肠道细菌介导中药代谢的研究概述

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摘要: 人体肠道中栖息着数量庞大、种类繁多的微生物, 这些微生物与其所寄居的肠道环境组成了肠道微生态系统。中药经口服后在胃肠道中被肠道微生物代谢, 其代谢产物吸收入血从而产生药理作用。本文就肠道菌群介导中药代谢的特点和影响因素进行综述, 同时归纳了近年来肠道细菌介导黄酮类、皂苷类、环烯醚萜类、木脂素类等中药成分代谢的研究进展, 为阐明肠道细菌与中药成分化学结构变化之间的关系、肠道细菌代谢中药成分的规律与机制研究提供依据。

关键词: 肠道菌群; 中药; 代谢特点; 影响因素; 有效成分

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Overview of research on intestinal flora mediating the metabolism of Chinese medicine

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Abstract: The human gut is inhabited by a large number and variety of microorganisms, which constitute the intestinal microecosystem with the intestinal environment where they reside. After oral administration, Chinese medicine undergoes metabolism by these intestinal microorganisms within the gastrointestinal tract. The resulting metabolites are absorbed into the bloodstream to produce pharmacological effects. This paper provides a comprehensive review of the characteristics and influencing factors related to the mediation of Traditional Chinese Medicine (TCM) metabolism by intestinal flora. Additionally, recent progress in the microbial-mediated metabolism of TCM components such as flavonoids, saponins, iridoids, and lignans is summarized. This serves as a foundation for understanding the connection between intestinal bacteria and the chemical structural alterations of TCM components. It also offers insight into the regulations and mechanisms governing the intestinal bacterial metabolism of TCM constituents.

Key words: intestinal flora; traditional Chinese medicine; metabolic characteristics; influencing factor; active ingredient

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肠道菌群作为肠道微生物的集合, 对维持肠道内环境稳定发挥重要作用[1]。中医认为人体是一个有机整体, 有“整体观”“天人合一”等理念,《黄帝内经·灵枢》曰: “肺合大肠, 大肠者, 传导之腑。心合小肠, 小肠者, 受盛之腑。”肺与大肠相表里, 心与小肠相表里, 体现了肠道菌群与中医整体观理论密切相关[2]。中药大多通过口服发挥作用, 进入消化道不可避免会与肠道菌群相互作用。中药中极性化合物较多, 生物利用度较低, 口服后难以原型形式直接突破胃肠道屏障进入体内而发挥药效作用[3], 只有代谢为活性成分才能发挥作用。肠道菌群富含的β-葡萄糖醛酸酶、β-葡萄糖苷酶、辅酶A连接酶等可以通过水解、氧化、还原等反应以及异构化、聚合等特征性代谢反应, 将中药极性分子转化为极性更小、脂溶性更高的代谢产物, 加速中药吸收, 提高中药的生物利用度[4], 进而对机体产生不同的生物学效应。此外, 参与肝肠循环的药物经肝脏解毒后其代谢物随胆汁分泌到肠道后, 会与肠道菌群再次接触, 也可能再次被肠道菌群代谢[5]。同时中药中丰富的化学成分能够对肠道菌群的组成和丰度起到调节作用[6], 还能保护肠道黏膜功能, 对维持肠道微生态系统平衡起着关键作用[7]。研究也表明中药代谢成分可以直接作用于微生物酶代谢系统, 或是通过干预免疫应答, 调控肠道菌群, 达到治疗疾病的目的。肠道菌群介导的中药代谢成分也可通过干预肠道菌群正向调节有益菌及其代谢产物, 降低致病菌丰度及有害代谢产物, 恢复人体内环境的“阴阳平衡”[8]。

