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Review 综述

肠道微生物改善高尿酸血症的研究进展

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摘　要：高尿酸血症(hyperuricemia, HUA)是人体内尿酸代谢紊乱、血尿酸水平持续高于正常值的一种病理现象。近年来，肠道微生态成为各种代谢性疾病的研究热点，因此肠道菌群有可能成为预防和治疗高尿酸血症的新靶标。本文综述了尿酸在人体内的代谢途径和生理作用，阐述了肠道菌群对高尿酸血症的调控机制，包括分解与内化嘌呤以抑制尿酸合成、分解尿酸并促进尿酸排泄、修复肠道屏障、影响肠道代谢产物、调节肠道免疫等方面。同时，总结了优化饮食结构、服用益生菌、益生元干预及粪便微生物移植等方法在高尿酸血症治疗中的潜在应用，为高尿酸血症的防治提供了新的思路与参考。

关键词：肠道微生物；高尿酸血症；嘌呤代谢

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Research progress in the amelioration of hyperuricemia by gut microbiota

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Abstract: Hyperuricemia is a pathological phenomenon in which the metabolism of uric acid in the human body is disrupted and blood uric acid levels remain above normal. In recent years, gut microbiota has become a research hotspot for various metabolic diseases, serving as a potential new target for the prevention and treatment of hyperuricemia. This article reviews the metabolic pathways and physiological effects of uric acid in the human body and elucidates the regulatory mechanisms of gut microbiota on hyperuricemia. Such mechanisms include inhibiting uric acid synthesis by the breakdown and internalization of purines, degrading uric acid and promoting uric acid excretion, repairing intestinal barriers, influencing intestinal metabolites, and regulating intestinal immunity. In addition, this article summarizes the potential applications of optimizing dietary structure, taking probiotics and prebiotics, and fecal microbiota transplantation in the treatment of hyperuricemia, providing new ideas and references for the prevention and treatment of hyperuricemia.

Keywords: gut microbiota; hyperuricemia; purine metabolism

高尿酸血症(hyperuricemia, HUA)是一种慢性代谢性疾病，其核心特征是血清尿酸(uric acid, UA)水平异常升高，源于嘌呤代谢紊乱[1]。随着我国社会经济的进步和民众生活水平的提高，该疾病在近年来的发病率显著上升，现已成为仅次于2型糖尿病的第二大常见代谢性疾病[2]。调查发现，中国HUA患病率为14%，其中男性患病率为24.4%，女性患病率为3.6%[3]。大量临床证据显示，HUA不仅可发展为痛风[4]，还显著增加高血压、高血脂、2型糖尿病、代谢综合征及慢性肾病等多种疾病的发生风险，是其公认的独立危险因素[2]，对人类健康构成严重危害[5]。

目前，药物治疗仍是控制高尿酸血症的主要手段[6]。临床常用药物包括尿酸合成抑制剂(如别嘌呤醇、非布司他)和促尿酸排泄剂(如苯溴马隆)等[7]。然而，这些药物虽有一定疗效，但存在诸多局限，如治疗成本较高、毒副作用明显以及患者依从性较差等[8]。作为关键的非药物治疗手段，饮食调整在降尿酸综合管理中的辅助价值已得到证实[9]，但受限于患者饮食习惯的惯性，临床依从度普遍较低[10]。这凸显了研发新型安全有效替代疗法的必要性。

人体大部分尿酸排泄在肾脏中完成[11]，但总尿酸排泄量的1/3发生在肠道[12]，并进一步由肠道菌群代谢[13]。作为肠-肾轴的核心调控因子[14]，肠道菌群对维持肾脏健康具有关键作用。肠道微生物也有可能成为深入研究HUA发病机制及相应治疗方法的新靶点[15]。本文综述了HUA与肠道菌群关联的最新研究进展，并进一步探讨了肠道菌群对HUA的调控机制，包括肠道菌群及其代谢物在分解和

内化嘌呤、促进尿酸排泄，以及通过调节肠道通透性来减轻炎症反应等方面的作用。最后，概述并展望了服用益生菌、益生元干预、粪便微生物移植和饮食调节等通过肠道菌群防治 HUA 的策略，以期为 HUA 的防治提供新的思路和参考。

