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Review 综述

益生菌缓解肠易激综合征症状的研究进展

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摘　要：肠易激综合征(irritable bowel syndrome, IBS)是一种以腹痛、腹胀及排便异常为特征的功能性胃肠疾病，其发病机制涉及肠道菌群失衡、免疫激活、肠-脑轴功能障碍等多因素交互作用。传统疗法虽能短期缓解症状，但存在药物副作用、疗效持续性不足等局限性，促使微生物靶向疗法成为研究热点。益生菌是活的微生物，已被证实对人体健康有益。现有研究表明，益生菌可通过定殖竞争抑制致病菌黏附，调节免疫应答，还能借助代谢产物修复肠屏障功能，改善肠道动力与渗透压平衡。本综述探讨了益生菌对 IBS 患者便秘、腹泻、腹痛腹胀及精神症状的具体作用效果和潜在作用途径。然而，益生菌临床应用仍面临挑战，包括菌株异质性、宿主个体差异以及缺乏标准化治疗方案等。未来需结合多组学技术筛选生物标志物，开发个体化干预策略，并通过动态监测优化疗效，为 IBS 治疗提供更精准的微生物靶向疗法。

关键词：肠易激综合征；益生菌；肠道菌群；肠-脑轴

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Research progress in probiotics for alleviating irritable bowel syndrome symptoms

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Abstract: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain, abdominal distension, and abnormal bowel movements. Its pathogenesis involves multiple factors such as imbalance of gut microbiota, immune activation, and dysfunction of the gut-brain axis. Although conventional therapies can alleviate symptoms temporarily, the limitations such as drug side effects and insufficient efficacy persistence have made microbial-targeted therapy a research hotspot. Probiotics are live microorganisms and have been proven to be beneficial to human health. Studies have shown that probiotics inhibit pathogen adhesion through competitive colonization, regulate immune responses, and repair the intestinal barrier function through metabolic products, thereby improving intestinal motility and osmotic balance. This review discusses the specific effects and potential pathways of probiotics on constipation, diarrhea, abdominal pain and distension, and mental symptoms in IBS patients. However, the clinical application of probiotics still faces challenges, including strain heterogeneity, host individual differences, and the lack of standardized treatment plans. In the future, it is necessary to combine multi-omics technologies to screen biomarkers, develop individualized intervention strategies, and optimize efficacy through dynamic monitoring, which are expected to provide more precise microbial-targeted therapy for the treatment of IBS.

Keywords: irritable bowel syndrome; probiotics; gut microbiota; gut-brain axis

肠易激综合征(irritable bowel syndrome, IBS)是一种常见的功能性胃肠疾病，显著影响患者的生活质量，其主要表现为腹痛、腹胀及排便异常，因个体差异存在腹泻型、便秘型等不同亚型。益生菌作为对人体健康有益的活微生物，具有调节肠道菌群、修复肠屏障、调节免疫应答及改善肠-脑轴(gut-brain axis, GBA)功能等作用，被视为缓解 IBS 症状的潜在方案。本文综述了益生菌在改善 IBS 患者便秘、腹泻、腹痛腹胀及精神症状方面的效果，探讨了其缓解 IBS 症状的潜力，以期为该病的治疗提供新见解。

1 肠易激综合征概述

1.1 肠易激综合征的定义与临床特征

肠易激综合征是一种常见的肠-脑相互作用障碍，属于功能性肠道疾病，其复杂的临床特征和发病机制引起了医学界的广泛关注[1-2]。根据罗马 IV 诊断标准，IBS 的诊断需在反复腹痛(过去 3 个月内平均每周至少发作 1 次)的基础上，并结合以下 2 项或 2 项以上的临床症状：

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(1) 排便后腹痛或腹部不适缓解；(2) 发作时排便频率的变化以及粪便形态的改变[3]。IBS 作为功能性胃肠疾病的典型代表，其临床症状具有显著特异性。根据罗马Ⅳ诊断标准，该疾病可分为 4 种亚型：腹泻型(irritable bowel syndrome with predominant diarrhea, IBS-D)患者以反复腹泻为主要特征，粪便呈松散或水样，常伴有急迫排便感；便秘型(irritable bowel syndrome with predominant constipation, IBS-C)主要表现为排便困难、粪便干硬及排便频率减少；混合型(irritable bowel syndrome with mixed bowel habits, IBS-M)患者在同一日内可能交替出现腹泻与便秘，粪便形状差异显著；未定型(irritable bowel syndrome unclassified, IBS-U)则指患者症状波动幅度较大，但不符合上述 3 种类型的分类标准；所有类型均伴随腹痛或腹胀，且症状反复发作、病程迁延，对患者的生活质量造成显著影响[4]。流行病学数据显示，全球 IBS 患病率约 11.2%，其中亚洲地区发病率显著上升，且存在明显的性别差异，女性患病风险高于男性，这可能与雌激素对内脏敏感性的调控作用有关[5-6]。