作为一个高度复杂的微生态系统, 肠道菌群介导的中药代谢过程非常复杂, 在中药临床疗效发挥方面扮演了重要角色。目前对于具体的肠道菌群介导中药成分的完整代谢途径, 即产生的代谢酶、发生的代谢反应和生成的代谢产物研究仍处于初步阶段, 肠道菌群介导中药代谢的规律尚不完全清晰。本文就研究较多的中药黄酮类、皂苷类、环烯醚萜苷类、木脂素类和醌类等6种结构类型成分的代谢进行总结, 归纳肠道菌群介导中药代谢的特点和影响因素, 探索肠道细菌介导中药的代谢规律, 为肠道菌群代谢中药成分的规律与机制研究提供依据。

1　肠道菌群介导中药不同结构类型成分的代谢

中药成分结构复杂多样, 不同的肠道细菌对其的代谢过程不同, 涉及水解、氧化 (裂变、甲基化、羟基化、氢化) 或还原 (脱水、脱氢、去甲基化、去羟基化) 等代谢反应及糖苷水解酶、氧化还原酶、裂解酶和转移酶等代谢酶, 具体代谢反应见表1[3,9-39]。以下主要阐述肠道细菌对黄酮类、皂苷类、环烯醚萜苷类等中药成分的代谢作用。

1.1　黄酮类成分　黄酮类化合物是指基本母核为2-苯基色原酮类化合物, 包括黄酮醇、二氢黄酮醇、异黄酮、查耳酮等类型, 多数以O-苷和C-苷形式存在, 少部分以游离态存在。黄酮苷在肠道细菌的作用下首先在肠道内水解生成苷元, 然后C环发生还原加氢, 其次C环中的O-C1键开环裂解, 生成酚酮类, 进而生成C6-C3型、C6-C2型酚酸及乙苯衍生物[40]。Hanske等[9]发现芹菜苷在肠道细菌细枝真杆菌和吉氏拟杆菌的代谢作用下转化成芹菜素 (4′,5,7-三羟基黄酮)、柑桔素 (4,5,7-三羟基黄烷酮) 和对羟基苯丙酸等主要代谢产物。

1.2　皂苷类成分　皂苷类成分在体内的生物利用度低, 肠内滞留时间长, 很难进入肠道直接发挥药效, 而是与肠道细菌作用后生成苷元入血发挥疗效[41]。肠道菌分泌的β-葡萄糖苷酶、β-木糖苷酶、α-鼠李糖苷酶、硝基还原酶等酶能够参与皂苷成分的转化, 发生羟基化、脱水、脱氢、去甲基化、去糖基化等代谢反应, 其中逐级水解脱糖生成次级糖苷或糖苷是苷类水解的主要方式[42]。Xiao等[21]采用变形菌门调节糖苷酶活性来影响三七总皂苷的去糖基化代谢, 发现变形菌门可以将三七皂苷R1转化为脱氢原人参三醇; Yan[15]在大鼠粪便和盲肠内容物中发现柴胡皂苷可先被肠道E.SP.A-44菌产生的SHGase酶水解为前柴胡苷元, 再通过PHFase0酶转化为柴胡苷元。

1.3　环烯醚萜苷类成分　环烯醚萜类成分属于单萜类化合物, 基本碳架含有10个碳, 即2个异戊二烯单位构成, 根据其环戊烷是否开裂, 分为环烯醚萜类和裂环醚萜类。肠道细菌首先通过产生β-葡萄糖苷酶, 催化环烯醚萜脱去糖基形成苷元, 然后半缩醛部分开裂, 醛基与肠道细菌氮代谢产生的氨进行加成反应, 最终生成含氮化合物[40]。Ke等[28]将富含大鼠肠道菌群的培养液与药物在厌氧条件下共同孵育24 h后, 芍药苷通过脱葡萄糖、脱苯甲酰基和四元环裂解重排等多个途径被完全代谢为芍药内酯苷元、脱酰基芍药内酯苷、脱酰基芍药内酯苷元和芍药内酯B等。

