基于“肠-肺轴”理论探讨培土生金法治疗慢性阻塞性肺疾病的科学内涵

黄浩轩[1,2], 李亚[1,2], 韩昕岐[3], 刘往[3], 张海龙[1,2,4*]

(1. 河南中医药大学 第一附属医院 国家区域中医(肺病)诊疗中心, 河南 郑州 450003;
2. 河南中医药大学 第一临床医学院, 河南 郑州 450003;
3. 河南中医药大学 中医学院(仲景学院), 河南 郑州 450046;
4. 河南中医药大学 呼吸疾病中医药防治省部共建协同创新中心, 河南 郑州 450046)

[摘要] 慢性阻塞性肺疾病(COPD)是以持续性气流受限为特征,易发恶化加重的异质性肺部疾病。近年研究揭示,肠道菌群失调可引发代谢紊乱、免疫异常及炎症反应,并通过“肠-肺轴”机制参与 COPD 的发生发展。“培土生金”法源于中医五行学说“虚则补其母”的治疗原则,通过增强脾胃(属土)功能以间接滋养肺脏(属金),体现脏腑相生的整体观。肠道作为脾胃运化的延伸,其微生态稳态实为“脾主运化”功能的现代体现。脾虚时肠道菌群失衡,浊毒内生上熏于肺,致正气不运,痰瘀互结。“培土”之义不仅在于补益中气,更涵盖胃肠功能改善、肠道菌群调控等多维度干预,恢复肺脾协调。“培土生金”治法可影响 COPD 患者消化系统微生物群,有效截断“脾虚-菌乱-肺损”的病理恶性循环,延缓疾病进展,减少急性加重。该法既彰显了中医整体思维的科学价值,也为 COPD 的中西医结合防治提供了重要路径,凸显“培土生金”在临床实践中的核心意义。

[关键词] 慢性阻塞性肺疾病; 培土生金; 肠道菌群; 肠道微生态

Scientific connotation of spleen-tonifying and lung-replenishing therapy in chronic obstructive pulmonary disease based on "gut-lung axis" theory

HUANG Hao-xuan[1,2], LI Ya[1,2], HAN Xin-qi[3], LIU Wang[3], ZHANG Hai-long[1,2,4*]

(1. *National Regional Chinese Medicine (Lung Disease) Diagnostic and Treatment Centre, the First Affiliated Hospital of Henan University of Chinese Medicine, Zhengzhou* 450003, *China*; 2. *the First Clinical Medical School of Henan University of Chinese Medicine, Zhengzhou* 450003, *China*; 3. *Traditional Chinese Medicine School (Zhong Jing School), Henan University of Chinese Medicine, Zhengzhou* 450046, *China*; 4. *Collaborative Innovation Center for Chinese Medicine and Respiratory Diseases Co-constructed by Henan Province & Ministry of Education, Henan University of Chinese Medicine, Zhengzhou* 450046, *China*)

[**Abstract**] Chronic obstructive pulmonary disease (COPD) characterized by persistent airflow limitation is a heterogeneous lung condition prone to exacerbations and progression. Recent studies have revealed that gut microbiota dysbiosis can trigger metabolic disorders, immune abnormalities, and inflammatory responses, contributing to the pathogenesis and progression of COPD through the gut-lung axis. The spleen-tonifying and lung-replenishing therapy originates from the five elements theory of TCM, specifically the principle of tonifying the source in the case of deficiency. Enhancing the function of the spleen and stomach (earth element) indirectly nourishes the lungs (metal element), embodying the holistic concept of organ interdependence. The gut, as an extension of the transformation function of the spleen and stomach, reflects the modern interpretation of the spleen′s role in transformation and

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[通信作者] *张海龙, 教授, 博士生导师, 研究方向为中医药防治呼吸疾病研究, E-mail: zhanghailong6@126.com

[作者简介] 黄浩轩, 硕士研究生, E-mail:15188350317@163.com

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transportation. When the spleen is deficient, gut microbiota dysbiosis leads to the accumulation of turbid toxins, which rise to affect the lungs, resulting in impaired flow of healthy Qi and the interplay of phlegm and stasis. The concept of tonifying the spleen not only involves tonifying the middle Qi but also encompasses multidimensional interventions such as improving gastrointestinal functions and regulating the gut microbiota to restore lung-spleen coordination. The spleen-tonifying and lung-replenishing therapy can influence the gut microbiota in COPD patients, effectively interrupting the pathological vicious cycle of spleen deficiency-microbiota dysbiosis-lung damage, slowing down disease progression, and reducing acute exacerbations. This method highlights the scientific value of the holistic thinking in TCM and provides a key pathway for integrating TCM and Western medicine in the prevention and treatment of COPD, underscoring the core clinical significance of tonifying the spleen and replenishing the lung.