1.2 IBS 的发病机制

在发病机制层面，IBS 已超越传统认知的单一肠道功能障碍，涉及遗传因素、部分饮食不耐受、胃肠道微生物体系失衡、肠道免疫激活、肠道通透性改变以及 GBA 功能异常等多个方面[7]。研究表明 IBS 患者的肠道菌群多样性和稳定性显著下降，患者粪便中肠杆菌科细菌数量较健康人群比例增加，而双歧杆菌等有益菌显著减少，这种失衡导致短链脂肪酸(short-chain fatty acids, SCFAs) (如乙酸、丙酸)代谢异常，与患者腹胀、腹痛等症状直接相关[8]。此外，芽孢杆菌门/拟杆菌门(*Bacillota*/*Bacteroidota*)比例异常会加剧肠道通透性改变[9]。IBS 患者的黏膜免疫系统呈现持续性低度炎症状态，肥大细胞密度、T 淋巴细胞($CD4^+$和 $CD8^+$)的数量和活性在 IBS 患者结肠黏膜中显著增加，肥大细胞释放的组胺和蛋白酶直接刺激肠道神经元，导致内脏高敏感性[10]。T 细胞的异常激活导致肠道局部的免疫反应失调，释放的细胞因子干扰素-γ (interferon-gamma, IFN-γ)、肿瘤坏死因子-α (tumor necrosis factor-alpha, TNF-α)、白细胞介素(interleukin, IL)-17 及 IL-6 失衡可能破坏肠黏膜屏障，增加肠道通透性，进而形成“代谢性肠漏”的恶性循环[11]。最新研究揭示，肠道菌群代谢产物(如吲哚丙酸)可通过迷走神经影响中枢神经系统，吲哚丙酸可激活肠道黏膜下的迷走神经传入纤维，直接抑制 γ-氨基丁酸(gamma-aminobutyric acid, GABA)能神经元活性。当 GABA 能神经元活性降低时前额叶皮质对边缘系统的抑制作用减弱，导致焦虑相关神经环路过度活跃，形成焦虑-肠道症状的恶性循环[12]。这些因素相互交织，共同造成肠道功能紊乱，引发 IBS 一系列症状。

2 益生菌与 IBS

目前，IBS 的治疗主要以缓解症状为目标。传统疗法，如解痉药(匹维溴铵)和止泻药(洛哌丁胺)虽能在短期内缓解症状，但效果通常不尽如人意，还可能导致便秘加重、药物依赖等副作用，患者满意度较低[13]。这一情况促使医学界探索多靶点干预策略，其中益生菌治疗展现出独特优势[14]。

2.1 益生菌的发展历程及在胃肠道疾病中的干预价值

益生菌是一类具有生理调节功能的活性微生物，其对健康的促进作用已成为现代微生物学和临床医学的研究重点。益生菌的发展可追溯至 19 世纪中期，1857 年巴斯德发现乳酸菌，开启了人类对益生菌的认知之旅[15]。1899 年蒂赛分离出双歧杆菌，1908 年梅契尼科夫提出“酸奶长寿”理论并被誉为“益生菌之父”[16]。1953 年“益生菌”一词首次被使用，2002 年联合国粮农组织(Food and Agriculture Organization of the United Nations, FAO) 和世界卫生组织(World Health