1.4　木脂素类成分　木脂素由两分子苯丙素衍生物聚合而成, 多呈游离状态, 少数与糖结合成苷。亚麻籽木脂素、罗汉松脂素、牛蒡苷等木脂素在肠道菌群的作用下, 通过糖苷水解、脱甲基、脱羟基、不对称加氢、环合等过程代谢为具有生物活性的肠内脂 (enterolactone, ENL)、肠二醇 (enterodiol, END)[43]。Quartieri等[32]发现亚麻木脂素可在肠道菌群的作用下去糖基化生成开环异松木醇, 开环异松木醇进一步发生脱羟基、去甲基化, 生成ENL和END。

1.5　醌类成分　醌类化合物具有醌式结构, 在植物体内以游离和结合的方式存在。醌类成分在肠道细菌的

Table 1 Intestinal flora-mediated the metabolism of Chinese medicines

Component	Botany	Typical compound	Associated intestinal bacteria	Enzyme	Main reaction	Main metabolite
Flavonoid[3,9-13]	Rue	Rutin Hesperidin	*Bifidobacterium catenulatum* *Pseudocatenultum*	*α*-*L*-Rhamnosidase	Deglycosylation Fissile	Aglycones
	Astragalus membranaceus	Quercetin Quercitrin	*Pediococcus* Q-5 *Streptococcus* S-3 *Bacteroides* JY-6 *Bifidobacterium* B-9 *Fusobacterium* K-60	Glucuronosyl transferase Biphasic enzymes such as UDPGT Specific glucosidase	Deglycosylation Aldolization	Aglycones
	Scutellaria baicalensis	Baicalin	*Lactobacillus brevis*	*β*-Glucosidase	Deglycosylation	Baicalein Oxylin A
Isoflavone[14]	*Pueraria lobata*	Puerarin	*Eubacterium rectale* Prevot A-44 *Streptococcus faecium* Orla-Jensen S-9 *Bifidobacterium longum* Reuter H1 *Corynebacterium* Niu-O16 *Eggerthella* sp. YY7918 *Eubacterium microcladum*	–	Hydrolysis	2-(4-Hydroxyphenyl)propionic acid
Triterpenoid saponins[15-27]	Notoginseng	Notoginseng saponin R1	Proteobacteria sp. Bacteroidetes sp.	*β*-Glucosidase *β*-Xylosidase Redox enzymes	Deglycosylation Dehydrogenation Oxidization Demethylation	Dehydroprotopanaxatriol
	Ginseng	Ginsenoside Rb1 Ginsenoside Rb2 Ginsenoside Rc	*Bifidobacterium* H-1 *Fusobacterium* K-60 *Bacteroides* JY-6 *Eubacillus* A-44 *Bifidobacterium* K-506	*β*-Glucosidase *β*-Xylosidase *α*-Arabinofuranosidase *α*-Arabinopyranosidase	Deglycosylation	Monoglycosylated ginsenoside compound K or protonaphthalenediol ginsenoside
	Ginseng	Ginsenoside Rg3 Ginsenoside Rg5 Ginsenoside Pk1 Ginsenoside Re Ginsenoside Rg1 Ginsenoside Rf	*Fusobacterium* K-60 *Bacteroides* JY-6 *Eubacillus* A-44 *Bacteroides* HJ-15	*α*-Rhamnosidase *β*-Glucosidase	Deglycosylation	Ginsenoside Rh1, Rh2, Rh3 Ginsenoside Rk2 or PPD Ginsenoside F1 Protoginsenoside alcohol
	Bupleurum	Saikosaponina Saikosaponind and its ringopening reduction products	*Bifidobacterium* sp. Saiko-1 Bifidobacterium sp. Saiko-2 *Eubacterium* sp. A-44	*β*-*D*-Glucosidase *β*-*D*-Fucosidase	Deglycosylation Dehydration	Sapogenin
	Chinese horse chestnut *Aesculus wilsonii*	Escin Ia	*Lactobacillus brevis* II-46	Lactobacillus shortus crude enzyme	Deesterification	Isoaesculin-I Decacylated aesculin-I *β*-*O*-Crotonyl proaescin Protoaesculin