[**Key words**] chronic obstructive pulmonary disease; tonifying the spleen and replenishing the lung; gut microbiota; gut microecosystem

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慢性阻塞性肺疾病(COPD)是一种以进行性气流阻塞为特征的异质性肺部疾病[1]。2019 年全球疾病负担研究显示,其患病率持续上升,已成为重要的公共卫生问题[2]。肠道菌群作为人体内庞大的微生物群落,与宿主维持着共生平衡,其稳态失衡与 COPD 发生发展及急性发作密切相关[3]。此外,COPD 患者普遍存在营养不良风险,而营养状态与肠道菌群组成及功能相互影响,形成复杂关联[4]。营养不良可加剧肠道菌群失衡和全身炎症,进一步损害呼吸功能与免疫力,形成恶性循环[5]。

中医学虽然没有直接提出“肠道微生态”这个概念,但其对人体与自然、脏腑与脏腑之间联系的整体性认识,以及对病机发生发展规律的洞察,都与现代肠道微生态研究存在高度的契合[6]。本文旨在通过分析脾胃运化功能、肠道微生态及 COPD 的关联性,剖析脾胃在人体水谷精微运化与能量转化中的核心枢纽作用,进而揭示“培土生金”这一中医治法干预 COPD 的现代科学内涵,以期为中医药防治该病,尤其是融合肠道菌群调控策略,提供现代生物学理论支撑。

1 培土生金法与肠道微生态的联系

在中医五行生克理论中,肺属金,脾属土,土能生金,故脾为肺之母,二者属母子相生之关系[7]。人体宗气的生成,赖于肺脾两脏协同:肺主呼吸,摄纳自然之清气;脾主运化,转输水谷之精微。清气与谷气在胸中相合而成宗气。正如《素问·经脉别论》所言:“食气入胃,浊气归心,淫精于脉。脉气流经,经气归于肺,肺朝百脉,输精于皮毛。”肺依脾土之上供而得以宣发精微、主持治节;脾借肺金之肃降而实现精微布散、灌溉四旁,因而有“脾为生气之源,肺为主气之枢”之论,肺气盛衰,实取决于脾气强弱。若肺病日久,兼见脾虚土弱,母病及子,则当以“培土生金”为治,补益中气,充实后天,使肺气得养。

溯及“脾与小肠相通”之论,早在《素问·六节藏象论》中“脾胃大小肠三焦膀胱者,仓廪之本,营之居也,……通于土气”便已将脾、胃、大小肠统归于“土”系,共司水谷受纳、精微化生与输布之职,体现了脾与肠的密切联系。明代李梴于《医学入门》明确提出“脾病宜泻小肠火,小肠病宜润脾土”,从病理互治角度阐明二者关系[8]。到清代,唐容川更以“膜网-微丝管”理论来阐释脏腑相通的形质基础[9]。脾主运化、散精微,为气血生化之源;小肠受盛化物、泌别清浊,为精微生成与传导之关键。二者协同,完成水谷消化、吸收与输布。若脾虚失运,清气不升,浊阴不降,则小肠受盛与泌别清浊功能受阻,可致水谷不化、湿浊内停,发为腹胀、泄泻、纳差等症。因此健脾益气以恢复小肠功能是“培土”的重要延伸,“培土”已涵括对肠腑功能之调燮。

小肠为“受盛之官”,其气机宜通、内境宜清,方能行使其正常生理活动。若脾虚湿困,食滞内停,浊邪蕴结肠腑,阻滞气机,清阳不升,则肠失其“藏清气”之能,这与现代医学所言肠道菌群失衡、内环境紊乱之理相贯通。中医之“脾”为一功能系统,主司消化、吸收、输布及气血生化,涵盖多系统生理活动。肠道微生态的平衡与否体现了脾是否健运,若菌群和调则为脾旺之征,菌群紊乱即为脾失健运之象。因此,“培土”不仅在于健脾气,更在于其调肠腑、化浊邪、复清肃,使肠境洁宁,如膏壤得润,有益微生物得以繁育,邪浊无以滋生。由此可见,脾之功能与肠道微生态密切相关,肠道微生态健康与肠道功能的正常运作是“脾主运化”的重要体现。