Organization, WHO)明确了其现代定义，即益生菌是指“当摄入足够数量时能够对宿主健康产生有益作用的活性微生物”[17-18]。经过半个多世纪的发展，全球已确认多种具有明确功能的益生菌菌株，其中乳杆菌属(*Lactobacillus*)、双歧杆菌属(*Bifidobacterium*)和芽孢杆菌属(*Bacillus*)构成了三大核心菌群[19]。益生菌在多种胃肠道疾病的干预中展现出独特的调节作用，其机制涉及肠道菌群平衡重建、代谢调控及免疫调节等多个方面[20-21]。在腹泻性疾病方面，多项随机对照试验证实益生菌干预可有效降低抗生素相关性腹泻和艰难拟梭菌(*Clostridioides difficile*)感染性腹泻的发病率[22-23]。其中，鼠李糖乳酪杆菌(*Lacticaseibacillus rhamnosus*) GG 株可有效降低儿童腹泻发病率，并减少腹泻持续时间[24]。Szajewska 等[25]的研究进一步证实，益生菌对轮状病毒性腹泻具有显著疗效。此外，植物乳植杆菌(*Lactiplantibacillus plantarum*) CCFM1143 在改善慢性腹泻患者症状方面效果显著，可显著降低排便频率并改善布里斯托尔大便评分[26]。在便秘治疗领域，益生菌显示出多方面的调节作用。临床研究显示，植物乳植杆菌 P9 能有效缓解成人慢性便秘症状，并显著改善患者生活质量[27]。最新随机对照试验(randomized controlled trial, RCT)研究(n=103)证实，两歧双歧杆菌(*Bifidobacterium bifidum*) CCFM16 可增加慢性便秘患者每周自发性排便(spontaneous bowel movements, SBM)次数并改善大便性状[28]。Koebnick 等[29]证实干酪乳酪杆菌(*Lacticaseibacillus casei*) Shirota 对便秘症状改善率达 89%，并显著提高排便频率。同时，Sabaté 等[30]发现长双歧杆菌(*Bifidobacterium longum*) 35624 在治疗期间使 IBS-U 患者的粪便性状恢复正常。另一项针对儿童便秘的研究表明，干酪乳酪杆菌 Lcr35 (8×10^8 CFU/d)治疗 4 周后排便频率明显改善且硬便减少，其疗效与氧化镁相当[31]。益生菌在腹胀腹痛相关胃肠道疾病中的作用同样得到了广泛关注。动物双歧杆菌乳亚种(*Bifidobacterium animalis* subsp. *lactis*) DN-173010 的发酵乳制品可有效缓解 IBS-C 患者的腹胀症状，并加速肠道传输；此外，该制剂还能改善肠易激综合征相关核心症状[32]。临床研究显示，嗜酸乳杆菌(*Lactobacillus acidophilus*) DDS-1 和动物双歧杆菌乳亚种 UABla-12 可显著降低腹痛严重程度[33]。植物乳植杆菌在 4 周干预后明显改善胃肠胀气症状，而唾液宿主关联乳杆菌(*Ligilactobacillus salivarius*)治疗 8 周后则显著降低腹痛频率和严重程度评分[34-35]。由此可见，益生菌在胃肠道疾病中展现出显著的调节作用和治疗效果，从理论机制和临床实践的双重角度来看，益生菌具有成为肠易激综合征(IBS)安全有效辅助治疗选择的巨大潜力(表 1)。

2.2 益生菌缓解 IBS 的作用机制

在治疗策略探索中益生菌的潜在应用价值受到持续关注。研究发现益生菌通过多种生物学机制发挥有益作用，主要包括与病原体的定殖竞争、调节机体免疫功能和产生细菌素等代谢物[44](图 1)。在定殖竞争过程中，*Lactobacillus* 和 *Bifidobacterium* 等常见益生菌通过占据肠道上皮细胞黏附位点形成生物膜屏障[45]。例如，嗜酸乳杆菌 AD125 通过其表面蛋白特异性识别肠道上皮细胞表面受体，并借助分子模拟机制与致病菌(如大肠埃希氏菌 O157:H7)竞争结合位点，从而降低致病菌的黏附率[46]。在免疫调节过程中，益生菌通过调控树突状细胞和调节性 T 细胞(regulatory T cells, Treg)的分化平衡 Th1/Th2 免疫应答，增加肠道免疫球蛋白 A (immunoglobulin A, Ig A)分泌量，降低 IL-6 等促炎因子表达[47-48]。在细菌毒素抑制方面，乳酸菌通过分泌细菌素(如 nisin)、短链脂肪酸和过氧化氢等物质发挥广谱抗菌作用，降低宿主感染风险[49-50]。典型例证包括布拉氏酵母菌(*Saccharomyces boulardii*, SB)可通过分泌 54 kDa 蛋白酶分解艰难拟梭菌毒素 A/B 的受体结合域，降低毒素活性，从而降低腹泻频率[51]。同时，研究发现除乳酸菌外，几乎所有细菌的必需营养素都含有铁，德氏乳杆菌(*Lactobacillus delbrueckii*)通过将氢氧化铁结