Continued

Component	Botany	Typical compound	Associated intestinal bacteria	Enzyme	Main reaction	Main metabolite
	Glycyrrhiza	Glycyrrhizin	*Eubacterium* sp. GLH *Ruminococcus* sp. PO1-3 *Clostridium innocuum* ES24-06 *Streptococcus* sp. LJ-22	–	Hydrolysis	Enoxolone
Iridoid glycosides[28-31]	*Rehmannia*	Catalpol	*Bacteroides* sp.45 *Enterococcus* 43-1 *Enterococcus* 8-2	β-Glucosidase	Deglycosylation Acetylationdimethylation Hydroxylation	Catalpol glycoside M1 Nitrogencontaining catalpol glycoside M4 Acetylated catalpol glycoside M2 Hydroxylated catalponin M3
	Gardenia	Glycosides Geniposide	*Fusobacterium nucleatum* Knorr *Bacteroides fragilis* *Peptostreptococcus* *Anaerobius*	–	–	Gardenia alkaloid Genipinine
Lignans[32,33]	*Linum usitatissimum*	Secoisolariciresinol diglucoside Pinoresinol Flaxseed	*Eubacterium* sp. SDG-2 *Ruminococcus bromii* *Ruminococcus lactaris*	–	Deglycosylation Demethylation Dehydroxylation	Enterodiol Enterolactone
	Burdock seed	Arctinoside	*Blautia* sp. AUH-JLD56	–	Deglycosylation Demethylation	Arctigenin Desmethylarctigenin
Quinones[34-36]	Arnebiae radix	Shikonin	*Bacteroides fragilis* *B. adolescentis* *B. breve* S-2 KZ 1287 *B. bifidum* aE319 *B. longum* IV-55 *C. butyricum* *C. innocuum* ES 24-06 *C. innocuum* KZ-633 *C. perfringens* To-23 *E. coli* O-127 *F. nucleatum* G-0470 *Gaffkya anaerobia* G-0608 *K. pneumoniae* ATCC 13883 *L. brevis* II-46 *L. acidophilus* ATCC 4356	–	Dehydrationdehydrocondensation (intramolecular cyclization)	Metaboshikonin I and II Shikometabolin A and B
	Rheum officinale	Rhein	*Bacteroides* sp. RHEIN-I *Bacteroides* sp. RHEIN-II	–	Reduction (intramolecular cyclic condensation) Glycosidic hydrolysis	Anthrone rhein Glucoside

Continued

Component	Botany	Typical compound	Associated intestinal bacteria	Enzyme	Main reaction	Main metabolite
	Sennae folium	Ennosides A	*Clostridium sphenoids*	*β-D*-Glucosidase	Deglycosylation	Sennogenin
		Sennosides B	*C. butyricum*		Condensation	Anthrone rhein
			B. adolescentis		Reduction	
			Eubacterium limosum			
			Eubacterium lentum			
			C. perfringens			
			L. brevis			
Alkaloids[37-39]	Aconiti Radix	Aconitine	*Bacteroides fragilis*	Cytochrome P450 enzyme	Esterification	6-O-Demethylaconitine
	Aconiti Kusnezoffii Radix		*K. pneumoniae*	Carboxylesterase	Acetylation	16-O-Desmethylaconitine
	Aconinti Lateralis Radix Praeparata		*C. butyricum*			Aconitine
						Hypaconitine
	Dutchman's log	Aristolochic acid I	*Staphylococcus aureus*	–	Amidation	Aristolactam IdIhydroberberine
		Berberine	*Enterococcus faecium*		Demethylation	
			Enterococcus faecalis		Dehydroxylation	
			Enterobacter cloacae			
			E. coli			
			Acinetobacter baumannii			
			Lactobacillus casei			

