

## · 专家论坛 ·

## “食药同源”的生物学原理

丁劲文<sup>1</sup>, 迟湘胤<sup>1</sup>, 张 玉<sup>1</sup>, 王璐璐<sup>2</sup>, 蒋建东<sup>1,2\*</sup>, 林 媛<sup>1\*</sup>

(1. 中国医学科学院、北京协和医学院药物研究所, 天然药物活性物质与功能国家重点实验室, 北京 100050;  
2. 中国医学科学院、北京协和医学院医药生物技术研究所, 北京 100050)

**摘要:** 随着社会快速发展以及“健康中国”战略的提出, 人民群众对生活质量和健康水平的需求日益增长, “食药同源”的理念也逐渐受到人们重视。“食药同源”概念在我国历史悠久, 是我国传统医学中食疗、药膳、养生及治未病等多种思想的凝练。“食药同源”具有坚实的科学基础, 其活性物质成分具有多种类、多机制和多靶点等特点, 经过口服吸收及代谢转化后, 发挥其生物学效应, 而且安全性好。本文从化合物、生物大分子及肠道菌群与肠道这三方面解析多种“食药同源”物质发挥药理活性的化学基础及生物学原理; 并以肠道菌群为主要研究内容, 重点分析了几个经典“食药同源”物质的生物学原理; 论述了研究“食药同源”的科学意义。本文旨在从现代医药学的角度来理解和探索“食药同源”这一传统理念的科学内涵, 为新药研发及人类健康发展提供理论参考。

**关键词:** 食药同源; 治未病; 肠道菌群; 化学基础; 药理作用; 标本兼治

中图分类号: R966 文献标识码: A 文章编号: 0513-4870(2024)06-1509-10

## Biological principles of "food and medicine homologous"

DING Jin-wen<sup>1</sup>, CHI Xiang-yin<sup>1</sup>, ZHANG Yu<sup>1</sup>, WANG Lu-lu<sup>2</sup>, JIANG Jian-dong<sup>1,2\*</sup>, LIN Yuan<sup>1\*</sup>

(1. State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China; 2. Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, China)

**Abstract:** With the rapid society development and broad recognition of "Healthy China", the demands for good life and health are increasing. Accordingly, the concept of "food and medicine homologous" have been attractive. The concept of "food and medicine homologous" has a long history in China, and is an essence of various ideas in traditional Chinese medicine, such as diet therapy, medicated diet, regimen and preventive treatment of disease, representing an important field in health science. Many studies have found that the active ingredients of "food and medicine homologous" substances are multiple types, multiple mechanisms and multiple targets, exerting their biological effects after oral administration and chemical or metabolic transformation. In this review, the chemical basis and biological principles of various "food and medicine homologous" substances were summarized as compounds, biological macromolecules and intestinal flora. By focusing on the intestinal flora, we discussed the detailed biological principles of several classic "food and medicine homologous" substances. The scientific significance of "food and medicine homologous" concept were also discussed. This review explores the concept of "food and medicine homologous" from the perspective of modern medicine, in order to provide insights for future drug development and human health.

**Key words:** food and medicine homologous; preventive treatment of disease; intestinal flora; chemical basis; pharmacological activity; Biao Ben Jian Zhi

收稿日期: 2024-03-28; 修回日期: 2024-04-22.

基金项目: 中国工程院战略研究与咨询项目 (2023-XZ-88); 中国医学科学院医学与健康科技创新工程重大协同创新项目 (2022-I2M-1-016).

\*通讯作者 Tel: 86-10-63017906, E-mail: jiang.jdong@163.com; linyuan@imm.ac.cn

DOI: 10.16438/j.0513-4870.2024-0284

随着科技的高速发展,研究者对祖国医学中一些观念也有了更多和深入的认识,“食药同源”是个例子。在我国传统医学中,某些食物被证实具有药用价值,可以通过食用来达到保健或治疗的目的,因此提出“食药同源”(food and medicine homologous)概念<sup>[1]</sup>。“食药同源”的理论认为食物和药物常具有相同的起源,因为它们之间存在相似或重叠的物质成分;这些物质不仅提供了人体必需的营养成分和能量,还可以帮助人们预防和改善慢性疾病以及其他健康问题。这种概念阐明了食物与药物之间的密切联系,提出了食物对人体健康的积极影响,因此有人说,最好的药物在餐桌上<sup>[2]</sup>。过去200年,由于现代化学、生物学、药学和医学的出现和快速进步,还原论思想形成主导,研究内容更注重分子细节,而逐渐淡化了“人与自然和谐相融”的道理。本文希望从现代药学的角度去触及这个传统概念的科学精髓,为今后更好的新药研究,以及对健康的探索提供参考。