表1 益生菌缓解IBS症状的临床研究

Table 1 Clinical studies on probiotics alleviating IBS symptoms

Strain (dose)	Object	Intervention cycle (d)	Number of subjects	Experimental design	Effect	References
Lactiplantibacillus plantarum (5.00×10^9 CFU/g)	Adult	56	Placebo group (*n*=25) Probiotic group (*n*=25)	Randomized controlled trial	The relative abundance of butyric acid producing bacteria ↑, IBS-SSS and IBS-QOL scores ↓	[36]
Bifidobacterium longum NCC3001 (2.00×10^9 CFU/g)	Adult	42	Placebo group (*n*=22) Probiotic group (*n*=22)	Randomized controlled trial	The levels of methylamine and aromatic amino acid metabolites in the urine of patients in the probiotic group ↓	[37]
Weizmannia coagulans MTCC5856 (2.00×10^{10} CFU/g)	Adult	90	Placebo group (*n*=20) Probiotic group (*n*=20)	Randomized controlled trial	Serum myeloperoxidase content and depression score ↓	[38]
Bifidobacterium adolescentis PRL2019 (2.00×10^{10} CFU/g)	4–18 years old	84	Placebo group (*n*=36) Probiotic group (*n*=36)	Randomized controlled trial	The frequency of constipation, the intensity of abdominal pain, and the frequency of abdominal pain in children with irritable bowel syndrome with predominant constipation ↓	[39]
Lactobacillus GG (1.00×10^{10} CFU/g)	6–20 years old	42	Placebo group (*n*=25) Probiotic group (*n*=25)	Randomized controlled trial	Frequency of abdominal distension ↓	[40]
Lactobacillus acidophilus DDS-1 (1.00×10^{10} CFU/g) *Bifidobacterium animalis* subsp. *lactis* UABla-12 (1.00×10^{10} CFU/g)	Adult	42	Placebo group (*n*=107) DDS-1 group (*n*=107) UABla-12 group (*n*=105)	Randomized controlled trial	Frequency of abdominal pain ↓ Frequency of normalization of stool shape ↑	[33]
Lacticaseibacillus casei Zhang (3.00×10^9 CFU/g) *Bifidobacterium animalis* subsp. *lactis* V9 (4.00×10^9 CFU/g) *Lactiplantibacillus plantarum* P-8 (3.00×10^9 CFU/g)	Adult	28	Placebo group (*n*=21) Probiotic group (*n*=24)	Randomized controlled trial	The levels of IL-6 and TNF-α in the serum ↓ The bacterial genera associated with the deterioration of IBS, such as *Bacteroides*, *Escherichia*, and *Citrobacter* ↓	[41]

(待续)

(续表1)

Strain (dose)	Object	Intervention cycle (d)	Number of subjects	Experimental design	Effect	References
Lactobacillus paracasei (1.00×10^8 CFU/g) *Lactiplantibacillus plantarum* (4.00×10^8 CFU/g) *Ligilactobacillus salivarius* (5.00×10^8 CFU/g)	Adult	28	Placebo group (*n*=26) Probiotic group (*n*=24)	Randomized controlled trial	The abdominal pain symptoms of the patients in the probiotic group were significantly relieved	[42]
Bifidobacterium animalis subsp. *lactis* (2.94×10^9 CFU/g) *Bifidobacterium longum* (2.94×10^8 CFU/g) *Bifidobacterium bifidum* (2.94×10^8 CFU/g) *Lactobacillus rhamnosus* (9.80×10^8 CFU/g) *Lactobacillus acidophilus* (4.90×10^8 CFU/g)	Adult	56	Placebo group (*n*=33) Probiotic group (*n*=35)	Randomized controlled trial	The observation results showed that the patient's incomplete defecation, bloating, pain, fecal pressure, and diarrhea symptoms all showed significant improvement	[43]

合到其细胞表面，使其他微生物无法利用它，进而缓解 IBS 症状[52]。此外，近年来研究还揭示了益生菌对肠-脑轴的双向调节作用。Pinto-Sanchez 等[37]研究表明，益生菌通过调节神经递质水平和神经活性化合物的产生调节肠道运动和敏感性。同时，益生菌通过下丘脑-垂体-肾上腺轴降低皮质酮等应激激素水平减轻压力对肠道功能的不良影响，最终缓解 IBS 症状[53]。