2 肠道微生态与肺脾的关系

2.1 肠道菌群与肺的关系

人体呼吸道微生物群和肠道微生物群是一个互作共生的微生态系统[10],二者共同参与人体生理及病理调控的互作通路,被称为“肠-肺轴”[11]。肠道微生物种类丰富,包含以拟杆菌门 Bacteroidetes、厚壁菌门 Firmicutes 在内的 150 种不同的细菌物种[12-13]。相比之下,呼吸道中微生物因环境原因个体差异较大,总体数量少于肠道微生物,二者在物种组成上有所不同,但在菌门分类水平上具有相似性[14]。

肠道菌群可影响免疫球蛋白 A(sIgA)的生成以调节免疫功能[15],也可通过代谢膳食纤维产生短链脂肪酸(SCFAs)等活性物质改善肺部炎症反应[16]。反之,肺部感染也会影响肠道微生物丰度、加剧肠道菌群失衡[17]。在一项动物实验中发现,通过小鼠模型结合多个菌门的共生菌定植实验,无论是在肠道还是上呼吸道中的细菌,只要能激活 Nod 受

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体,均可通过 IL-17A/GM-CSF 信号轴增强肺部的免疫防御[18]。上述研究揭示了肺部与肠道微生物群微环境变化的相关性及同步性,为“肺-肠轴”关联的潜在物质基础提供了证据。

2.2 肠道菌群与脾的关系

中医“脾”的功能与肠道菌群在消化吸收、能量代谢和免疫防御等方面高度契合。研究发现,脾虚证模型大鼠的肠道微生物丰度存在厚壁菌门及拟杆菌门失衡,拟杆菌门和纤维杆菌门 Fibrobacteres 的相对丰度降低等异常,并伴有线粒体功能障碍[19]。另有研究表明,作为反映肠道菌群稳态重要指标的双歧杆菌 Bifidobacterium 与大肠埃希菌 *Escherichia coli* 比值(B/E)及厚壁菌门与拟杆菌门的比值(F/B)失衡是脾虚患者肠道菌群改变的特征性规律[20]。

肠道微生态平衡在人体营养代谢方面发挥重要作用,并与脾胃受纳水谷、转运并输布精微物质的“脾主运化”特性高度契合。肠道菌群失衡可导致短链脂肪酸、胆汁酸等代谢物失调,破坏肠道共生菌群的免疫稳态,进而引发代谢紊乱[21-22]。肠道菌群失衡可诱发线粒体功能受损及肌肉萎缩,其对骨骼肌质量的影响与“脾主肌肉”的内涵相符[23]。研究显示,肠道菌群失衡是 COPD 患者肌肉衰减综合征的潜在诱因之一[24]。肠道菌群作为“后天精微”的转化者,其菌群稳态可直接影响脾胃运化精微滋养肌肉四肢的效能。

脾的生理功能与思虑意念相关,肠道菌群调节神经递质是“脾在志为思”理论的重要体现。研究显示,约 24.6% 的 COPD 患者并发抑郁症[25],且肠道微生态平衡与抑郁症具有潜在关联[26]。多项实验表明,肠道菌群可通过“脑-肠轴”调控胆碱代谢以减少肠道神经递质和代谢产物对大脑的负面影响,从而改善情绪状态[27-30]。因此“脾在志为思”与“脑-肠轴”理论对于防治 COPD 相关情志共病具有重要价值。

