Advances in Clinical Medicine 临床医学进展, 2024, 14(12), 1016-1023
Published Online December 2024 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2024.14123180

Hans汉斯

茯砖茶对肠道菌群及代谢综合征的调节作用研究进展

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收稿日期：2024年11月20日；录用日期：2024年12月13日；发布日期：2024年12月23日

摘　要

茯砖茶是一种传统的后发酵茶，其中所含冠突散囊菌(*Eurotium cristatum*)，也被称为“金花”，是其区别于其他茶叶的关键。研究表明长期饮用茯砖茶具有抗肥胖、降糖、降脂、调节肠道菌群、抗炎等多重药理作用。代谢综合征(Metabolic syndrome, MS)是一组代谢紊乱性疾病的总称，其特征是向心性肥胖、血脂异常、血压升高、高血糖状态，已成为全球性的公共卫生问题。目前没有单一药物能够全面治疗代谢综合征的所有症状，人们越来越关注天然食品在预防和治疗代谢综合征中的作用。茯砖茶中的活性成分，如茶多酚、茶多糖等，可以通过调节肠道菌群的结构和功能，进而影响宿主的代谢过程。本文综述了茯砖茶通过调节肠道菌群改善MS的研究进展，以期为MS的防治提供新思路。

关键词

茯砖茶，肠道菌群，代谢综合征

Research Progress on the Regulatory Effects of Fuzhuan Brick Tea on Gut Microbiota and Metabolic Syndrome

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Received: Nov. 20th, 2024; accepted: Dec. 13th, 2024; published: Dec. 23rd, 2024

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文章引用: 李雪, 王军奎, 邢琳. 茯砖茶对肠道菌群及代谢综合征的调节作用研究进展[J]. 临床医学进展, 2024, 14(12): 1016-1023. DOI: 10.12677/acm.2024.14123180

Abstract

Fuzhuan brick tea is a traditional post-fermented tea, in which the presence of *Eurotium cristatum*, also known as "golden flower", is a key distinguishing feature from other tea varieties. Studies have shown that long-term consumption of Fuzhuan brick tea has multiple pharmacological effects, including anti-obesity, anti-diabetes, anti-lipid, regulation of gut microbiota, and anti-inflammation. Metabolic syndrome (MS) is a group of metabolic disorders characterized by central obesity, dyslipidemia, hypertension, and hyperglycemia, and has become a global public health problem. Currently, there is no single drug that can comprehensively treat all symptoms of MS, and people are increasingly paying attention to the role of natural foods in the prevention and treatment of MS. Active components in Fuzhuan brick tea, such as tea polyphenols and polysaccharides, can regulate the structure and function of gut microbiota, thereby influencing the host's metabolic process. This review summarizes the progress of research on how Fuzhuan brick tea regulates gut microbiota to improve MS, with the aim of providing new insights into the prevention and treatment of MS.

Keywords

Fuzhuan Brick Tea, Gut Microbiota, Metabolic Syndrome

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1. 茯砖茶与肠道菌群

1.1. 茯砖茶

中国茶根据加工工艺和发酵程度分为六大类：绿茶(未发酵)、白茶、黄茶和乌龙茶(部分发酵)，红茶(完全发酵)、黑茶(后发酵) [1]。茯砖茶是黑茶的代表之一，主要生产于以陕西咸阳为中心的关中地区，采用湖南、陕南、四川等地的鲜叶为原料，经过选料、筛制、渥堆、压制、发花、烘干等工艺制成，茶型似砖，色泽黑褐，汤色红浓，香气浓郁，口感滑润。其独特的风味品质和化学成分与复杂的微生物发酵过程有关。茯砖茶在发酵过程中，冠突散囊菌的代谢作用会在茶叶表面形成金黄色的颗粒，俗称"金花"，这是茯砖茶独有的特征之一[2]。

1.2. 茯砖茶对肠道菌群的调节作用

肠道菌群指生活在人体肠道中的大量和多样化的微生物群，约 90%属于厚壁菌门和拟杆菌门，其余微生物如变形菌门、疣菌门、放线菌门、梭杆菌门等仅占很小一部分[3]，其中厚壁菌门/拟杆菌门(Firmicutes/Bacteroidetes)的比例通常用于反映肠道微生物群的健康状况，并且与脂肪变性和肥胖密切相关[4]。在正常情况下，肠道菌群的结构稳定，处于动态平衡的状态。在炎症刺激和肠道菌群失衡等病理条件下，肠粘膜屏障受损，导致肠道通透性增加，肠道致病产物可能通过受损的肠粘膜屏障进入血液循环，引起一系列疾病。