## 1 “食药同源”的起源

食物为人体提供能量和营养,满足人类生存的基本需求。某些食物还可以被用作治疗疾病,校正人体的机能,最常见的如素食,有助于减脂降糖等。从生物学角度看,食物与药物常无明显界限(如维生素),一些食物和药物之间存在着相似或重叠的化学成分及生物学活性。所以,在一定的用法和用量下,某些可食用的植物、微生物、动物或矿物等物质也可以用于治疗疾病,被中医称为“食药同源”,也叫做“药食同源”或“医食同源”<sup>[3-5]</sup>。

“食药同源”的概念由来已久。自春秋战国时期起,有关食物和药物的传世著作开始逐渐丰富起来。《黄帝内经》是中国第一部关于医学理论的专著,书中记载了“毒药攻邪,五谷为养,五果为助,五畜为益,五菜为充,气味合而服之,以补精益气”,以及“食宜同法”、“药以祛之,食以随之”等说法,即认为谷物蔬果补充人体精气,以辅助药物治疗疾病,不仅奠定了食疗的理论基础,而且记载了许多关于食疗的配方<sup>[4]</sup>;东汉张仲景所著的《金匮要略》中也采用了大量的饮食调养方法来配合治疗;至唐代,孙思邈的《千金方·食治》中记载“安身之本,必资于食;救疾之速,必凭于药”、“食能排邪而安脏腑,悦情爽志以资气血”、“夫为医者,必须先洞晓病源,知其所犯,以食治之;食疗不愈,然后命药”等,这表明食物对人体的调节功能与药物不同,食物性质平和,缓慢补益,而药物性质猛烈,可快速祛病<sup>[6]</sup>;宋代官方修订的《太平圣惠方》则专设“食治门”,对食疗方剂进行论述,往后又有《饮膳正要》《本草纲目》《清宫秘方》等医药论著,均存在对食药同源的概念

运用和实践发展<sup>[5]</sup>。

随着国家对食药同源、食养文化等传统医学的推广,“食药同源”理念已经被越来越多的国人所熟悉与推崇。从广义上看,食药同源物质是基于这一理念的指导,在我国传统中医学和食疗学中使用的、既可食用又可药用的中药材物质。狭义的食药同源物质是从广义的食药同源物质中选择已有国家中药材标准,经过食品安全风险评估,认为长期服用对人体无害的动物和植物可使用部分。2002年,卫健委发布了87种食药同源物质名录;之后,食药同源物质名单不断扩展,直至2021年11月15日,国家卫健委食品安全标准与监测评估司发布了《按照传统既是食品又是中药材的物质目录管理规定》的通知,我国食药同源物质已达到102种,未来还将根据科学研究的进展逐步扩充。目前,我国已经对既是食品又是中药材的物质以及可用于保健食品的中药名单进行规定,前者共102种物质,包括山药、山楂、枣、姜、栀子等;后者共113种物质,包括人参、白芍、巴戟天、五味子等。

绝大部分食药同源物质都取之于自然,经过现代科学的多方验证,应用于医学实践。如山药中的山药多糖可用于降糖、抗氧化,酸枣仁中的酸枣仁皂苷能够安神和改善睡眠等,这不仅体现了食药同源理念的正确性,更体现了人与自然相互连接、相互和谐的基本道义。食药同源理念提倡“治未病”,即在日常饮食中对身体机能进行调节,防病于未然。同时,某些食药同源物质在经过机体代谢后往往产生多种药理效应,达到数管齐下、标本兼治的效果。“食药同源”这一古老智慧的科学含义,可以作为现代人类健康生活的指南,通过精确了解食药同源物质的成分和效应,使之在现代医学和健康领域得到更加有效的应用,在日常膳食中逐步提升人们的生活质量和健康水平。

## 2 “食药同源”的中医药实践

在中医药学理论和实践中,许多药物都源自食物。如生姜、葱、蒜等常见的食材在中医中也被用作治疗感冒、消化不良等疾病的药物<sup>[7,8]</sup>;枸杞、山药、燕窝等食品在中医中也被用作补肾益气、滋阴润燥等方面的药物<sup>[9-11]</sup>。近年来,随着人们对健康和营养的关注不断提高,越来越多的食品也被发现具有一定的药用价值。如黑豆、葡萄、红枣等食品中含有丰富的抗氧化剂和营养成分,可以用于调节血糖、降低血脂和增强免疫力等<sup>[12-14]</sup>;紫苏、芝麻、胡麻等食品中富含维生素E、不饱和脂肪酸等营养素,可以用于抗氧化和保护心血管健康<sup>[15,16]</sup>。需要注意的是,虽然一些食品具有药用价值,但并不意味着它们可以完全替代药物进行治疗,应该遵循医嘱,根据具体情况和症状选择适当的食材,同时

遵循适量、适时、适法的原则,以避免出现不良反应或者贻误病情。同时,一些中药材也可以作为食物使用。如常见中药材中的枸杞是一种食物,富含多糖、维生素、矿物质和抗氧化剂,被广泛用于保健和滋补;黄芪也是一种食材,它富含多种氨基酸、多糖和微量元素,被用于提高免疫力和调理身体;当归被广泛用于食物烹饪,它富含铁、维生素和矿物质,常用于调理女性身体和补血;莲子富含蛋白质、脂肪和淀粉,常用于补养身体和滋补食品。