2.3 益生菌缓解 IBS 典型症状

2.3.1 便秘

IBS-C 作为肠易激综合征的常见亚型，结肠动力异常是其核心病理特征，具体表现为患者结肠传输速度显著低于健康人群[37]。在改善这一病理状态的过程中，相关研究揭示了益生菌发挥作用的多方面规律，且这些规律与 5-羟色胺(5-hydroxytryptamine, 5-HT)信号系统调控、胆汁酸代谢、肠道屏障功能及菌株特性等密切相关。从 5-HT 信号系统调控来看，其是改善 IBS-C 结肠动力异常的关键突破口。肠道作为人体最大的神经内分泌器官，肠嗜铬细胞分泌的 5-HT 占全身总量的 95%，该物质兼具刺激局部肠神经反射以增强肠道分泌功能、通过迷走神经调控平滑肌收缩节律的双重作用[54]。同时，肠嗜铬细胞释放的 5-HT 存在双向调节机制，既能通过加速肠道运动减少水分重吸收，又能通过增加粪便含水量改善便秘症状，这为益生菌发挥作用提供了重要基础[55]。益生菌对 5-HT 信号系统的调控呈现出明确的菌株特异性规律。不同菌株通过不同方式调节 5-HT 水平及相关功能：植物乳植杆菌 AR495 通过抑制色氨酸羟化酶-1 的过度激活使肠嗜铬细胞密度降低 32%，从而将结肠 5-HT 水平恢复至健康对照组范围[56]；特定乳杆菌则能提升肠道 5-HT 生物利用度 1.8 倍，并增强 5-HT 转运体(serotonin transporter, SERT)表达效率[57]；长双歧杆菌 NCC3001 则通过上调 SERT 转运体表达使肠腔 5-HT 再摄取效率提高 45%，在促进肠道规律收缩的同时还能避免因过量 5-HT 产生而引发内脏高敏性[37]。这些不同菌株的作用方式虽有差异，但最终都指向对肠道动力的改善，表明益生菌在该调控过程中方式多样且目标统一的特性。在胆汁酸代谢层面，存在益生菌可能通过间接路径影响肠道动力的规律。研究发现便秘患者存在特异性胆汁酸合