作用下先被水解为苷元, 然后蒽醌苷元加氢发生氢化反应, 或者进一步发生乙酰化反应[44]。大黄酸可在肠道细菌*Bacteroides* sp. RHEIN-I, *Bacteroides* sp. RHEIN-II的作用下发生还原和糖苷键水解反应代谢转化为大黄酸蒽酮葡萄糖苷[34]。紫草中的紫草醌可在*Bacteroides fragilis* ss. *thetaotus*, *B. adolescentis*, *B. breve* S-2 KZ 1287等多种细菌的作用下脱水脱氢缩合生成单体(metaboshikonin I and II) 和二聚体 (shikometabolin A and B)[35]。

1.6　生物碱类成分　生物碱是含氮的碱性有机化合物, 大多有复杂的环状结构, 氮素多包含在环内。双酯二萜类生物碱在肠道细菌的作用下可以发生羟基化、脱氧、去甲基化及C-8位与长短链脂肪酸的酯交换过程等, 完成生物转化[37]。Gao等[22]首次利用软电离串联质谱技术研究了乌头碱在人肠内细菌中的生物转化规律, 研究表明, 乌头碱可被肠道细菌*Bacteroides fragilis*, *K. pneumoniae*, *C. butyricum*介导转化为6-O-去甲基乌头碱、16-O-去甲基乌头次碱、乌头原碱、乌头次碱, 细胞色素P450酶、羧酸酯酶参与代谢发生酯化和乙酰化作用[38]。

2　肠道菌群介导中药成分代谢的特点

2.1　不同细菌菌株促进同一化合物代谢　部分细菌如直肠真杆菌*Eubacterium rectale* revot A-44、屎肠球菌*Streptococcus faecium* Orla-Jensen S-9和游离双歧杆菌*Bifidobacterium longum* Reuter H1可以将葛根素转化为大豆苷元[14]。大豆苷可以被几乎所有的肠道菌水解。芒柄花苷能被人体多种肠道细菌代谢产生去甲基化产物、羟基化产物、氢化产物及去糖基化产物等7种代谢产物[45]。此外, 肠道内不同的细菌可以相互作用, 协同促进某一特定化合物的代谢, *Bifidobacterium* K506、*Eubacterium* A-44、*Prevotellaoris*、*Fusobacterium* K-60和*Paecilomyces bainier* sp. 等细菌通过协同作用共同参与人参皂苷成分代谢[46]。

2.2　单个细菌菌株转化不同的化合物　单个细菌菌株可以通过产生不同类型的酶或调控不同的代谢途径转化多种不同的化合物, 表现出多样化的代谢能力。多种菌株具有*β-D*-葡萄糖苷酶活性, 如*Bifidobacterium adolescentis*、*Bifidobacterium longum*、*Enterococcus faecalis*、*Bacteroides ovatus*等[47], 而*β-D*-葡萄糖苷酶的底物特异性较差, 可以广泛裂解含C-O、C-S、C-N和C-F等*β*-糖苷键的苷类化合物[48], 实现了单个菌株介导了不同的代谢反应。细枝真杆菌在体外可通过去糖基、加氢、环开裂转化芦丁 (槲皮素-3-*O*-芸香糖) 和芹菜苷两种不同结构的化合物[40]。