### 3 “食药同源”的生物学原理

口服药物和食物及所含化学物质都需要在胃和肠道进行消化、转化、代谢和吸收,吸收入血的物质还可能在肝脏和血液中与CYP450等宿主酶相互作用,然后进入各组织器官;而难以吸收的成分则在肠道与肠道菌相互作用(纤维素、黄酮类、生物碱等),产生不同的微生物代谢产物(短链脂肪酸等)再进入循环发挥作用。它们有的组分或代谢物主要为身体提供营养和能量(氨基酸、葡萄糖、维生素、微量元素等),而有的组分或代谢产物则提供给机体治疗的效果及或不良反应(如生物碱)。就口服的途径而言,因为有着非常相似的代谢转化过程,为食药同源的原理解析铺垫了基础;而更进一步的科学基础还来自以下几个方面。

**3.1 “食药同源”化合物** 某些食物中的活性成分与药物中的成分相似或相同,这使得它们具有类似的药理作用。植物中富含的生物碱类、黄酮类、酚类、皂苷类等化学成分可通过抗氧化、抗炎、调节免疫功能和其他机制促进机体健康<sup>[17-20]</sup>,而表1<sup>[16,21-44]</sup>列出的只是一些常见例子。如生姜含有姜黄素,具有抗炎和抗氧化特性,它可以缓解消化不良、减轻恶心和缓解关节炎疼痛;大蒜含有硫化物,如大蒜素,被认为具有抗菌、抗炎和氧化的特性;绿茶富含多酚类化合物,如儿茶素和咖啡碱,具有抗氧化、抗炎、抗菌和降低胆固醇的作用,绿茶还可以提供一些咖啡因,具有提神的效果;荞麦富含维生素、微量元素及矿物质等多种营养成分,具有抗氧化、降血糖和降血压等多种功效;铁皮石斛中的石斛碱具有保护神经系统、清热止痛及抗甲型流感病毒等多种作用。

**3.2 “食药同源”生物大分子** 除小分子化合物外,多糖及核酸类等成分也是食药同源物质中不可或缺的大分子活性成分群,广泛存在于食品菜肴或药方汤剂中。然而这些大分子成分具有多种生物活性,还可作为人体基因表达的调节剂,促进人体健康。

多糖是一种广泛存在于食药同源物质中的天然生物大分子。研究表明,多糖具有促进糖原合成、增加缺

**Table 1** Classification and biological activities of representative "food and medicine homologous" substances. SCFAs: Short-chain fatty acids

Category	Source	Active ingredient	Biological activity	Ref.
Alkaloid	Mulberry leaf	Mulberry leaf alkaloids	Inhibits glycogenolysis, antiviral infection, etc	[21]
	Officinal dendrobium stem	Dendrobine	Anti-neuronal apoptosis, etc	[22]
	Malt	Malt alkaloids	Treatment of hyperprolactinemia, etc	[23]
	Portulaca oleracea	Oleracein E	Anti-inflammatory, improve intestinal inflammation, etc	[24]
	Lotus	Nuciferin	Regulates disorders of lipid metabolism, etc	[25]
Flavonoids	Ginger	Turmerone	Anti-tumor, etc	[26]
	Fructus hippophae	Seabuckthorn flavone	Anti-inflammatory, improve insulin resistance, etc	[27]
	Ginko	Total Ginkgo flavone	Promotes the proliferation of human fibroblasts, etc	[28]
	Shiso	Apigenin, luteoline	Antibacterial, anti-allergic, etc	[29]
	Lobed kudzu vine root	Puerarin	Regulates intestinal flora, SCFAs, etc	[30]
Phenols	Green tea	Catechin, caffeine	Antioxidant, anti-inflammatory, antibacterial and cholesterol-lowering, etc	[31]
	Ma-yuen Jobstears seed	Gallic acid	Anti-tumor, antibacterial, etc	[32]
	Lycium barbarum	Procyanidin	Antioxidant, inhibition of fatty acid synthesis, etc	[33]
	Grape	Resveratrol	Antioxidant, anti-aging, etc	[34]
	Ginger	Curcumin	Inhibition of retinal neovascularization, etc	[35]
Saponins	Spine Date seed	Jujuboside	Calms the nerves, etc	[36]
	Ginseng	Ginsenoside	Regulates the central nervous system, anti-fatigue, etc	[37]
	Gardenia	Geniposide	Antioxidant, regulate lipid metabolism, etc	[38]
	Licorice	Licoricesaponin	Improve chronic liver injury, etc	[39]
	Grandiflorum	Platycoside D	inhibition of pathological neovascularization, etc	[40]
Others	Hawthorn	Maslinic acid	Regulates lipid metabolism, etc	[41]
	Garlic	Garlicin	Hypotensive, inhibits platelet clotting and improves blood circulation, etc	[42]
	Cassia seed	Aurantio-obtusin	Hypolipidemic, regulates cholesterol metabolism, etc	[43]
	Black sesame	Vitamin E, unsaturated fatty acid	Cardiovascular protection, etc	[16]
	Buckwheat	Trace element, minerals	Inhibits the formation of cholesterol and improves immunity, etc	[44]