1 高尿酸血症概述

1.1 尿酸代谢机制

尿酸作为嘌呤代谢的终末产物[16]，其来源分为内源性与外源性途径：内源性嘌呤源于细胞衰亡释放的核酸、腺嘌呤及鸟嘌呤[17]，经代谢最终生成 UA；外源性嘌呤则来自高果糖饮料、动物内脏及海产品等膳食[18-19]，主要在肝、肠及血管内皮细胞转化为 UA[20]。UA 的生物合成涉及复杂酶级联反应。初始底物单磷酸腺苷(adenosine monophosphate, AMP)和单磷酸鸟苷(guanine monophosphate, GMP)经不同酶促途径转化[21]。AMP 可经脱氨酶催化生成单磷酸肌苷(inosine monophosphate, IMP)，再经核苷酸酶去磷酸化为肌苷[22]；也可经核苷酸酶水解为腺苷，后由脱氨酶转化为肌苷[14]。GMP 经核苷酸酶可直接转化为鸟苷[23]。肌苷与鸟苷在嘌呤核苷磷酸化酶(purine nucleoside phosphorylase, PNP)作用下分别生成次黄嘌呤与鸟嘌呤[24]。二者随后经黄嘌呤氧化酶(xanthine-oxidase, XOD)和鸟嘌呤脱氨酶(guanine deaminase, GD)催化形成黄嘌呤[25]。在终末反应中，黄嘌呤由黄嘌呤氧化酶不可逆氧化为 UA (图 1)，最终经肾脏或肠道排出。

1.2 肠道菌群改善高尿酸血症现状

肠道微生态系统承载着数以十万亿计的微生物[26]，各类微生物在持续的能量物质交换中形成互作平衡，保障群落结构稳定性[1]。HUA 病理进程伴随肠道微生态重构[27]。研究表明，HUA 组较健康对照组微生物组成显著改变，多样性指数与菌群丰度明显降低[28]，且芽孢杆菌门(*Bacillota*)与拟杆菌门(*Bacteroidota*)的比例下