2.3　肠道菌群介导中药代谢具有结构特异性　肠道

细菌在介导的代谢活性和代谢产物的选择上存在差异, 即肠道菌群对中药代谢呈现结构特异性。如糖苷类成分通过逐步水解代谢, 水解产物继续通过骨架保留修饰 (如三萜苷)、骨架裂变 (如类黄酮类) 或者骨架重塑 (如环烯醚萜苷类) 过程进一步转化[49]。Li 等[50]将乌头碱、中乌头碱、次乌头碱在健康大鼠粪便的GAM培养基中培养7天后, 产生了包括胺醇型、单酯型及酯型生物碱的代谢产物。脂型生物碱的产生主要通过肠内菌中酶的作用C-8位乙酰基水解, 之后在C-8位的羟基与肠内菌中不同的短链脂肪酸结合。胺醇型和单酯型生物碱为母体化合物的分解产物, 主要通过脱乙酰基、脱苯甲酰基和脱氢基反应。山莨菪碱与东莨菪碱虽来源不同但结构相似, 山莨菪碱结构中醇部分在6位有一个*β*-取向的羟基, 使山莨菪碱分子极性增强, 难以通过血脑屏障, 而东莨菪碱的醇部分在6,7位间有一个*β*-取向的氧桥基团, 使东莨菪碱的脂溶性增强, 易进入中枢神经系统。有报道将山莨菪碱、东莨菪碱分别与大鼠肠内菌体外厌氧温孵培养后, 山莨菪碱经脱水及水解代谢为脱水山莨菪碱、6*β*-羟基托品和托品酸, 东莨菪碱水解为莨菪品[51,52]。再如, 具有不同类黄酮骨架的杂环吡喃酮, 即黄酮、黄酮醇和异黄酮, 被肠道微生物选择性地解离生成C6-C3酚酸、C6-C2酚酸和乙基苯酚衍生物[53]。

根据糖苷的苷元结构、结合的糖基种类以及糖基连接到苷元上的位置不同, 对其产生水解作用的糖苷酶也不同。肠道菌群的主要酶系为*β*-*D*-葡萄糖苷酶与*β*-*D*-葡萄糖醛酸苷酶等。*β*-*D*-葡萄糖苷酶是糖苷类成分水解的常见酶, 能水解结合于末端非还原性的*β*-*D*-葡萄糖苷键, 释放出*β*-*D*-葡萄糖和相应的配基, 同时参与糖酵解途径, 是参与双歧杆菌糖代谢的有关酶系之一[54]。而肠道菌群中*β*-*D*-葡萄糖醛酸苷酶活性的表达只在一些梭菌聚集的厚壁菌内, 可以从糖苷链上非还原的聚多糖端裂解*β*-*D*-葡萄糖醛酸残基, 催化各种类型的*β*-*D*-葡萄糖醛酸苷水解, 该酶为参与Ⅱ相代谢反应的重要酶系[41]。

3　肠道菌群介导中药代谢的影响因素

正常情况下, 肠道菌群相对稳定, 其对中药成分的代谢依赖于菌群的种类、比例、产酶类型等。当种属、地域、生理病理状态等机体的状态因素发生变化, 肠道菌群会受到影响, 进而影响肠道菌代谢[55]。

3.1　机体内部环境变化影响肠道菌群介导中药代谢　肠道菌群介导的中药代谢过程中, 机体的遗传背景或病理状态会影响肠道菌群对中药的代谢。豆科植物中的大豆苷元经肠道菌群代谢可以生成雌马酚[56], 雌马酚的抗癌作用要显著强于大豆苷元, 但是只有1/3的人能将大豆苷元代谢为雌马酚[57], 该过程具有个体差异性。研究还发现病理状态紊乱的肠道菌群会影响中药的代谢, 与正常机体状态存在代谢差异。黄芩提取物在2型糖尿病模型小鼠中, 代谢物黄芩素的含量明显高于正常小鼠, 且代谢物木蝴蝶素A仅存在于模型组, 正常组还产生了氢化和甲基化的黄芩苷代谢物[58]。

3.2　机体外部环境变化影响肠道菌群介导中药代谢　当机体外部环境发生变化时, 敏感肠道菌就会被抑制, 未被抑制的肠道菌就会快速繁殖引起菌群失调, 形成破坏生理性、病理性组合的现象, 如Guo 等[59]研究显示林可霉素诱导的大鼠肠道菌群失调会影响体内人参皂苷Rg3的肠道脱糖代谢, 这可能是因为抗生素处理后*β*-葡萄糖苷酶活性降低, 影响人参皂苷Rg3在肠道菌群中的脱糖基代谢, 进而改变了人参皂苷Rg3及其脱糖基代谢产物人参皂苷Rh2吸收入血后的药代动力学行为。研究发现, 高原低氧环境下, 大鼠肠道菌群表现为双歧杆菌减少, 大肠埃希菌增加[60]。食物中含有蛋白质、脂肪及碳水化合物等多种成分, 这些成分的摄入都会使人体内肠道菌群发生变化。不健康的高脂饮食能够导致肥胖的关键原因之一就是肠道菌群的结构发生了改变。Liu 等[61]对控制饮食的小鼠肠道微生物菌群结构信息进行了分析, 发现高脂饮食的小鼠肠道中乳酸杆菌、双歧杆菌及肠球菌的数量显著减少。