氧耐受性及调节脂质代谢、改善肥胖等多种生物学活性。如黄芪多糖通过降低机体血清中乳酸积累并增加脑的氧储备来缓解疲劳,提高运动能力,同时还可以提高肝脏中超氧化物歧化酶和谷胱甘肽过氧化物酶活性,对机体中氧化应激具有保护作用<sup>[45]</sup>。灵芝多糖通过调节 LXR $\alpha$ -ABCA1/ABCG1 信号通路促进胆固醇逆转运,抑制脂肪生成并促进脂肪分解,同时抑制下丘脑中神经肽 Y 的活性,减少饥饿刺激信号的发出,进而降低食欲、减轻体重<sup>[46]</sup>。

有些食药同源物质中还含有核酸类生物大分子活性成分。其中,小 RNA (sRNA) 是一类重要物质,它属于非编码 RNA,转录后能够调节体内多种内源性基因的表达。而植物(如冬虫夏草等多种食药同源类植物) sRNA 是煎煮后,可能通过口服脂质汤剂体(sRNA、植物脂质、化合物分子及蛋白)的形式,实现跨物种进入体内,入肺入血,实现植物 sRNA 调控哺乳动物基因表达,发挥相应的生物学功能<sup>[47]</sup>。如红景天汤剂体中 sRNA (HJT-sRNA-m7) 能有效降低肺泡细胞中肺纤维化标志基因的表达,显示出较好的抗肺纤维化作用<sup>[48]</sup>;蒲公英汤剂体中 sRNA (PGY-sRNA-6) 能够抑制 NF- $\kappa$ B 介导的炎症信号通路的激活,发挥缓解急性肺损伤的作用<sup>[49]</sup>;半枝莲汤剂体中的 sRNA (BZL-sRNA-20) 能有效抑制细胞因子风暴中关键因子 TLR4 和促炎细胞因子,缓解新冠与细菌诱导的小鼠急性肺损伤<sup>[50]</sup>。

**3.3 “食药同源”物质与肠道菌群及对肠道免疫功能的调节作用** 肠道是食物消化吸收的主要场所,同时也是人体最大的免疫器官,发挥重要的免疫屏障功能<sup>[51]</sup>。肠道微生态稳态是一种主要由肠道菌群及其代谢物、肠上皮屏障、黏膜免疫屏障等因素组成的动态平衡状态,对于维持人体健康至关重要<sup>[52]</sup>。近年来,随着肠道微生态研究的兴起,食药同源物质与肠道菌群的相互作用逐渐引起人们的重视。

食药同源物质通过影响肠道菌群的丰度和组成,增加益生菌的数量,改善肠道菌群代谢产物,调控肠道稳态,从而达到预防或改善疾病的作用。如芹菜素、类黄酮、白藜芦醇、槲皮素等,可以通过增加有益菌嗜黏蛋白阿克曼氏菌 (*Akkermansia muciniphila*) 的相对丰度,从而增加肠道菌群有益代谢产物如短链脂肪酸 (short-chain fatty acids, SCFAs) 的水平,进而改善代谢,降低糖脂代谢紊乱的发生概率<sup>[53]</sup>;白藜芦醇可以通过增加乳酸杆菌和双歧杆菌的丰度,降低血清中氧化三甲胺 (trimethylamine oxide, TMAO) 的水平,调节胆固醇代谢和炎症反应,改善动脉粥样硬化<sup>[54]</sup>;决明子是一种常用的中药,常用于清热解毒和润肠通便,研究发

现,决明子能够改善肠道菌群的组成,增加有益菌如双歧杆菌的数量,同时减少有害菌如大肠杆菌等。而肠道菌群中,有一类特殊的菌群,即益生菌可以促进消化、增强免疫功能和改善肠道健康。一些食物本身含有益生菌或益生元,可以促进肠道菌群的生长和多样性。如酸奶、酸菜、酸黄瓜等发酵食品富含益生菌,豆类、蔬菜、水果、全谷物和纤维食物则是益生元的良好来源。

食药同源物质也可以通过肠道菌群来源的代谢酶进行生物转化,产生生物利用度更高的活性代谢物,进而发挥药理活性。如栀子豉汤中的栀子苷可以被真杆菌属产生的  $\beta$ -葡萄糖苷酶转化为京尼平活性成分,进而发挥抗抑郁作用<sup>[55]</sup>;人参中皂苷类成分可被双歧杆菌属、球菌属产生的  $\beta$ -葡萄糖苷酶、鼠李糖苷酶、木糖酶等糖苷酶水解,脱糖基生成活性更高的活性产物,从而发挥类似益生元的作用<sup>[56]</sup>。

