技术与人工智能,推动精准化干预策略的开发。

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