3 从肠道菌群失调认识 COPD 的发病机制

3.1 肠道菌群失调是 COPD 的重要表现

肠道属于中医“藏象”理论中广义脾胃系统范畴。肠道菌群失调是“百病由生”的重要原因[31]。肠道菌群与肺可通过“肠-肺轴”实现双向调控而相互作用[32]。

健康人群肠道内,拟杆菌门是丰度最高的门类,其次是厚壁菌门 Firmicutes[33]。COPD 患者肠道菌群的组成和多样性常发生失衡,且菌群失衡程度与疾病的进展速度和严重程度密切相关[34-36]。无论在急性加重期或稳定期,COPD 患者肠道中变形菌门 Proteobacteria 丰度均显著增加[37],并与乳酸杆菌属 *Lactobacillus* 数量呈负相关[38]。这种菌群失衡进一步加剧 COPD 患者体内的炎症反应和氧化应激状态[39-40]。此外,肠道菌群变化与 COPD 急性加重的风险相关,如普雷沃菌 *Prevotellaceae* 和肠球菌 *Enterococcus* 等菌属的变化常提示急性加重的发生[41]。一项双样本孟德尔随机化和全基因组关联研究证实,毛螺旋菌 NK4A136 群 Lachnospiraceae_NK4A136_group 丰度增加可降低急性加重风险,而梭状芽孢杆菌 1 组群 Clostridium 丰度增加则与急性加重风险升高相关[42]。来自芬兰的队列研究发现,肠道微生物群对 COPD 的患病具有预测能力,即患者在出现疾病症状前肠道微生物群就已经发生改变[43]。吸烟作为 COPD 的最主要诱因之一,其与肠道微生物群的关联已得到充分证实。烟雾中有害物质可抑制自然杀伤细胞活性,同时可溶性烟雾成分可引起胃肠黏膜损伤和溃疡修复延迟,进而导致肺-肠轴微生态失调及病原菌过度定植[44-45]。益生菌灌胃干预可显著调控 COPD 大鼠肠道内乳酸杆菌、双歧杆菌、肠球菌及肠杆菌含量[46],并改善大鼠气道高反应性、缓解气道重塑[47]。上述研究进一步证实肠道菌群失调与 COPD 病理过程的密切关联。

3.2 肠道屏障受损是 COPD 进展的诱因之一

肠道菌群广泛参与肠道屏障的构成,具有维持肠道屏障的稳定性、保护肠道屏障等作用,可有效防止病原体及毒素从肠道渗透入血引发炎症和免疫反应[48-50],并竞争性抑制病原菌的黏附,减少有害菌的定植[51]。当肠道菌群失调时,肠道屏障的功能可能受损诱发“肠漏”[52]。研究表明,肠道菌群可通过改变紧密连接蛋白(TJ)的表达和分布以改变肠道屏障功能,例如在幼年大鼠体内定植老年大鼠的肠道菌群后,发现幼年鼠的肠道通透性对应增加,佐证肠道菌群可通过改变 TJ 的表达和分布以改变肠道屏障功能[53]。

肠道屏障的完整性对于防止有害物质进入体内至关重要[54]。炎症是 COPD 患者病情恶化的关键诱因,当炎症产生的分泌物或渗出物阻塞小气道,影响肺通气和换气功能时,血液中气体分压升高,诱发肠道积气,进而导致肠道功能紊乱。若炎症持续存在,肠道与血液中升高的气压促使积气向压力较低的部位弥散,侵入疏松的黏膜下层形成气泡,甚至引发局部黏膜脱落形成溃疡,进一步加重肺通气和换气障碍,加剧肺部病情进展[55]。此外,肠道免疫系统受损时,肠道黏膜中的淋巴细胞可迁移至肺部,引发肺黏膜免疫应答[56]。当肠黏膜屏障完整性受损时,拟杆菌和肠杆菌等致病菌可通过通透性增加的肠道进入循环系统并到达肺部,诱导促炎因子 TNF-α 和 IL-6 等释放,加剧 COPD 的进一步发生发展[57]。

3.3 肠道微生态失衡是 COPD 急性加重的潜在机制

微生物失调是 COPD 加重的关键因素[58-59]。AECOPD 是由“肠-肺轴”紊乱造成微生物多样性降低、菌群组成改变、代谢产物紊乱、促炎性细胞因子生成增加和免疫应答功能障碍等多种因素共同作用的结果[60]。肠道菌群能够促进小肠及结肠中免疫细胞的诱导、抑制和迁移[61]。如双歧杆菌可调控 T 细胞的极化,促进 Th1 和调节性 T 细胞(Treg)的生成,抑制 Th2 和 Th17 介导的炎症反应,对维持免疫稳态具有重要意义[62]。而普雷沃菌、分节丝状菌(SFB)则是 Th17 发育、活化的重要影响因素,前者主要通过刺激骨髓来源树突状细胞上的 TLR2 发出信号,诱导 Th17 极化细胞因子的产生[63-64],后者则是通过黏附增强和主动内化的双重机制介导