此外,食药同源物质还可以通过调节肠道免疫细胞、维持肠道屏障完整性及纠正肠道炎症因子分泌紊乱等方式增强肠道免疫,改善肠道炎症,恢复人体健康。肠道作为人类重要的免疫器官,分布了 70%~80% 的免疫细胞<sup>[51]</sup>。在肠上皮层和固有层含有大量 T 淋巴细胞,其中,调节性 T (Treg) 细胞在维持肠道免疫稳态中具有关键作用。巨噬细胞具有独特的吞噬功能和杀菌活性,还可以行使抗原呈递功能等。食药同源物质及其活性成分通过增强肠道免疫细胞活性,调节淋巴细胞比例等提高肠道黏膜免疫功能及肠道屏障保护作用。因此,通过食药同源物质调节肠道免疫对维护人体健康十分重要。如山药主要活性成分薯蓣皂苷元可以通过上调肠道炎症反应部位的 Treg 细胞来介导免疫应答,减弱过敏原诱导的肠道炎症<sup>[57]</sup>;山药多糖还可以促进淋巴细胞的增殖和自然杀伤细胞的活性从而恢复肠道免疫状态<sup>[58]</sup>。枸杞多糖可显著提高巨噬细胞的活性,促进巨噬细胞与多糖或糖蛋白结合,从而分泌 IL-1 $\beta$ 、IL-6、TNF- $\alpha$  等炎症因子杀死肿瘤细胞,起到免疫调节作用<sup>[59]</sup>。此外,枸杞多糖还可通过刺激肠道黏膜中 B 细胞增殖产生分泌型免疫球蛋白 A (sIgA),与病原体表面抗原结合,保护肠道黏膜屏障的完整性,从而阻断病原体对人体的感染<sup>[60]</sup>。另外,灵芝多糖也可促进回肠中 sIgA 的表达,增强黏膜免疫屏障的保护作用,还可以显著提高 IFN- $\gamma$ 、IL-2 和 IL-4 的表达以发挥肠道免疫调节功能<sup>[61]</sup>。

#### 4 食药同源研究走进科学前沿的例子

**4.1 白芍** 白芍 (*Paeoniae Radix Alba*) 是一种常见的食药同源/可用于保健食品的物质,为毛茛科植物芍药 (*Paeonia lactiflora* Pall) 的干燥根。《本经》记载其能“主

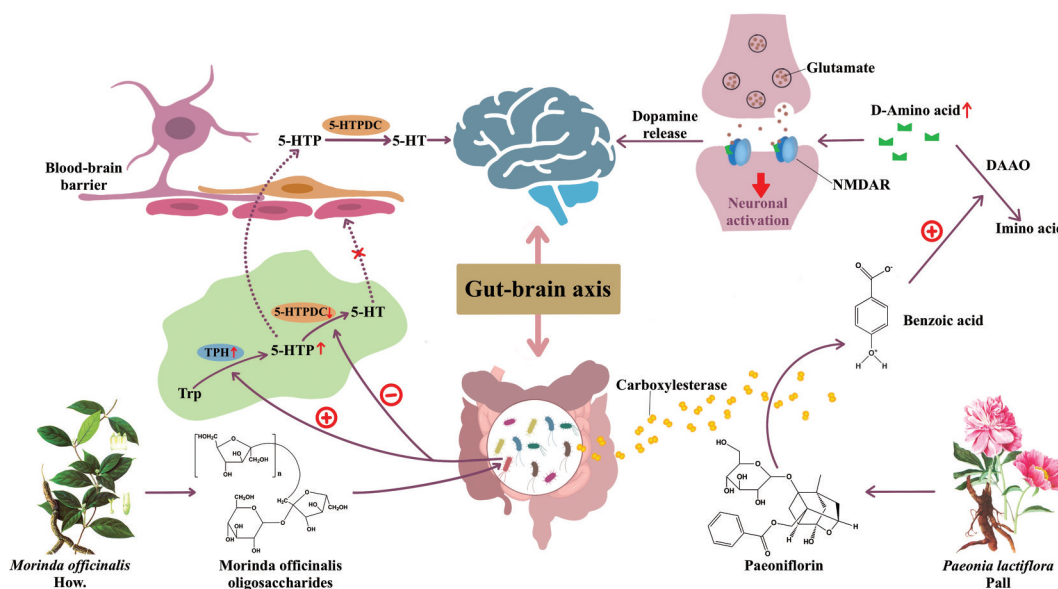
邪气腹痛、除血痹、破坚积寒热、止痛、利小便、益气”<sup>[62]</sup>。作为一种食药同源物质,白芍可通过煲粥、炖汤、煮茶、制酒等方式入膳,也可直接入药,如中药经典方剂逍遥丸中就含有白芍,其能够“养血敛阴,柔肝缓急”<sup>[63]</sup>。现代药理学研究表明,白芍中的白芍总苷是其发挥生物学活性的有效成分,而其中芍药苷(paeoniflorin)为主要成分<sup>[64]</sup>。芍药苷已经被证明具有多种药理功能,其中芍药苷的抗抑郁作用越来越受到研究人员的关注。