越来越多的研究表明茶的健康益处可能部分源自其对肠道菌群的调节作用。茯砖茶及其组分可以调节肠道菌群的代谢途径和代谢物。例如，茶多糖可以改善肠道菌群的结构，显著提高短链脂肪酸(Short chain fatty acids, SCFAs)的水平，包括乳酸、乙酸和丙酸，并丰富淀粉和蔗糖的代谢途径[5] [6]，进而显著

影响免疫平衡、能量代谢和黏膜完整性维护等生理活动。此外，它还可以改善溃疡性结肠炎患者肠道微生物的色氨酸代谢，增加粪便中吲哚-3-乙酸和吲哚-3-乙醛的含量[7] [8]。茯砖茶及其成分在体外实验中显示出对肠道菌群有显著的调节作用。它们能够降低厚壁菌门与拟杆菌门的比例，减少有害菌群如埃希氏菌和 *γ-Proteobacteria*_B38 的相对丰度，并增加有益菌群如拟杆菌、双歧杆菌和粪杆菌的数量[9]。此外，茯砖茶还能提高肠道菌群的系统发育多样性，降低厚壁菌门/拟杆菌门的比例，并增加有益菌群如乳杆菌、拟杆菌、双歧杆菌科、梭菌科、拟杆菌科、Muribaculaceae、Prevotellaceae 和 Lachnospiraceae 的丰度，同时抑制促炎或致病性菌群如 *Allobaculum*、*Helicobacter*、Ruminococcaceae、Peptococcaceae、Peptostreptococcaceae 和丹毒杆菌科。这些作用有助于维护肠道微生态平衡，促进宿主健康[5] [10]-[12]。

2. MS 与肠道菌群

肠道菌群紊乱是多种身体系统疾病的病因或促成因素。肠道菌群的典型功能是分解食物残渣、调节免疫系统、合成维生素和氨基酸以及代谢药物[13]，通过调节人体内的肠道微生物组，可以增强肠道免疫能力、抵抗致病菌、改善胰岛素抵抗[14]，进而减少脂肪肝和高脂血症。肠道微生物组还通过调节宿主基因的表达来影响宿主生理过程[15]。越来越多的证据表明肠道微生物群在代谢性疾病中扮演关键角色。肠道菌群被认为是一个重要的“新陈代谢器官”和“内分泌器官”，与肥胖、糖尿病、血脂异常等疾病的发生密切相关。

2.1. 肥胖与肠道菌群

肠道菌群组成会影响人体获取营养物质和调节能量使用的能力，在肥胖及相关疾病的发生和发展中起着重要作用[16] [17]。在肥胖中，杆菌属，例如乳酸杆菌属(*Lactobacillus*)、双歧杆菌属(*Bifidobacterium*)、拟杆菌属和肠球菌属(*Enterococcus*)，以及厚壁菌门与拟杆菌门的比例上调，而梭状芽胞杆菌属(*Clostridium*)，包括钩状梭菌(*Fusobacterium mortiferum*)和肠杆菌属(*Enterobacter*)均下调[18] [19]。SCFAs 是由肠道中特定厌氧菌，主要包括拟杆菌门和厚壁菌门，通过发酵膳食纤维和抗性淀粉产生的主要代谢产物，是参与调控结肠黏膜能量和肝脏能量的重要能量来源，也是肌肉和脂肪组织能量的部分来源，其中乙酸是调控能量代谢的重要信号分子[20]。目前大量研究证实 SCFAs 可刺激饱腹感激素产生。研究发现，SCFAs 与 G 蛋白偶联受体(G-protein-coupled receptors, GPCRs)结合产生的 GLP-1、PYY、瘦素等内分泌激素，可增加饱腹感来改善肥胖。动物实验发现，喂食菊粉 14 周可刺激野生型或 Ffar2$^{-/-}$小鼠 SCFAs 的产生，驱动分泌 PYY 的细胞数量增加，使 PYY 释放增加，进而抑制食欲来控制肥胖[21]。GLP-1 激素增加使胰岛素敏感性增加，并抑制脂肪组织中的脂肪蓄积，从而维持体内能量稳态[22]。

2.2. 糖尿病与肠道菌群

Meta 分析显示，T2DM 患者肠道双歧杆菌含量减少，而大肠杆菌含量增加，提示肠道菌群的改变可能在糖尿病的发病机制中发挥重要作用[23]。首先，肠道菌群参与调控宿主的能量吸收和脂肪代谢，影响肥胖和胰岛素抵抗；肠道菌群的代谢产物可通过肠促胰素如 GLP-1 影响胰岛素分泌和糖代谢[24]。此外，肠道菌群可能通过调节炎症标志物(脂多糖和连蛋白等)影响肠屏障功能，进而影响糖尿病的进展。