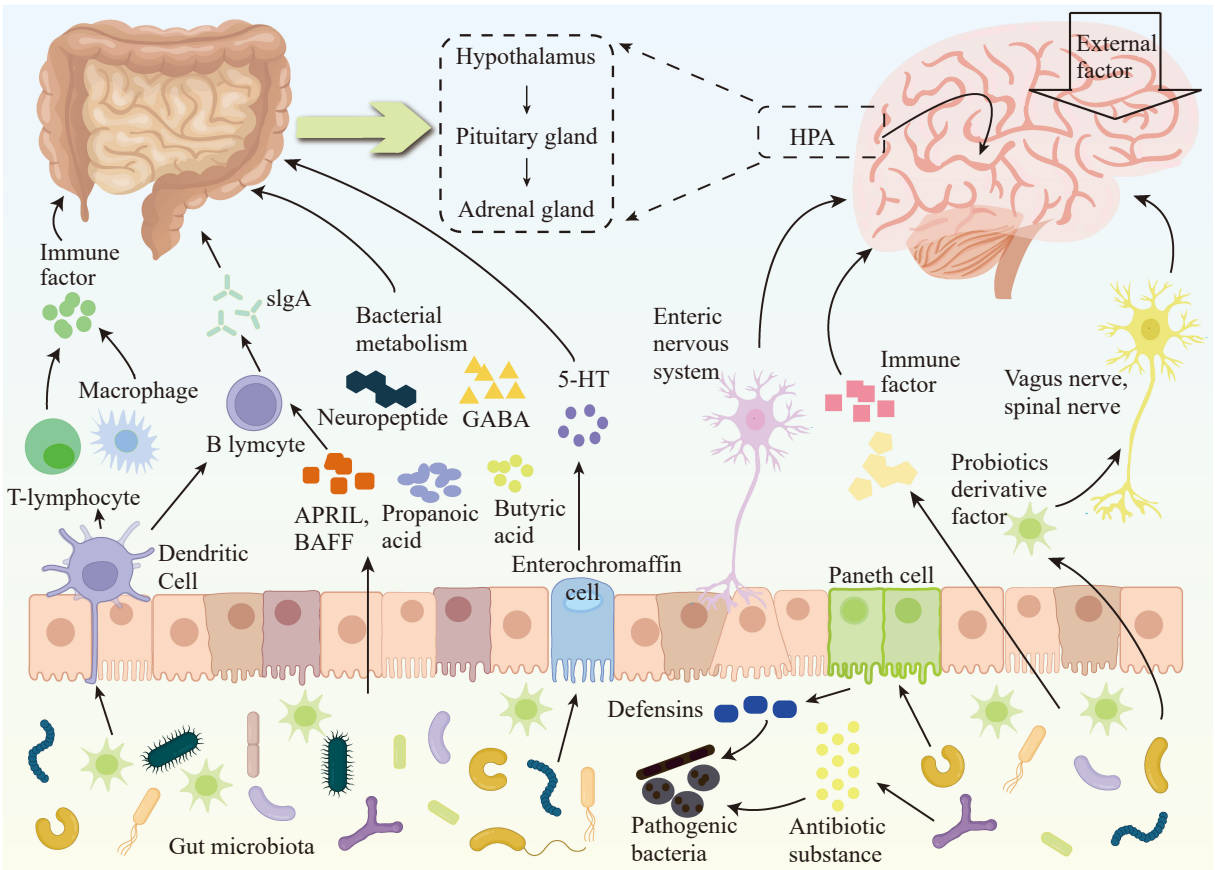

图1 益生菌改善IBS的机制。HPA：下丘脑-垂体-肾上腺轴；APRIL：增殖诱导配体；BAFF：B淋巴细胞活化因子。

Figure 1 Mechanism of probiotics in improving IBS. HPA: Hypothalamic-pituitary-adrenal; APRIL: A proliferation-inducing ligand; BAFF: B-cell activating factor of the TNF family.

成障碍[58]，而临床试验已证实，鹅去氧胆酸及回肠胆汁酸转运抑制剂能通过激活 Takeda G-protein-coupled receptor 5 (TGR5)受体及协同释放 5-HT、降钙素基因相关肽等机制，有效缩短肠道转运时间[59-60]。益生菌对肠道屏障功能的修复也呈现出一定规律，既存在共性的作用方向，又因菌株不同而效果有差异。其共性作用主要围绕抑制促炎因子、保护紧密连接蛋白结构及调控黏蛋白产生等方面：动物双歧杆菌乳亚种 TY-S01 可显著抑制 TNF-α、IL-6 等促炎因子表达，从而有效保护紧密连接蛋白结构，防止肠道屏障破坏[61]；丁酸梭菌则通过增加丁酸分泌，不仅使 IBS-C 患者的结肠转运时间缩短 12 h，还能显著提高肠屏障功能标志物紧密连接蛋白(zonula occludens-1, ZO-1)的含量[62]。在黏蛋白调控上，不同菌株的作用差异明显，VSL#3 能通过上调 MUC2 基因诱导结肠黏蛋白产生，乳杆菌在发挥黏蛋白分泌作用方面与 VSL#3 效果相当，而双歧杆菌和唾液链球菌的作用则最小[63]。临床研究结果进一步证实了益生菌疗效具有显著菌株特异性的规律。含乳杆菌和双歧杆菌的复合益生菌制剂可通过增加肠道中 SCFAs 的浓度，显著改善 IBS-C 患者的排便频率和粪便稠度[64]。具体到单一菌株，类干酪乳杆菌 (*Lactobacillus paracasei*) HA-196 在增加 IBS-C 患者的自发排便和自发完全排便次数方面