芍药苷的抗抑郁作用生物学原理主要和其与肠道菌群之间的相互作用有关<sup>[65]</sup>(图1)。作为一种脂溶性较低的单萜类苷,口服后芍药苷原型药的整体吸收率和生物利用度均较低,但可在厌氧环境下被肠道菌如双歧杆菌、嗜酸乳杆菌、金黄色葡萄球菌等中的羧酸酯酶(carboxylesterase)催化代谢后转化为活性成分苯甲酸,后者的血浆浓度及整体分布均提高,可以大量通过血脑屏障<sup>[65]</sup>。而苯甲酸作为一种D型氨基酸氧化酶(D-amino acid oxidase, DAAO)抑制剂,可以减少D型氨基酸(如D-丝氨酸)降解,后者作为N-甲基-D-天冬氨酸受体(N-methyl-D-aspartic acid receptor, NMDAR)的协同激动剂,其浓度水平的增加将改善NMDAR功能低下,从而刺激多巴胺神经元,增加多巴胺释放<sup>[66]</sup>。人体随机双盲试验显示,苯甲酸治疗可有效缓解受试患者的抑郁症状,改善其认知功能,减轻心理感知压力<sup>[66,67]</sup>。因此苯甲酸很可能是芍药苷通过肠道菌群作用发挥抗抑郁的重要代谢物。此外,芍药苷还可以调节肠道菌群组成,增加乳杆菌属(*Lactobacillus*)、毛螺

菌属(*Lachnospira*)、罗氏菌属(*Roseburia*)等有益菌的丰度<sup>[65]</sup>,它们的丰度变化很可能进一步增加了芍药苷的抗抑郁作用<sup>[68,69]</sup>。

**4.2 巴戟天** 巴戟天(*Radix Morindae Officinalis*)是一种经典食药同源/可用于保健食品的物质,来自于茜草科植物巴戟天(*Morinda officinalis* How.)的干燥根。其入膳可以通过与怀牛膝浸酒、与肉苁蓉或杜仲等煲汤,也可以红茶冲泡饮用,能够补肾壮阳、强体祛湿,和槟榔、砂仁、益智并称为我国“四大南药”<sup>[70]</sup>,其主要有效成分即是巴戟天寡糖(*Morinda officinalis* oligosaccharides)。由军事医学科学院药物研究所研制的巴戟天寡糖胶囊于2012年被批准上市,用于治疗抑郁症,是目前唯一以寡糖单体为主要成分的抗抑郁中药,对比研究显示其疗效并不弱于氟西汀(选择性5-羟色胺再摄取抑制剂),且不良反应较轻<sup>[71-73]</sup>。

研究表明,巴戟天寡糖与肠道菌群之间的相互作用或许是其产生抗抑郁效应的关键<sup>[74]</sup>(图1)。将巴戟天寡糖与SD大鼠肠道菌在体外进行共同培养,发现其可以通过提高肠道菌如丁酸梭菌中的色氨酸羟化酶(tryptophan hydroxylase, TPH)活性,同时降低5-羟色氨酸脱羧酶(5-hydroxytryptophan decarboxylase, 5-HTPDC)活性,对“色氨酸→5-羟色氨酸→5-羟色胺”这一代谢途径进行调节,使培养体系中的5-羟色氨酸水平升高。5-羟色氨酸作为5-羟色胺的合成前体,可以透过血脑屏障,在脑内被进一步代谢成5-羟色胺,进而能够改善抑郁动物的脑功能和抑郁行为<sup>[74]</sup>。进一步研究表明,巴戟天寡糖中的五糖是其抗抑郁的主要活



**Figure 1** Biotransformation mechanism of paeoniflorin and *Morinda officinalis* oligosaccharides associated with gut microbial. Trp: Tryptophan; 5-HTPDC: 5-Hydroxytryptophan decarboxylase; 5-HT: 5-Hydroxytryptamine; TPH: Tryptophan hydroxylase; 5-HTPDC: 5-Hydroxytryptophan decarboxylase; NMDAR: N-Methyl-D-aspartic acid receptor; DAAO: D-Amino acid oxidase

性成分,能够提高脑内色氨酸羟化酶和四氢生物蝶呤的水平,降低5-羟色氨酸脱羧酶的活性和维生素B6的浓度,从而促进脑内5-羟色胺的生成<sup>[74]</sup>。巴戟天寡糖还能够降低肠道菌群中与抑郁症发生相关的菌群丰度,包括苏黎世杆菌属、经黏液真杆菌属、狭义梭菌、毛螺菌等发挥抗抑郁作用<sup>[74]</sup>。