2.3. 血脂代谢与肠道菌群

肠道菌群对血脂水平的影响涉及多种生理机制，众多研究证实，肠道菌群可通过胆汁酸(Bile acids, BAs)、SCFAs、氧化三甲胺(Trimethylamine N-oxide, TMAO)等代谢产物影响脂质代谢。

胆汁酸既可以调控机体的脂质代谢，又可以调节肠道菌群的组成。初级胆汁酸在肝脏合成后释放到小肠中，可促进机体对脂质或脂溶性维生素的吸收，大约 5%的胆汁酸进入到结肠后，经过肠道共生菌的

转换，作用于宿主的多种核受体和 GPCRs，参与调控宿主的胆固醇代谢和能量平衡[25]。此外，初级胆汁酸还可减少低密度脂蛋白胆固醇(Low density lipoprotein cholesterol, LDL-C)以及甘油三酯(Triglyceride, TG)的累积[26]。

SCFAs 主要包括乙酸盐、丙酸盐、丁酸盐[27]，多由未消化吸收的碳水化合物经结肠厌氧菌酵解产生。乙酸盐可以通过分泌 GLP-1、PYY 和其他肠道激素，对宿主的能量代谢产生有益作用，降低全身脂肪分解和促炎细胞因子水平，增加能量消耗和脂质氧化[28]。丙酸盐通过 AMPK/LSD1 通路促进小鼠的肠道脂肪分解和能量稳态[29]。丁酸盐是结肠的主要能量来源，肠上皮细胞的大部分能量来自丁酸盐的氧化。肠道微生物群中产生丁酸盐的细菌增加了丁酸盐的产生，从而通过丁酸盐-SESN2/CRTC2 途径改善脂质代谢[30]。

TMAO 是近年发现与心血管疾病相关肠道菌群代谢物的明星分子。膳食摄入的胆碱、甜菜碱和左旋肉碱等 TMAO 的前体物质，在肠道中被特定细菌如 *L. saccharolyticum* 代谢转化为三甲胺，运输至肝脏，在黄素单加氧酶(如 FMO3)的作用下氧化生成 TMAO，最终释放入血液循环。临床研究表明，血浆中 TMAO 水平与心血管疾病风险正相关，这可能与其影响脂质和激素稳态有关[31]。研究表明，TMAO 与 TG 水平正相关，与高密度脂蛋白胆固醇(High density lipoprotein cholesterol, HDL-C)水平负相关。TMAO 被发现能够减少胆固醇代谢关键酶 CYP7A1 的表达，影响胆固醇的代谢过程[32]。

3. 茯砖茶与 MS

3.1. 茯砖茶的抗肥胖作用

在过去几年中，减肥已被公认为是控制和预防冠心病、高血压等心血管疾病的关键因素。适度的体重减轻，即使只是初始体重的 5%，也可以在很大比例的超重患者中减少或预防这些疾病[33]。长期研究表明，持续适度的体重减轻 10%，可减少胰岛素抵抗、改善血糖控制[33]，更好地控制或预防高血压，增加 HDL-C、降低 LDL-C 和极低密度脂蛋白(Very low density lipoprotein, VLDL)，改善心脏舒张功能，减少室性心律失常的风险。茯砖茶具有预防肥胖的功能[34]-[36]，相关研究表明，茯砖茶减轻了高脂饮食饲养小鼠的体重、肝脏重量、腹部脂肪重量、谷丙转氨酶(Alanine aminotransferase, ALT)和谷草转氨酶(Aspartate transaminase, AST)活性[37]。茯砖茶中活性成分可从不同途径发挥抗肥胖作用。Ye 等[38]发现茶多酚可降低全身脂多糖水平，进一步抑制 NF-κB 的活化，显著降低高脂饮食小鼠血清肿瘤坏死因子(Tumor necrosis factor, TNF)-α、白细胞介素(Interleukin, IL)-1β 和 IL-6 水平，从而减轻肥胖诱导的炎症反应。茯砖茶多糖可改善肠道中 SCFAs、BCAA 和 AAA 的代谢，并调节 SCFA-GPR 信号通路以达到抗肥胖作用[39]。而茶褐素通过 SCFAs 和 AMPK-PGC1α 途径调节产热和炎症基因[40]。研究表明茯砖茶可以通过激活 AMPK 通路减少脂肪的分解合成以及 TG 和总胆固醇(Total cholesterol, TC)的积累，同时促进脂肪酸的氧化分解[41]；此外，茯砖茶可下调关键的脂肪生成转录因子(C/EBPα、PPAR-γ 和 SREBP1c)及其下游靶基因(aP2 和 FAS)，抑制脂肪和肝脏组织的脂肪生成[42]，从而达到减脂减肥的目的。茯砖茶通过增强肩胛间棕色脂肪组织活性和诱导腹股沟白色脂肪组织褐变，增加热调节基因的表达，促进能量消耗，最终抑制高脂喂养小鼠的肥胖及肥胖诱导的脂质和葡萄糖紊乱[42]。