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细菌-上皮相互作用,最终驱动 Th17 介导的免疫反应[65]。脆弱拟杆菌 *Bacteroides fragilis*、梭状芽孢杆菌等也参与诱导 Treg 形成的过程[66]。Th1 分泌 TNF-α 及 IL-12 等促炎因子参与 AECOPD 的发生,Th17 和 Treg 则是连接肠道菌群和胃肠道免疫功能的关键细胞亚群,Th17 作为肠道免疫屏障的重要组成部分,可分泌炎症因子诱导肠道上皮细胞产生紧密连接蛋白及抗菌肽以维持肠道屏障的完整性,从而参与炎症反应[67]。Th17/Treg 分化失衡会加剧免疫炎症反应[68]。因此,调节免疫是肠道菌群参与 COPD 急性加重的重要机制。

4 培土生金法介导肠道微生态调控 COPD 的机制与应用

肠道微生物在调节宿主生理过程和药物代谢中发挥重要作用[69]。肠道微生物群落作为中医脾胃系统的外延体现,其生态稳态特征与中医理论所强调的整体协调及阴阳动态平衡理念高度契合。因此,通过调控肠道菌群微生态以恢复其功能平衡为培土生金法在 COPD 的治疗中提供了创新性的理论依据。

4.1 肠道菌群作用于 COPD 的机制

COPD 是由慢性炎症和结构变化驱动,其急性加重由细菌或病毒感染或非感染性因素引起,炎症和损伤等恶性循环可加速肺部衰老并促进肺部炎症。炎症刺激促使 $CD4^+$T 细胞分化为 Th1 或 Th2 细胞。Th1 主导细胞免疫,Th2 主导体液免疫。COPD 稳定期以 Th1 活跃为主,AECOPD 则偏向 Th2 反应,Th2 细胞介导的炎症反应与气道高反应性相关[70]。因此调节免疫系统中 Th1/Th2 细胞的平衡,可缓解 AECOPD 症状。Treg 是免疫系统中的一种重要细胞类型,能抑制其他免疫细胞的活化和炎症反应的发生[71]。肠道菌群可通过调节 T 细胞亚群产生抗炎性代谢产物,从而调节全身和局部的免疫反应进而起到治疗 COPD 的作用[72]。临床研究也表明益生菌干预可重塑肺病患者的肠道微生物群,减轻炎症损伤[73],乳酸杆菌可通过黏附竞争和免疫调节方式降低卡他莫拉菌在气道上皮细胞的黏附和相关炎性因子的表达程度,减轻炎症反应[74]。

脂多糖(LPS)是革兰阴性菌外膜的重要组成部分,通过激活 Toll 样受体 4(TLR4)引发免疫反应[75]。TLR4 是一种模式识别受体,在先天免疫中发挥关键作用[76]。当 LPS 与 TLR4 结合时,会激活细胞内的信号通路,如髓样分化因子 88(MyD88)和核因子-κB(NF-κB)通路,导致促炎细胞因子和趋化因子的产生,从而引发炎症反应[77]。六酰化 LPS(P-LPS)作为一种促炎性脂多糖,能够有效地激活 TLR4,从而促进炎症反应的发生。然而,并非所有 LPS 都是促炎的,五酰化和四酰化 LPS(A-LPS)作为抗炎性脂多糖,可以通过竞争性地抑制 P-LPS 的活性来减弱炎症反应[76]。肠道菌群在 LPS 的产生和修饰中起着关键作用[78],A-LPS 竞争性抑制 P-LPS 活性可能是调节肠道菌群改善 COPD 炎症反应的潜在机制之一。