**4.3 人参** 人参 (Ginseng) 是五加科植物人参 (*Panax ginseng* C. A. Meyer) 的干燥根,始载于《神农本草经》,是应用最广泛的药用植物之一。自古以来,人参就有“百草之王”、“神仙草”和“不老药”等称号。如今,人参成为“食药同源”的养生上品,以人参为食材烹制的药膳越来越受到人们的青睐。如长寿药膳人参蜂蜜饮、补肝肾药膳人参枸杞粥、大补元气药膳人参鸡汤等。

人参中含有人参皂苷、多糖、挥发油、蛋白质等多种活性物质,人参皂苷 (ginsenoside) 是现阶段研究最广泛的活性成分,在抗炎、抗肿瘤、调节中枢神经系统、抗疲劳、延缓衰老等方面作用显著<sup>[75]</sup>。虽然人参皂苷的生物活性较低,但经过肠道菌群的生物转化,发现有289种人参皂苷(包括游离人参皂苷)的活性代谢物生物利用度显著提高<sup>[76]</sup>。其中,人参皂苷 Rb1 (ginsenoside Rb1) 作为人参皂苷中最主要的活性成分之一,在真杆菌属 (*Eubacterium*) 和双歧杆菌属 (*Bifidobacterium*) 作用下,能够从苷元 C-20 羟基位取代基的末端水解一分子葡萄糖 (glucose, Glc),从而产生中间代谢物人参皂苷 Rd (ginsenoside Rd)。人参皂苷 Rd 在拟杆菌属 (*Bacteroides*) 和乳杆菌属作用下,苷元 C-3 取代基的两分子 Glc 被水解,生成人参皂苷 CK (ginsenoside CK)。此外,在拟杆菌属和梭杆菌属 (*Fusobacterium*) 介导下,人参皂苷 Rd 还可以先被水解掉其苷元 C-3 取代基末端一分子 Glc,产生人参皂苷 F2 (ginsenoside F2),再在拟杆菌属、真杆菌属和双歧杆菌属作用下继续水解苷元 C-3 取代基处的 Glc,最终产生人参皂苷 CK。人参皂苷 Rb1 经过肠道菌群的去糖基化作用,产生了更容易被人体吸收的人参皂苷 CK,

具有保肝、抗炎及治疗动脉粥样硬化等生物活性,增强了人参的药理作用<sup>[77,78]</sup> (图2)。

**4.4 五味子** 五味子 (Chinese Magnoliavine Fruit) 来源于木兰科植物五味子 [*Schisandra chinensis* (Turcz.) Baill.] 的干燥成熟果实,是一种富含不饱和脂肪酸、矿物质、维生素和蛋白质的功能性食品<sup>[79]</sup>。五味子最早记载于《神农本草经》,具有收敛固涩、益气生津、补肾宁心等功效。五味子的化学成分主要包括多糖和木脂素类。五味子多糖可以降低血清中甘油三酯 (TG)、总胆固醇 (TC)、低密度脂蛋白 (LDL)、谷丙转氨酶 (ALT) 和谷草转氨酶 (AST) 的水平,同时还能减轻肝细胞脂肪变性和坏死,降低肝脏 TC 和 TG 含量,从而发挥调节血脂和保护肝脏的作用<sup>[80]</sup>。木脂素类化合物是五味子中重要的活性成分,主要包括五味子素 A 和五味子丙素。五味子素 A 具有抗氧化、抑制细胞凋亡、调节免疫等多种药理作用。五味子素 A 可通过调节 AdipoR1/AMPK-ROS/线粒体损伤信号通路来减轻糖尿病肾病患者肾脏细胞的铁死亡和 NLRP3 炎症小体介导的细胞焦亡,从而缓解其肾损伤程度<sup>[81]</sup>。五味子丙素可以降低血清中 ALT 的含量,是五味子果实中抗肝损伤最有效的化合物,但其含量一般在 0.08% 以下。以五味子丙素为基础,中国医学科学院药物研究所的研究人员研发了首个具有自主知识产权的国家一类抗肝炎新药双环醇,具有抗肝炎病毒复制、抗肝纤维化、抗肝损伤和诱导肝细胞蛋白合成等多种药理活性和较高的生物利用度<sup>[82]</sup>。

食药同源物质兼具食品和药品的属性,除了作为药膳被广泛食用外,还可以用于养生保健,发挥“治未病”的作用。研究发现,食药同源物质大多性质平和,且发挥生物活性的化合物是多成分、多机制、多靶点<sup>[83]</sup>,因此,传统的单靶点药物理念并不适用于解释食药同源物质的治疗功效及原理。随着肠道菌群研究的兴起,为研究者探索食药同源物质提供了新的研究方向。口服食药同源物质后,在肠道菌群的作用下,产生