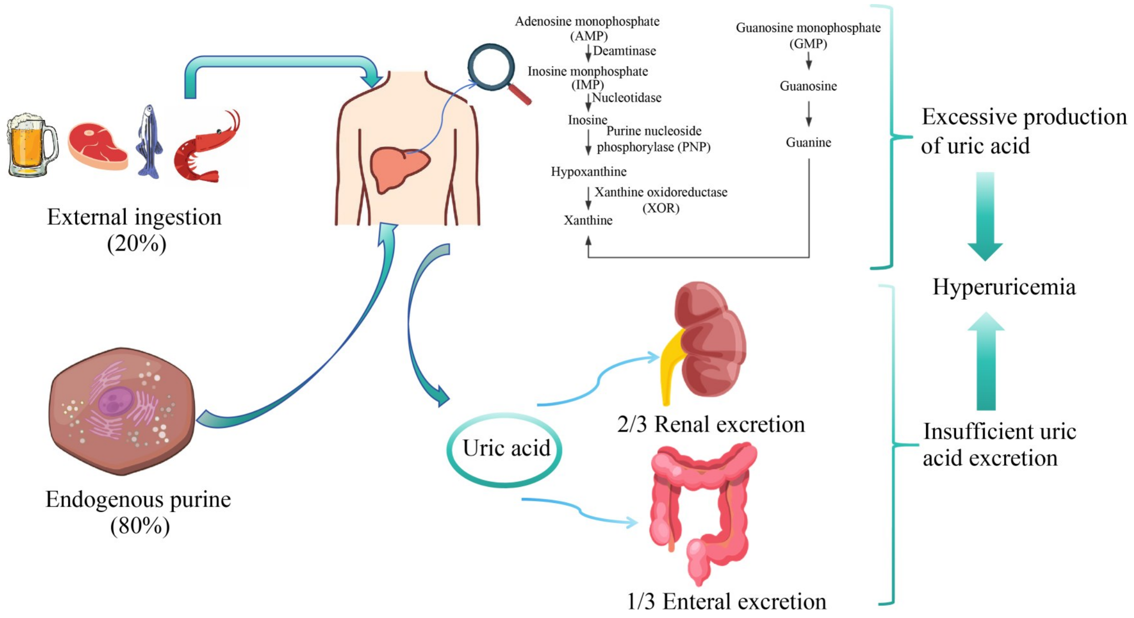

图1 高尿酸血症发病机制。血尿酸水平受尿酸形成和排泄的动态平衡调控。当尿酸合成过多、排泄障碍或两者兼有时血尿酸水平升高，进而诱发HUA。

Figure 1 Pathogenesis of hyperuricemia. Blood uric acid levels are regulated by the dynamic balance of uric acid formation and excretion. When uric acid synthesis is excessive, excretion is impaired, or both, the blood uric acid level rises, which in turn induces HUA.

降。此外，HUA 组的粪便样本中，拟杆菌属(*Bacteroides*)、普雷沃氏菌属 (*Prevotella*)、梭杆菌属(*Fusobacterium*)等菌属较为富集，而粪球菌属 (*Coprococcus*)、瘤胃球菌属 (*Ruminococcus*)、乳杆菌属 (*Lactobacillus*）和粪杆菌属(*Coprobacillus*)则有所减少[29]。

用于调控 HUA 的益生菌主要来源于乳酸菌(lactic acid bacteria, LAB)[30]，该类微生物在肠道菌群中占据关键生态位。LAB 的肠道定植能力使其可重塑 HUA 微生态环境，优化嘌呤-尿酸代谢通路[31]。另外 LAB 通过刺激产短链脂肪酸(short-chain fatty acids, SCFAs)菌群增殖，增强肠道 SCFAs 生成，由此下调肝脏及血清 XOD 酶活性，实现 HUA 的病理缓解[32]。研究发现，唾液宿主关联乳杆菌(*Ligilactobacillus salivarius*) CECT 30632 展现强效嘌呤代谢能力：肌苷与鸟苷完全转化，尿酸转化率达 50%[13]。对比研究表明，发酵黏液乳杆菌 (*Limosilactobacillus fermentum*) GR-3 强化型酸奶相比常规产品显著降低血尿酸水平[33]，该效应源于菌群-宿主互作，通过微生态调控抑制炎症、促进尿酸清除，并维持肾脏与肠道生理功能。

目前，关于肠道菌群缓解 HUA 的研究尚处于发展早期，以动物实验为主，临床循证研究相对匮乏。未来研究需深化机制认识，加快向临床转化的步伐。

2 肠道菌群对高尿酸血症的调控机制

肠道菌群及其代谢物通过协调嘌呤代谢、增强尿酸清除率及抑制炎症反应多靶点干预 HUA 发展进程(图 2)。

2.1 肠道菌群分解与内化嘌呤抑制尿酸合成

嘌呤的肠道分解与内化过程高度依赖菌群调控[34]，微生物通过特异性代谢酶实现嘌呤衍生物转化。鉴于嘌呤是重要的肠道有机氮源，微生物进化出多途径利用策略[35]。有氧嘌呤分解途径存在于克雷伯氏菌属(*Klebsiella*)等特定菌属，依赖氧气环境实现嘌呤降解；厌氧尿囊素代谢存在于部分肠杆菌属(*Enterobacter*)菌株，在缺氧条件下分解尿囊素，伴随草酰乙酸同化[36]；而厌氧尿酸分解代谢途径存在于大肠埃希氏菌(*Escherichia coli*)和克雷伯氏菌的某些菌株中，目前这一机制尚未完全阐明，其嘌呤分解可能关联厌氧尿酸分解过程[37]。