4.2 培土生金法调节肠道菌群的具体应用

4.2.1 改善脾胃功能并维持免疫稳态 营养不良在 COPD 患者中普遍存在[79],欧洲呼吸学会(ERS)将营养评估和饮食干预作为 COPD 患者综合管理的基本组成部分[80]。营养摄入是影响肠道微生物群的关键因素,合理调节饮食结构可改善肠道微生物状态并影响宿主健康[81]。培土生金类中药可通过增强脾胃运化功能,从而提高 COPD 患者的营养吸收效率[82]。针对 AECOPD 患者的一项研究发现,营养不良组的肠道菌群相较于营养良好组患者存在明显差异,厚壁菌门、放线菌门的丰度在营养不良组丰度较高,而梭杆菌门、疣微菌门、互养菌门、蓝藻菌门的丰度则较低[83]。人参、黄芪、白术等培土生金类单味中药可促进肠道乳酸杆菌的增殖[84-86]。乳酸杆菌代谢益生元产生的乳酸和丁酸能通过 G 蛋白结合受体 GPR41 和 GPR43 的途径促进肠细胞和结肠上皮细胞的生长,从而增加营养物质吸收的表面积,进而有效促进营养吸收[87]。瘤胃球菌是参与人体营养代谢的重要细菌,能降解碳水化合物,并分泌降解纤维物质帮助细胞吸收糖分,为宿主提供营养物质[88]。玉屏风颗粒可显著上调 COPD 模型大鼠瘤胃球菌丰度,提高其营养吸收效率[89]。临床研究也表明补脾类方药可以增强胃肠蠕动,改善消化吸收功能,提高患者的营养摄入[90]。

菌群失衡会引发免疫反应失常,降低其对病原体的敏感性[91]。胃肠道微生物群经“肠-肺轴”与呼吸道微生物群密切关联,并通过代谢产物的吸收、协调免疫反应以对抗机体的免疫紊乱现象,影响呼吸系统疾病的发展。培土生金复方可修复损伤的肠黏膜,防止细菌继发性易位以维持免疫稳态,如发酵的玉屏风多糖能够增加菌群多样性和纤维分解细菌的丰度,降低肠球菌和链球菌的丰度,并通过上调空肠和回肠中的细胞连接蛋白、膜蛋白的水平,促进表皮生长因子 mRNA 的表达,从而保护肠黏膜免疫屏障[92-93]。参苓白术散在改善 COPD 模型大鼠的营养状态和免疫功能、缓解呼吸肌疲劳等方面也效果显著,可有效阻止 COPD 的病理进展[94]。升阳益胃汤在降低 IL-6 及 RORγt mRNA 表达、升高 IL-10 及 Foxp3 mRNA 表达方面呈剂量依赖性,可通过调节 Th17/Treg 平衡来综合改善 COPD 肺脾气虚证大鼠呼吸道及肠道炎性损伤[95]。

4.2.2 维持肠道微生态稳定并降低炎症水平 肠道微生态稳定性表现是指肠道菌群的多样性维持、有益菌占比平衡、代谢产物正常,以及与宿主免疫、代谢系统的协同作用。培土生金法通过调理脾胃功能,维持肠道微生态稳定,从而发挥抗炎作用,与现代医学的“肠-肺轴”机制相呼应[96]。SCFAs 通过抑制 Th2 细胞激活、维持 Th1/Th2 平衡、减少促炎因子释放,从而降低肠漏风险和气道炎症[97]。参苓白术散通过其多糖成分能促进脾气虚证大鼠肠道内 SCFAs 的产生[98]。补中益气汤、黄芪多糖等通过优化肠道菌群结构,减少 IL-1β 和 TNF-α 等促炎因子释放,间接缓解 COPD 相关肺部炎症[99-100]。西洋参多糖联合人参皂苷通过逆转淋巴细胞亚群比率,刺激小肠中的 $CD4^+$ T 细胞和 IgA 分泌的方式直

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接改善免疫功能障碍[101]。肠道炎性环境常显示 F/B 降低，并与 COPD 的急性发作次数和运动能力相关[102]，芪参地黄汤、黄芪甲苷均可提高肠道菌群的 F/B 比值，缓解肠道炎症反应，从而减少肠黏膜屏障损害，避免肠上皮细胞破坏引发的免疫功能紊乱[103-104]。