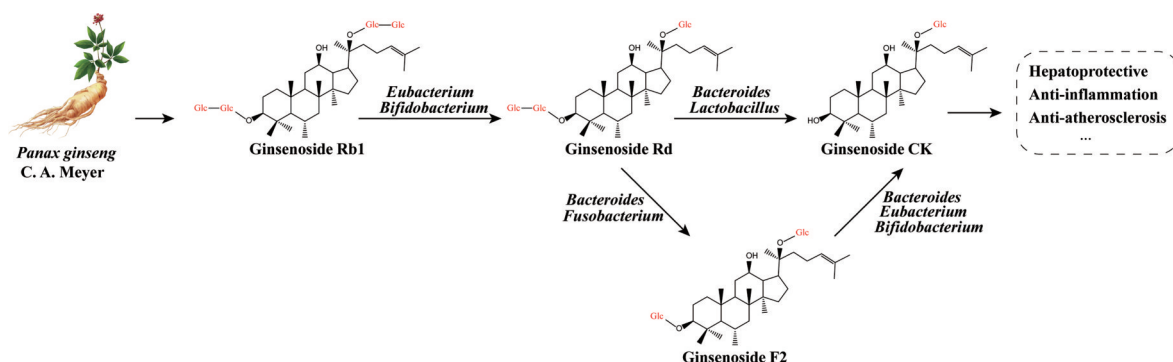


Figure 2 Biotransformation and pharmacological activity of ginsenoside Rb1 in gut microbiota

与其相关的活性化学物质和/或中间生物活性分子,这些物质与机体能量代谢相关通路或靶点分子相互作用,改善疾病的症状(如降低血脂,治标),同时减少炎症、恢复机体免疫力、改善肠道壁或肠道菌群状态等,实现对疾病根源的治疗(治本),这种复杂的多重效应充分体现了食药同源物质“标本兼治”的治疗特点<sup>[84]</sup>。前文提到的白芍和巴戟天通过肠-脑轴机制增加多巴胺、5-羟色胺等释放从而发挥抗抑郁的作用,也能够调节肠道菌群的数量和组成,恢复机体稳态,实现“标本兼治”的药理学效应。此外,食药同源物质大多具有“补益”的属性,如枣、百合、枸杞子、阿胶等活性成分可以调节肠道菌群,增强免疫,对慢性病、失眠、肥胖等有很好调理及预防作用<sup>[85,86]</sup>。然而,口服食药同源物质的生物活性成分通常甚微,对于患者而言可能需要长期服用。虽然见效较慢、作用微弱,但因其具有安全性、普遍性的特点,食药同源物质仍然备受青睐。

## 5 研究“食药同源”的科学意义

防病于未然是健康中国建设的关键内容之一,涉及每个人的日常生活,所以科学诠释“食药同源”具有具体和实际的意义。研究“食药同源”的化学基础及生物学原理,从整体把握食药同源物质发挥药理活性的规律,兼顾“治标效应”和“固本效应”,形成“标本兼治”,尽可能全面解释其整体的生物信号分子及之间相互作用机制,有助于探索“食药同源”物质的药学细节,让科学知识走进千家万户,达到“润物细无声”的治疗效果。在大健康概念的背景下,食药同源物质既满足人们对天然食品的需要,又能够实现防治未病的功效,是健康中国、回归自然的重要例子。

食药同源物质还是新药发现的源泉。有很多新药都是从食药同源的实践效果中获得提示的。如五味子有益于肝脏,不仅在我国已有2 000多年临床应用历史,在食疗方中的应用也不胜枚举。我国第一个具有国际自主知识产权的治疗肝炎的一类化学新药双环醇,就来源于食药同源物质五味子。此外,源于芹菜籽的脑血管创新药物丁苯酞的发现,就与芹菜本身对心血管系统的益处的提示相关;古医书中桑树之材可治疗消渴症,所以科学家在桑枝中提取分离得到的降血糖新药桑枝总生物碱等。随着人们科学知识的增加,食药同源的实践也可能成为发现原创新药的有效手段。

比较特别的是,肠道菌群在“食药同源”的科学原理中极为重要,包含了人体-肠道菌-植物之间天然存在的相互作用。宏基因组技术出现后,研究人员可以深入研究肠道菌群的复杂结构、新陈代谢、化学内涵和许多细节;以此作为深入研究的基础,相信今后10年

会涌现出更多的对人类健康认识的新知识,帮助研究人员找到疾病的原因、药物治疗的原理和标本兼治甚至有助长寿的药物。

药食同源是一种科学理念,深含“人与自然”的哲学道理,需要大量的以现代科学技术为引领的研究来支撑(如文中例子所示),代表着未来药物治疗与健康生活相结合的大智慧。深入了解两者的差异及相通之处,研究其中的化学基础和生物学原理,并合理运用于医疗卫生的实践之中,就可能对人类健康产生重要的益处。

**作者贡献:** 丁劲文、迟湘胤、张玉、王璐璐负责文献整理和撰写;林媛、蒋建东负责文稿的统筹和修改。

**利益冲突:** 所有作者均声明不存在利益冲突。

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