当前乳酸菌嘌呤代谢研究聚焦双轨路径：其一为降解菌株的筛选，核心筛选标准为菌株能否将嘌呤底物解聚为无嘌呤环结构的小分子，或催化其转化为其他嘌呤衍生物[38]。研究结果表明，大多数乳酸菌能够降解肌苷和鸟苷，只是降解能力差异较大[39]。另一方面为乳酸菌降解嘌呤的机理机制研究[40]，乳酸菌降解嘌呤的一种假设机制是乳酸菌利用嘌呤进行生长。刘银辉等[41]研究表明，核苷酸前体的吸收刺激了乳酸菌的生长。因此，比较乳酸菌在嘌呤化合物存在和不存在的情况下的生长速率可以证明乳酸菌生长对嘌呤的利用[42]。

作为次黄嘌呤和黄嘌呤转化为 UA 的关键限速酶，黄嘌呤氧化还原酶由黄嘌呤氧化酶和黄嘌呤脱氢酶组成，广泛分布于微生物及哺乳动物体内[43]。该酶活性增强将促进尿酸生物合成，导致血尿酸水平异常升高[44]。值得注意的是，肠道内革兰氏阳性与阴性菌的黄嘌呤代谢呈现功能分化[45]。多数具有强分解能力的革兰氏阴性菌，如假单胞菌属(*Pseudomonas*)和克雷伯氏菌属携带 XOD 基因[46]，而革兰氏阳性菌中仅少数菌株存在 XOD 基因且代谢效率低下。这种菌群代谢能力的异质性表明，微生物组成变化可直接干预肠道嘌呤向 UA 的转化通路[47]。