比长双歧杆菌 R0175 更为有效[65]。因此，益生菌可能为 IBS-C 患者提供一种综合的治疗策略。

2.3.2 腹泻

在肠易激综合征腹泻型(IBS-D)的病理机制中毒素作用与代谢异常是两大关键环节。毒素作用的致病规律方面，艰难拟梭菌感染是重要诱因[64]，其定殖后分泌的 TcdA 与 TcdB 毒素存在协同致病特点。具体而言，TcdA 通过抑制 Wnt 信号通路阻碍 β-catenin 向细胞核转移，进而影响细胞增殖相关基因的表达；TcdB 则通过与卷曲同源物(frizzled homolog, FZD)受体及硫酸软骨素蛋白聚糖 4 (chondroitin sulfate proteoglycan 4, CSPG4)蛋白结合，直接造成肠道黏膜组织损伤；二者的协同作用会显著提升肠屏障通透性，引发肠道分泌功能异常，最终导致分泌性腹泻的表型[66-67]。针对这一机制，益生菌的干预呈现靶向毒素的规律。克劳斯氏嗜碱盐芽孢杆菌(*Alkalihalobacillus clausii*) O/C 可通过分泌碱性丝氨酸 M-蛋白酶及细菌素 clausin，降低艰难拟梭菌毒素的细胞毒性[68]。LGG 的作用具有双重性，一方面在临床中对 32 例参与者干预 2 个月后，84% 实现临床痊愈且所有患者症状均有改善，显示出对艰难拟梭菌相关性腹泻的根治潜力[69]；另一方面还能诱导肠上皮细胞合成热休克蛋白，增强细胞应激保护能力[70]。SB 的干预则体现“中和毒素+修复屏障”的协同性，其构建的四聚体特异性抗体可高效中和 TcdA 与 TcdB，在动物模型中能阻断毒素与宿主细胞结合、抑制酶活性并标记毒素供免疫系统清除[71]；其 CNCM I-745 菌株还可通过 Rab11A 依赖性途径促进内吞的 E-钙黏蛋白向细胞质膜传递，从结构层面恢复肠道屏障功能以减少腹泻发作[72]。代谢异常的致病规律主要体现在 2 方面：(1) SCFAs 异常，不仅会激活黏膜免疫反应，还能通过改变肠道渗透压及神经信号传导加剧腹泻症状[73]；(2) 产乳酸菌代谢缺陷，IBS-D 患者肠道内产乳酸菌(如乳杆菌)丰度显著降低，导致乳酸合成不足，这会削弱肠道防御屏障，增加肠腔渗透负荷，形成恶性循环[74]。干酪乳酪杆菌可有效抑制志贺氏菌诱导的核因子 κB (nuclear factor kappa-B, NF-κB)信号通路活化，显著降低促炎因子、趋化因子和黏附分子的表达水平[75]。在临床转化中植物乳植杆菌 CCFM8610 表现出多效性，为期 12 周的随机双盲安慰剂对照实验显示，其可降低肠易激综合征病情严重程度量表(irritable bowel syndrome severity scoring system, IBS-SSS)总分、提高肠易激综合生活质量量表(irritable bowel syndrome quality of life, IBS-QOL)总分，还能特异性富集产丁酸菌群，其代谢产物丁酸盐通过激活 GPR109A 及抑制蛋白激酶 B (protein kinase B, PKB)和 NF-κB p65 信号通路改善肠上皮屏障功能障碍[36,76]。综上所述，益生菌通过靶向相应环节实现干预，为 IBS-D 治疗提供了相对完整的机制解释与临床依据。

2.3.3 腹痛和腹胀

在 IBS 患者中腹痛和腹胀是常见症状。研究揭示，肠道菌群及其代谢产物与腹痛、腹胀等症状密切相关。结肠细菌发酵未消化物质产生肠道气体，而肠道菌群失衡会加剧腹胀，如产气能力较强的肠杆菌科和梭状芽孢杆菌过度增殖可加重病症，这提示调节肠道微生物是缓解气体相关症状的关键[77-78]。多项研究表明，部分益生菌作用存在亚型特异性或广谱性，酿酒酵母 I-3856 仅在 IBS-C 亚组中显著降低腹胀评分，长双歧杆菌婴儿亚种(*Bifidobacterium longum* subsp. *infantis*) 35624 则对各类 IBS 亚型的腹胀、胀气等均有疗效，且双歧杆菌能通过调节免疫(增加 Treg 比例、降低 IL-6 和 TNF-α 表达、促进 IL-10 分泌)来调节肠道菌群，缓解整体症状及改善生活质量[79]。在腹痛调节上，益生菌可通过信号通路与代谢途径发挥作用。嗜酸乳杆菌 NCFM 与上皮细胞接触时经 NF-κB 途径诱导 Mu 阿片受体(Mu opioid receptors, MOR) 1 和 CB2 表达以调节内脏痛觉感知[80]；植物乳植杆菌 CCFM8610 能通过调节菌群(降低甲烷短杆菌丰度、提高产丁酸菌属比例)及代谢

产物(丁酸上调 GPR43 表达影响神经功能)缓解腹胀和腹痛[36,81]。此外，饮食与益生菌联用存在协同效果，低可发酵的低聚糖、双糖、单糖和多元醇(fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, FODMAP)饮食结合益生菌可增加双歧杆菌丰度，减少肠道发酵气体及不适感，降低 IBS-SSS 总分以缓解症状[82]。益生菌代谢产物也有积极作用，如热处理的长双歧杆菌 CECT 7347 可缓解腹痛、改善焦虑及生活质量[83]；Sinn 等[84-85]在随机对照试验中发现，给予 2×10^9 CFU/d 嗜酸乳杆菌-sdc 2012、2013 时能缓解腹痛，而在 LAB4 联合研究中益生菌组疼痛天数显著减少。菌株选择上，单一与复合制剂效果存在差异。单一益生菌[如凝结魏茨曼氏菌(*Weizmannia coagulans*) MTCC 5856、双歧杆菌 MIMBb75]可有效缓解 IBS 症状[86]。复合益生菌(如含鼠李糖乳酪杆菌 NCIMB 30174 的 Symprove)连续服用 12 周后可显著降低腹痛严重程度评分及 IBS-SSS 总分。同时，复合益生菌在改善生活质量、腹胀和腹痛方面均优于单一菌株[87]。需注意的是，并非所有益生菌均对腹胀患者有缓解作用[35,88]。研究显示，与安慰剂相比，LGG 对以腹部张力下降为主诉的 IBS 患者无效果[77]。长双歧杆菌婴儿亚种比唾液宿主关联乳杆菌在减轻腹痛方面更有效[35]。同样地，植物乳植杆菌与燕麦汤联用方案也未改善腹胀症状[34]。