4.2.3 调控肠道微生物代谢产物并修复肠黏膜屏障损伤 丁酸作为 SCFAs 的组成部分，能够影响肠上皮细胞的增殖、分化和凋亡，同时具有增强肠黏膜屏障的功能[87,105]。产丁酸菌作为丁酸的主要生产者，其代谢活动直接决定了肠道内丁酸的丰度。参苓白术散能够有效恢复大鼠肠道产丁酸菌丰度，并通过调节该菌群的结构、分布及丰度以恢复菌群多样性、改善肠道微生态环境失稳[106]，其多糖成分可进一步通过调控产丁酸菌的多样性与组成结构进一步促进丁酸生成[107]。

乳酸杆菌属、双歧杆菌属在内的益生菌可改善肠黏膜屏障、帮助消化吸收，还能降低 COPD 患者的炎性因子水平改善预后[108-109]。联用双歧杆菌活菌胶囊能优化 COPD 伴呼吸衰竭患者的营养和炎症指标[110]。培土生金类单味中药及其多糖成分对益生菌属也有一定的调节作用，如白术被证实可显著增加小鼠肠道双歧杆菌和乳杆菌数量，减少肠杆菌数量[111]，其提取的异质酸性杂多糖，可以增加肠芳烃受体的表达，进而上调紧密连接蛋白、抗菌肽和黏蛋白的表达来降低全身性脂多糖，以改善肠道屏障功能[112]。茯苓可回调哮喘小鼠拟杆菌门的异常升高并促进丁酸盐生成[113]。党参可显著提高肠道乳杆菌水平并降低大肠杆菌水平[114]，其多糖成分可通过上调双歧杆菌和乳杆菌等与免疫呈正相关的菌群的生长，抑制脱硫弧菌和幽门螺杆菌等致病菌的生长，改善肠黏膜屏障，恢复肠道微生态平衡[115]。黄芪多糖可促进双歧杆菌、乳酸杆菌的生长，调整肠道微生态并修复肠道屏障损伤，提高机体的免疫力[116]。黄芪多糖可降低体内肠球菌和肠杆菌的含量[117]。紧密连接蛋白与肠道物理屏障密切相关[118]，黄芪多糖可增加小鼠肠中紧密连接蛋白（ZO-1、Occludin、Claudin-1）的表达水平，并富集乳杆菌，抑制 TLR4/MyD88/NF-κB 信号通路，减少促炎因子释放[119]。玉屏风颗粒也能有效降低 COPD 患者血液中 LPS 与紧密连接蛋白（Occludin、ZO-1）的水平，修复 COPD 患者的肠黏膜损伤[120]。上述干预通过优化肠道微生态和屏障功能，为 COPD 的治疗提供了潜在策略。

5 总结与展望

“培土生金”基于《黄帝内经》理论，是中医药防治 COPD 的重要治法，通过调理脾胃功能促进肺气生成，与现代医学“肠-肺轴”理论高度契合。本研究通过论证脾胃运化功能与肠道微生态在器官联系、生理机制及病理演变中的内在一致性，阐明脾主运化与肠道微生态的内在关联，并系统归纳中药干预对肠道菌群的调控作用，以期为 COPD 的精准治疗提供理论依据。目前，部分中医药辨证论治 COPD 随机对照试验已将肠道菌群检测纳入结局指标，多维度证实其疗效[121-122]。今后仍需通过大样本前瞻性临床研究，系统评估中药治疗 COPD 的疗效及其对肠道菌群的调节机制，并厘清菌群改变与免疫通路的因果时序关系。建议未来研究深化以下方向：①引入粪菌移植、无菌动物模型等因果验证手段以增强推断的可靠性，全方位探讨中医药调控肠道菌群治疗 COPD 的作用机制；②整合多组学技术深入揭示“微生物-宿主”互作机制，探究肠道菌群对 COPD 病程进展的预测能力；③积极探索中医证候分型与菌群特征的对应关系，如研究发现肺脾两虚[123]、肺气虚[124] COPD 模型大鼠存在不同菌群特征，未来仍需更多支持“证型-菌群”相关的循证依据；④推动“培土生金”治法与益生菌、益生元及饮食营养干预策略的结合，益生元可选择性刺激营养吸收相关肠道细菌的活性[125]，足量膳食纤维的摄入则能显著降低 COPD 的发病率[126]，因此未来需深入探究中医药结合饮食干预在 COPD 患者中的特定代谢模式及其潜在作用机制，为基于肠道菌群特征的个体化营养建议提供重要的理论依据和实践指导。

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