总之，肠道微生物能通过吸收核苷或降解嘌呤来抑制尿酸合成，最终实现血尿酸水平的调控。

2.2 肠道菌群分解尿酸和促进尿酸排泄

在哺乳动物体内，尿酸向(S)-尿囊素的氧化

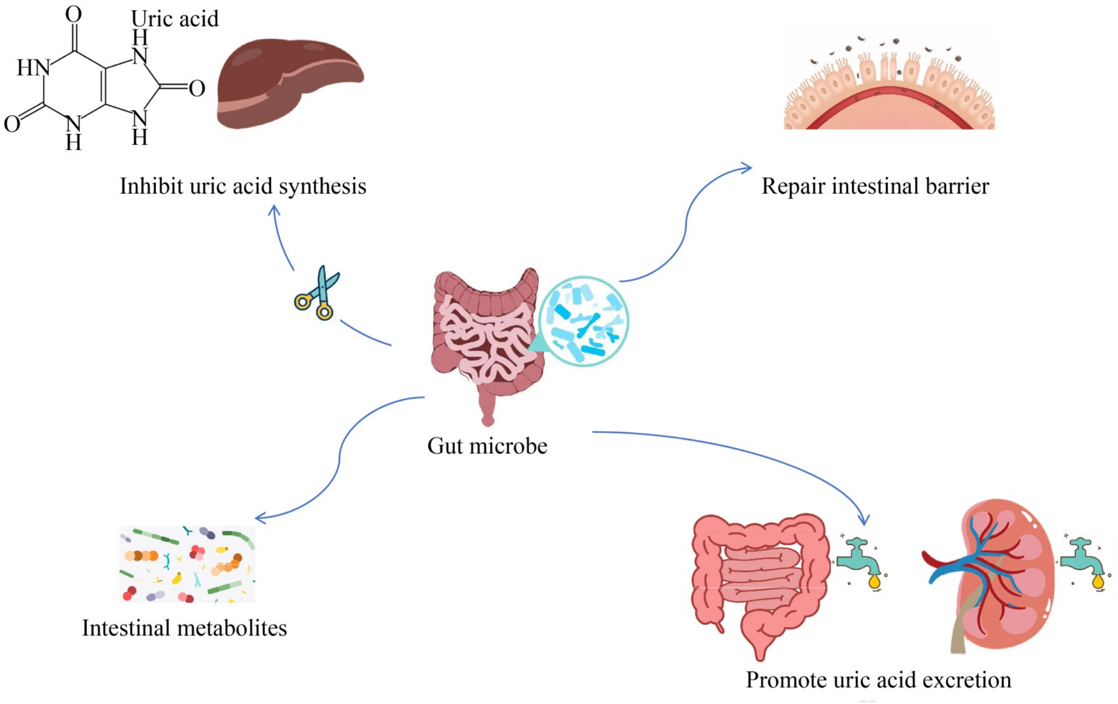

图2　肠道微生物对高尿酸血症的调控机制。肠道菌群可多途径缓解高尿酸血症，其作用机制主要包括分解和内化嘌呤抑制尿酸合成、分解尿酸和促进尿酸排泄，以及调节肠道屏障。

Figure 2　The regulatory mechanism of gut microbiota on hyperuricemia. The gut microbiota can alleviate hyperuricemia through multiple pathways, mainly by decomposing and internalizing purines to inhibit uric acid synthesis, decomposing uric acid, and promoting uric acid excretion, as well as regulating the intestinal barrier.

转化是解离尿酸结晶的核心生化反应[48]。在尿酸酶的作用下，尿酸首先被氧化形成不稳定的5-羟基异尿酸盐(5-hydroxyisourate, HIU)，随后通过 HIU 水解酶水解或自发分解为 2-氧基-4-羟基-4-羧基-5-脲基咪唑啉[12]。最后，在脱羧酶的催化下进一步脱羧，生成可溶性较好的(S)-尿囊素[49]。肠道微环境中存在大量能厌氧降解尿酸的细菌[50]，其代谢终产物包括黄嘌呤、乳酸、乙酸盐与丁酸盐。分泌至肠腔的尿酸可被驻留菌群，如大肠埃希氏菌和尿酸戈特沙尔克氏菌(*Gottschalkia acidurici*)快速分解，经尿酸氧化酶作用生成可溶性尿囊素[51]。

人体生成的尿酸在尿酸转运蛋白的作用下通过肾脏和肠道排泄出体外[52]，以维持体内尿酸水平的平衡。尿酸转运蛋白分为尿酸重吸收转运蛋白和尿酸分泌蛋白，广泛分布于肝脏、肾脏、肠道等组织中，共同维持尿酸重吸收和分泌的动态平衡。近期研究证实，肠道菌群通过调节尿酸转运蛋白表达促进宿主尿酸排泄[53]。鹅肌肽(anserine)作为天然抗 HUA 制剂[54]，其功效与肠道内梭菌属(*Clostridium*)和乳杆菌属(*Lactobacillus*)的富集密切相关。其关键机制在于鹅肌肽对 ABCG2、URAT1 和 GLUT9 转运蛋白的调节具有菌群依赖性[55]。

2.3　肠道屏障影响高尿酸血症

肠道屏障的完整性是机体健康的基石[56]。其双向调节功能体现在不仅能吸收营养物质和液体，还能阻断病原体及毒素侵袭[57]。当肠黏膜受损时，在缺氧和炎症刺激的病理条件下会导致紧密连接(tight junction, TJ)蛋白内转移[1]。细胞间孔隙扩张肠黏膜通透性增加，促使肠道菌群易位[36]。释放入血的脂多糖(lipopolysaccharide, LPS)可扩散至肝脏等器官，成为多种疾病的启动因子[58]。研究表明，肠道屏障功能障碍是代谢性疾病的一个突出特征[30]。值得注意的是，高尿酸血症小鼠的肠道通透性随着年龄和 LPS 水平的增加而增加，因此老年小鼠发生高尿酸血症的可能性更高。在一些研究中，患有高尿酸血症的小鼠的特征是肠道通透性增加、TJ 蛋白表达水平下调，以及血清 LPS、炎症因子水平显著升高[59]。临床案例研究也能反映痛风与肠黏膜屏障之间的关系。例如，Xie 等[60]对 11 名痛风患者进行了洗涤微生物群移植(washed microbiota transplantation, WMT)，并比较了治疗前后的症状，结果显示 WMT 治疗后痛风患者痛风症状和肠道屏障功能得到改善。此外，肠道黏膜屏障损伤及通透性增加不仅促使 UA 直接入血诱发 HUA[61]，更会导致病原体相关分子模式与细菌 LPS 移位增加[62]。这种双重病理效应可能加剧肠道菌群失调并触发广泛性肠炎，从而恶化痛风进程。相关分子机制仍需深入实验解析。