3.2. 茯砖茶的降糖作用

长期高血糖可导致动脉粥样硬化，引发冠心病、心肌梗死、脑卒中等疾病，糖尿病患者发生心血管疾病风险是正常人的 2~4 倍。同时，糖尿病可引起心肌病变，使患者出现心力衰竭、心律失常等症状，长期高血糖还会影响心脏自主神经功能，增加猝死风险[43] [44]。胰岛素抵抗是 MS 和 T2DM 的核心机制，MS 的各种因素(如肥胖和血脂异常)会加剧胰岛素抵抗，最终导致 T2DM 的发生。

茯砖茶及其提取物通过多靶点和通路改善胰岛素抵抗[45]。茯砖茶通过下调信号调节蛋白(Signal regulatory protein, SIRP)-α的表达，激活胰岛素信号通路中的蛋白激酶B (即Akt)和葡萄糖转运蛋白4型(Glucose transporter type 4, GLUT4)，可能在改善由高脂饮食诱导的胰岛素抵抗中发挥作用[46]。Huang等[47]发现结合了多酚成分的茶渣可以激活INS-R/IRS2/PI3K/AKT/Glut-4/PPAR-γ等胰岛素通路，促进葡萄糖在肝脏的运输和储存，减少糖异生，表现出显著的降糖活性。茶多酚还被证明可调节氨基酸合成、核糖体合成、碳代谢和脂质代谢等代谢途径的基因表达，并通过上调AMPK磷酸化，调节碳水化合物代谢，发挥降糖作用[48]。茯砖茶水提物在T2DM小鼠HepG2细胞中具有自由基清除活性、良好的糖苷酶抑制、缓解胰岛素抵抗和降糖活性，并能激活IRS1/PI3K/Akt信号通路，调节糖脂代谢，改变与糖脂代谢相关的关键酶的活性[45]。茯砖茶中的新型酰基糖苷黄酮(AGFs)被发现具有对α-葡萄糖苷酶和HMG-CoA还原酶的抑制活性，这可能有助于降低餐后血糖水平，为预防和治疗2型糖尿病提供了潜在的途径[49]。

3.3. 茯砖茶的降脂作用

高脂血症是动脉粥样硬化的主要危险因素之一。血液中过多的脂质会沉积在动脉壁上，形成粥样斑块，使动脉管腔狭窄，影响血液流通。随着斑块的不断增大和破裂，可能导致心肌梗死、脑卒中等严重心血管事件[50]。茯砖茶多糖可促进氨基酸代谢、脂质代谢、糖代谢和其他次生代谢产物的生物合成[6]，降低血清TG、TC、LDL-C、游离脂肪酸，提高HDL-C水平；同时降低肝脏中TG含量，从而减少脂肪积累。茯砖茶可降低与脂肪生成和积累相关的基因或蛋白表达，如FAS、SREBP-1c和PPAR-γ；提高脂质分解代谢相关基因或蛋白的表达，包括CCAAT/C/EBP-α、CPT1和PPAR-α [34] [51] [52]。其中PPAR-γ的表达在动物的脂肪组织中最丰富[53]，可以促进脂肪细胞中游离脂肪酸的沉积。当肝细胞表现出脂质沉积诱导的脂肪变性时，肝脏中PPAR-γ的表达显着增加，大量的PPAR-γ表达促进脂质合成，导致肝脏中更多的脂质沉积[54]。

4. 结论与展望

本文综述了茯砖茶的独特加工工艺及其对肠道菌群的调节作用，深入探讨了茯砖茶在改善MS中的潜在益处。茯砖茶含有的茶多酚、茶多糖和茶褐素等活性成分，通过影响肠道菌群的结构和功能，对肥胖、糖尿病和血脂异常等代谢性疾病展现出积极的调节作用。这些发现不仅为茯砖茶的药理功能提供了新的科学依据，也为MS的治疗提供了新思路。虽然动物模型和体外研究为茯砖茶对MS的防治作用提供了证据，但未来需要更多的临床试验来验证茯砖茶对人体健康的益处。此外，茯砖茶调节肠道菌群的具体靶点和分子机制探索仍处于初级阶段，尚需进一步阐明。未来的研究应进一步探索茯砖茶在临床上的应用潜力，聚焦于茯砖茶中的活性成分，完成活性成分提取、对肠道菌群和宿主代谢的调节机制及靶点探索，以期开发出更加安全有效的干预策略，造福人类健康。

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