2.3.4 益生菌缓解 IBS 精神症状

肠道与大脑的关联是 IBS 发病与干预的重要视角，相关理论为其提供了生物学依据，该理论通过内分泌、神经和免疫三大通路实现肠道与中枢神经系统的双向交流，而 IBS 作为典型脑-肠互动疾病，其临床特征与之相印证[89]。IBS 患者常存在“肠-脑互扰”的情况，约 1/3 的患者伴随焦虑或抑郁症状，这些精神类疾病不仅影响生活质量，还会形成恶性循环[90]。从脑功能层面看，IBS 患者前额叶皮层(prefrontal cortex, PFC)中 GABA 浓度与焦虑程度呈正相关，且 PFC 与前扣带回皮质(anterior cingulate cortex, ACC)的功能连接显著减弱，ACC 作为情绪调节中枢，其功能异常可能是患者出现精神症状的重要机制[91]。在益生菌干预方面，迷走神经是重要调节通路。鼠李糖乳酪杆菌 JB-1 可通过降低 PFC 中 GABA mRNA 的表达，调节迷走神经以缓解焦虑症状[92]；将抑郁模型动物的菌群移植至健康小鼠，会诱发膈下迷走神经的脑-肠-微生物群轴失调性激活，而益生菌干预能逆转该效应[93]。抑制炎症因子与菌群调节也是干预的重要途径。联合使用长双歧杆菌 35642®和长双歧杆菌 1714®可恢复皮质醇反应，改善 IL-6、CRP 和 TNF-α 等炎症因子水平，进而改善 IBS 症状并降低抑郁评分[94]；鼠李糖乳酪杆菌 Probio-M9 能调节压力大成人肠道菌群的稳定性，影响相关有益代谢物，从而改善其心理和生理生活质量[95]；gQlab 多菌株益生菌可改善 IBS-M 患者的 IBS-QOL 评分，能缓解烦躁不安情绪、减轻对自身健康的担忧，还对改善人际关系有显著效果[96]。然而，益生菌的情绪调节作用存在争议。Asad 等[97]通过 20 项试验的荟萃分析发现，益生菌缓解焦虑症状的效果优于抑郁症状。含瑞士乳杆菌(*Lactobacillus helveticus*)和长双歧杆菌的复合制剂干预 8 周后，患者的抑郁、焦虑自评量表得分无显著改善[98]。接受干酪乳酪杆菌或菊粉治疗的大鼠，在血浆皮质酮水平测量中表现出更高水平的焦虑行为和压力[99]。

3 益生菌缓解 IBS 的挑战和未来方向

尽管益生菌在改善 IBS 症状方面展现出潜力，但其临床应用仍面临多重挑战。首先，益生菌的疗效具有显著的菌株特异性。不同菌株的代谢活性、免疫调节能力及宿主互作机制差异巨大，导致研究结果难以统一。此外，IBS 患者的高度异质性进一步制约疗效。肠道菌群组成、遗传背景(如胆汁酸代谢相关基因多态性)、

环境暴露(如饮食模式)及精神心理状态的差异，使得同一种益生菌在不同个体中可能产生截然不同的效果。同时，现有研究在菌株组合、剂量及疗程设计上缺乏标准化，导致不同临床试验的结论难以横向比较。

未来研究需向精准化与个体化治疗方向突破，开展大规模、多中心随机对照试验，明确不同菌株的适应规律及长期安全性。同时，需关注益生菌对 IBS 精神共病(如焦虑、抑郁)的调节机制，揭示菌群代谢产物(如丁酸、γ-氨基丁酸)通过肠-脑轴影响中枢神经系统的具体路径，推动益生菌从“广谱干预”迈向“精准治疗”，最终为 IBS 患者提供更高效、个性化的解决方案。

作者贡献声明

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