2.4 肠道代谢物对高尿酸血症的影响

肠道菌群不仅可以修复肠道屏障，还能极大地影响肠道代谢产物，从而影响高尿酸血症的发生和发展[63]。一些代谢物是维持人体健康和生命功能的关键成分，如 SCFAs、必需氨基酸和 LPS[58]。膳食纤维可被肠道微生物群利用产生 SCFAs。作为碳链长度不超过 5 个碳的脂肪酸，SCFAs 是微生物代谢研究中被广泛关注的核心产物[64]。在肠道微环境中，乙酸盐、丙酸盐及丁酸盐的丰度最高[65]。乙酸盐及其相关代谢产物乙酰辅酶 A (acetyl-coenzyme A, Acetyl-CoA)参与机体中多个代谢通路，包括能量生产、脂类合成和蛋白乙酰化等[66]。Daien 等[67]发现乙酸盐通过转化为乙酰辅酶 A，然后经过三羧酸循环(tricarboxylic acid cycle, TCA)和氧化磷酸化(oxidative phosphorylation, OX-PHOS)提供燃料，增加能量可用性，以及通过乙酰辅酶 A 合成酶 2 (acetyl-coenzyme A synthetase 2, ACSS2)进行蛋白质乙酰化方式诱导产生白细胞介素 10 (interleukin-10, IL-10)的 B10 细胞分化发挥抗炎作用。Henson[68]通过使用丁酸盐作为痛风疾病的特定代谢标志物构建群落代谢模型进行计算代谢建模，研究结果显示低痛风组丁酸盐含量较高，高痛风组琥珀酸盐含量较高。Chu 等[69]通过宏基因组研究分析了短链脂肪酸合成中编码关键酶的基因丰度，发现负责丙酸盐和丁酸盐生物合成的基因在健康对照中相对丰度更高。由此可以得出结论，膳食纤维在肠道微生物作用下分解的 SCFAs 会影响痛风的进程。同时，SCFAs 还能抑制 XOD 活性[70]，并为肠道内尿酸的排泄提供能量，从而起到降低尿酸的效果。另外，对于其他肠道菌群代谢产物的研究，Song 等[71]发现在尿酸氧化酶基因敲除的小鼠模型中，异亮氨酸、色氨酸、缬氨酸、精氨酸和谷氨酰胺的相对丰度明显升高。此类必需及条件必需氨基酸主要经肠道菌群合成，其水平升高可诱导嘌呤代谢通路紊乱，进而影响尿酸稳态。吲哚-3-甲醛(indole-3-carboxaldehyde, I3A)是色氨酸经肠道菌群代谢后的吲哚衍生物，其可通过激活肠道 AhR/IL-10/Wnt 信号通路和增加有益菌丰度从而维持肠道屏障功能[72]。除了 SCFAs 和必需氨基酸，LPS 也是一种不可忽视的微生物代谢物[13]。革兰阴性菌细胞壁组分 LPS 在肠道中的水平随该类菌丰度升高而增加[36]。LPS 能激活 XOD 的转录表达，增强其酶活性，进而加速尿酸生成[73]。

因此，由于 SCFAs、必需氨基酸和 LPS 等肠道代谢物的存在，肠道代谢物在高尿酸血症发生发展中的作用不容忽视。

2.5 肠道免疫系统

肠道作为人体最大的免疫器官，肠道菌群能够通过免疫调节作用影响全身免疫稳态。肠道免疫系统对 HUA 的发生和发展也有巨大的影响[56]。肠道菌群通过调节机体的免疫反应，减轻炎症状态，缓解肾脏、肝脏、肠道损伤，修复组织屏障，改善其通透性，恢复尿酸代谢能