4　肠道菌群介导中药代谢的意义

4.1　增强吸收, 提高疗效　肠道菌群能够增强中药成分吸收、提高药物疗效, 相关研究较多。大肠杆菌菌株产生的姜黄素转化酶, 可转化姜黄素为二氢姜黄素和四氢姜黄素[62,63]。糖苷由于不能被普通的消化酶代谢, 很难通过小肠壁, 因此难以被机体利用, 双歧杆菌和类杆菌可以产生*α*-葡萄糖苷酶和*β*-葡萄糖醛酸酶[64], 能够将糖苷转化为极性更低、亲脂性更强的次级糖苷, 利于吸收入血[65]。

4.2　减毒或增毒作用　肠道菌群除了能够转化中药的有效成分, 将其代谢为新的生物活性代谢物外, 还能对中药中的有毒成分产生减毒或增毒的作用。雷公藤甲素在体内代谢会引起肝损伤, 对生殖系统、循环系统和免疫系统均有一定的毒副作用, 研究发现三七和地黄在体内经肠道菌群代谢产生的活性成分能通过调控核呼吸因子1及其下游基因线粒体转录因子A, 有效降低雷公藤甲素诱导的L-02细胞肝毒性[66]。对香加皮中的杠柳毒苷进行研究发现其经肠道菌群代谢后会生成杠柳次苷, 能够减缓毒性从而增强药效[67]。动物实验表明, 苦杏仁苷注射给药后在大鼠体内主要以原型分布和排泄, 而灌胃给药后肠道菌群水解苦杏仁苷的糖苷键, 释放出苦杏仁腈, 引起毒性反应[68], 说明肠

道菌群是导致苦杏仁苷产生毒性的关键因素。

5 结语与展望

随着中药学、微生物学和分析技术的发展, 肠道菌介导中药代谢的研究不断深入。肠道菌群通过编码多种酶, 影响口服中药在体内的吸收、代谢、转化等过程, 进而影响中药疗效的发挥。研究肠道菌对中药各类成分代谢规律有利于了解其在体内的整个代谢过程, 阐明发挥药效的物质基础。然而, 肠道菌群是非常丰富多样性的群体微生物, 中药又具有多种类、多成分、多靶点等特点, 肠道菌群介导中药代谢的特点和影响因素非常复杂, 目前中药中各类化学成分的代谢规律、参与代谢的细菌种类及其参与的酶仍不完全清晰, 尤其是复方中不同成分对肠道不同细菌生长的抑制或促进作用存在差异, 会导致细菌种类和数量的变化, 这种变化又反过来影响中药复方的成分代谢。综上所述, 肠道菌群代谢药物的研究仍面临巨大挑战, 建立批式发酵模型、人体肠道芯片模型 (HITChip) 等体外肠道微生态模型, 将越来越多的分析技术和测试手段如肠道菌群孵育技术、分离培养技术、基因检测技术和质谱检测技术等应用于肠道菌群的代谢研究至关重要。本文总结肠道菌群介导中药黄酮类、皂苷类、环烯醚萜苷类等成分的代谢途径, 阐述肠道细菌介导中药的特点, 发现菌群与化合物的相互作用也存在一对多和多对一, 同时具有结构特异性, 这有利于深入了解肠道菌群的代谢功能, 认识宿主、菌群及药物之间复杂的互作关系, 丰富中医药理论, 提高中药的药理作用和临床疗效, 加快中药现代化进程。

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