力，从而有助于降低尿酸水平。HUA 则可能会影响肠道免疫细胞和微生物群，产生免疫因子，如白细胞介素 1、1β、6、12 和肿瘤坏死因子 α (tumor necrosis factor alpha, TNF-α)，从而导致炎症[74]。牛春华等[75]通过筛选获得一株具有降尿酸功能的植物乳植杆菌 (*Lactiplantibacillus plantarum*) UA149，动物体内实验测试显示，植物乳植杆菌 UA149 可显著降低高尿酸血症模型大鼠白三烯、血栓素和炎症因子水平，并可以显著上调丝裂原活化蛋白激酶(mitogen-activated protein kinase, AMPK)、去乙酰化酶 1 (sirtuin 1, SIRT1)蛋白表达，降低核因子-κB (nuclear factor kappa B, NF- κB)、核因子 κB 抑制蛋白 α (inhibitor of nuclear factor kappa B alpha, IκB-α)、NOD 样受体家族 Pyrin 域蛋白 3 (NOD-like receptor family pyrin domain-containing protein 3, NLRP3) 和凋亡相关颗粒样蛋白 (apoptosis-associated speck-like protein containing a CARD, ASC)表达，通过调节 AMPK/NF-κB/NLRP3 信号通路来减缓 HUA 引起的肾脏炎症反应。在另一项研究中，痛风患者的肠道微生物群紊乱和淋巴细胞浸润会产生炎症因子[76]，包括 TNF-α、IL-1β、IL-6 和 IL-12。Lv 等[74]发现，在 *Uox*-KO 小鼠模型中，促炎微生物扩增通过激活 Toll 样受体(Toll like receptors, TLR) 2/4/5 信号轴，诱导 IL-1β 与 TNF-α 过量释放，引发免疫稳态失衡及肠屏障损伤；此级联反应最终促使微生物突破屏障进入循环系统，触发系统性炎症；他们发现，高尿酸血症小鼠肠道组织和血清中的 TNF-α 水平均升高，进一步证明了肠道免疫系统在痛风发展中的重要作用。此外，肠道炎症也与微生物群高度相关[77]。有证据表明，微生物群通过改变抗炎物质的水平、降低细菌丰富度、改变微生物相互作用或产生细菌代谢物来影响肠道免疫[78]。炎症因子和免疫细胞会导致肠道稳态失衡，引起通透性的变化和菌群失调，促进高尿酸血症的发展[79]。

3 基于肠道微生物的 HUA 干预策略

肠道微生物在人体嘌呤-尿酸代谢通路中发挥核心调控作用，因此靶向调节肠道菌群是治疗 HUA 的关键干预策略(表 1)。

饮食是影响肠道微生物群组成的重要因素之一[84]。终止高血压膳食(dietary approaches to stop hypertension, DSAH)近年来受到广泛关注，在此饮食中碳水化合物被微生物酵解为 SCFAs[80]，可优化菌群结构，进而促进尿酸排泄。除碳水化合物外，该饮食所含的天然多酚通过抑制 XOD 酶活性[85]进一步减少尿酸的产生[86]。

益生菌具有改善肠道菌群结构与血尿酸水平的双重功能，使其成为 HUA 治疗领域的前瞻性生物疗法。益生菌能够抑制高尿酸引发的炎症反应[87]，减轻肾脏和全身炎症[70]。此外，益生菌能够抑制尿酸吸收，促进尿酸排泄[88]。益生元被定义为非宿主代谢依赖性物质，通过选择性激活益生菌的代谢通路及增殖机制协同维持微生态稳态[87]。常用的益生元有双歧因子、菊粉型果聚糖、低聚糖、抗性淀粉和非淀粉多糖[89]。因其安全性高、疗效显著，已逐渐成为 HUA 的替代性疗法[90]。本课题组从云南特色发酵食品中分离获得具有强效嘌呤核苷分解活性的乳酸菌，在分子水平上阐明了其体外降解嘌呤的关键机制，并在动物模型中证实其能显著降低血尿酸水平，为开发降尿酸益生菌制剂提供了核心种质资源，同时为 HUA 的微生态疗法开辟了新路径。

粪便微生物移植(fecal microbiota transplantation, FMT)是一种基于菌群重构的治疗策略：将健康者粪便经生物处理获得的功能性微生物群植入患者肠道，以恢复菌群多样性与代谢稳态，从而达到疾病治疗目的[91]。HUA 的代谢紊乱本质与肠道微生物失调密切相关[60]，因此 FMT 成为创新治疗选择[65]。一项有关洗涤微生物群移植

表1　基于肠道微生物的HUA干预措施

Table 1　HUA intervention measures based on gut microbiota

Intervention	Specific measures	Mechanism of action	References
Dietary structure adjustment	DASH diet The mediterranean diet Low purine diet Ketogenic diet	Reduce exogenous purine intake Promote SCFAs production inhibit uric acid synthase (XOD) Competitive inhibition of renal tubular uric acid reabsorption by whey protein Polyphenolic substances inhibit inflammation and XOD activity	[80]
Probiotic intervention	*Bifidobacterium adolescentis* *Lactobacillus acidophilus* *Lactiplantibacillus plantarum* *Lacticaseibacillus rhamnosus*	Direct degradation of intestinal purine/uric acid Strengthening the intestinal barrier and reducing the entry of endotoxins into the bloodstream Inhibition of xanthine oxidase (XOD) activity Regulating Th17/Treg immune balance to alleviate inflammation	[81]
Probiotic supplementation	Soluble fiber: oligofructose (FOS), inulin Resistant starch: green banana, cold rice Polyphenols: green tea extract, berries	Selective promotion of probiotic (*Bifidobacterium*/*Lactobacillus*) proliferation Fermentation produces SCFAs such as butyric acid, which downregulate the URAT1 transporter protein Antioxidant effect reduces systemic inflammation	[82]
Fecal microbiota transplantation	Screening of healthy donor microbiota (characteristics of low uric acid type microbiota) Delivery *via* colonoscopy/capsule	Rebuilding gut microbiota structure: increasing uric acid degrading bacteria (such as *Bacillus subtilis*), reducing pro-inflammatory bacteria (such as *Prevotella*), restoring intestinal barrier integrity	[83]

的临床研究表明，WMT 不仅可降低血清尿酸含量，还可有效恢复肠屏障完整性[92]。

4　总结与展望

HUA 是当前高发的代谢性疾病，其病理进程与多种疾病显著相关。近年研究表明，HUA 与肠道微生物密切关联，以肠道菌群为靶点的诊疗策略正逐渐成为研究热点。本综述总结了肠道微生物对 HUA 的调控机制，肠道菌群可通过多途径缓解 HUA，其作用机制主要包括分解和内化嘌呤以抑制尿酸合成、分解尿酸和促进尿酸排泄以及调节肠道屏障。同时，探讨了基于肠道菌群干预的防治手段，如服用益生菌、益生元干预和粪便微生物移植在重塑微生态平衡及调控尿酸水平方面的潜力，为 HUA 的临床治疗提供了新视角。

目前，肠道菌群与 HUA 的病理关联仍需更充分的研究支撑。鉴于肠道微生物组成具有高度异质性、代谢通路具有复杂性，且其与尿酸代谢存在多靶点互作特征，二者间确切的因果机制尚未明晰。基于肠道菌群的干预策略比较分析表明，益生菌疗法通过富集有益菌群改善宿主健康，但存在口服生物利用度低的问题，影响定植效率与疗效持续性，且长期使用可能破坏菌群稳态，产生定植抗性；益生元干预选择性促进益生菌增殖以优化微生态，但响应周期长，且个体疗效差异显著；FMT 可快速重建菌群平衡，但其侵入性强、供体筛选标准化缺失及长期安全性不确定，构成临床转化障碍。

未来研究需整合跨学科技术体系，依托肠道微生物多组学分析与人体全基因组测序数据，系统解析菌群-基因组-HUA 的互作网络，进而建立更精准高效的 HUA 防治路径。同时，应着力推进新型降尿酸菌株的发掘与功能验证，拓展菌种资源储备，深化作用机制研究，转化优化治疗产品，基于菌株特性开发靶向制剂。以

肠道微生态调控为核心的 HUA 治疗策略有望成为未来研究的关键突破口。

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