

鼠李科植物枣多糖的活性机制及其结构特征研究进展

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摘 要 鼠李科枣属植物包含原变种枣 (*Ziziphus jujuba* Mill. var. *jujuba*)、无刺枣 (*Ziziphus jujuba* var. *inermis*)、酸枣 (*Ziziphus jujuba* var. *spinosa*) 等许多品种, 而其中大枣在全国各地有最丰富的栽培变种, 如哈密大枣、黄河滩枣等。枣属植物品种丰富且药食两用, 多糖作为枣的主要活性成分之一, 是其发挥功效的重要药效物质基础。枣多糖已被发现具有促进造血、抗氧化、抗肿瘤、修复肝损伤、免疫调节、抗炎等多种药理活性。本文通过对不同品种和不同产地来源的枣类多糖文献进行全面归纳分析, 综述了枣多糖发挥生物活性的潜在作用机制, 汇总了枣多糖相对分子质量、单糖组成、糖残基连接方式等一级结构特征, 并对枣多糖硫酸化、磷酸化、羧甲基化、硒化、乙酰化的取代基修饰进行总结, 以期对枣类在多糖创新药物、功能食品等领域的研究与开发利用提供参考。

关键词 枣多糖; 生物活性机制; 结构分析; 结构改造

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Research progress on active mechanism and structure feature of polysaccharides from *Ziziphus jujube* in Rhamnaceae plants

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Abstract The genus *jujube* (*Ziziphus jujuba* Mill.) within the Rhamnaceae family encompasses numerous varieties, such as *Ziziphus jujuba* Mill. var. *jujuba*, *Ziziphus jujuba* var. *inermis*, and var. *spinosa*, etc. Among these, the *jujube* fructus has the most abundant cultivated variants across the country, including *Ziziphus jujuba* cv. *Hamidazao* and *Ziziphus jujuba* cv. *Huanghetanzao*. *Jujube* plants are rich in variety and are used for both medicinal and food purposes. Polysaccharides, one of the main active ingredients of *jujube*, are important medicinal components that contribute to its efficacy. *Jujube* polysaccharides have been found to promote hematopoiesis, exhibit antioxidant and anti-tumor activities, repair liver damage, regulate the immune system, and

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provide anti-inflammatory effects. By comprehensively summarizing and analyzing the literature on jujube polysaccharides from different varieties and origins, this paper reviews the potential mechanisms of action of jujube polysaccharides in exerting biological activities. It also summarizes the primary structural features, such as relative molecular mass, monosaccharide composition, glycosidic linkage, and the substituent modifications of jujube polysaccharides by sulfation, phosphorylation, carboxymethylation, selenization, and acetylation. This review aims to provide a reference for the research and development of jujube in the fields of innovative polysaccharide drugs and functional foods.

Key words jujube polysaccharide; bioactive mechanism; structural analysis; structural modification

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枣主要包括无刺枣、酸枣等变种以及栽培变种,枣属植物在亚洲与美洲均有分布^[1],《中华人民共和国药典》(2020 版)所记载的大枣(*Jujubae fructus*)与酸枣仁(*Ziziphi spinosae semen*)分别属于鼠李科枣属植物的果实与种子,是中国传统常用的大宗中药材^[2]。随着现代中医药的发展,枣中多种化学成分已被发现,如多糖、皂苷、黄酮类等^[3-4]。

近年来医药、食品产业快速发展,目前国内外研究重点主要聚焦在枣多糖生物活性及结构特征方面,但因多糖的结构复杂,生物活性多样,所以其活性机制至今仍未详细阐明。本文主要对枣的原种及栽培变种等枣多糖文献进行归纳整理,简要总结枣多糖发挥不同生物活性的调节作用机制以及初级结构、化学修饰等结构特点,以期药食两用的鼠李科植物枣在糖类创新药物、功能食品研究以及挖掘枣多糖资源应用潜力提供理论依据。

1 枣多糖生物活性机制

1.1 促造血机制

近年来有研究发现,中药多糖、硫酸乙酰肝素等糖类物质与造血密切相关,如促进血细胞恢复及减少凋亡、调节造血干细胞等^[5-6],多糖铁复合物还

被报道作为潜在补血剂,具有生物利用度高、安全低毒、胃肠道刺激小等特点^[7]。动物实验表明(表 1),枣多糖造血机制主要有促进造血细胞增殖、刺激造血因子分泌、升高血常规水平、改善造血器官骨髓和脾脏等。此外,在若羌枣的研究中发现其多糖铁制剂品质稳定、制备工艺简单^[12]。因此,多糖作为枣发挥补血作用的重要药效物质基础,有望开发成为一种新型大分子补血剂。

1.2 抗氧化机制

多糖的化学结构中带有半缩醛羟基,可与活性氧发生氧化还原反应^[13],且大分子结构有利于捕获多种自由基或与金属离子络合,因此多糖具有良好的抗氧化活性^[14-15]。故推测枣多糖是一种有效的天然抗氧化剂,具有良好的抗氧化活性。枣多糖抗氧化活性在体内外实验均得到验证(表 2),其机制包括直接清除自由基、提高自由基清除酶活性、降低过氧化物水平、增强氧化细胞活性、抑制氧化应激损伤。

1.3 抗肿瘤机制

大分子多糖已被发现对癌细胞具有细胞毒性而不损害健康组织、抑制肿瘤免疫逃逸等特点^[16-27],充分展现了天然来源多糖抗肿瘤潜力。而枣多糖也被

表 1 大枣多糖促造血活性研究

实验设计	结果	文献
5/6肾切SD大鼠除贫血模型 ELISA试剂盒	血清促红细胞生成素(EPO)水平、肾脏EPO mRNA与EPO蛋白↑,肾性贫血减轻可能与HIF-α蛋白上调相关,红细胞、血红蛋白、血细胞比容和血小板计数↑;	[8]
昆明小鼠 放血与环磷酸胺所致小鼠气血双虚模型	大枣多糖200 mg/kg剂量最显著,血红蛋白、白细胞、红细胞和血小板↑,多糖通过升高血清粒-巨噬细胞集落刺激因子,而呈现出促进骨髓造血和兴奋免疫的作用;	[9]
Wistar雄性大鼠 放血与环磷酸胺所致小鼠气血双虚模型	骨髓有核增生、骨髓红系比↑,脾脏、胸腺萎缩↓;	[10]
Wistar雄性大鼠 放血与环磷酸胺所致小鼠气血双虚模型	血红细胞、血红蛋白、血小板↑,改善能量代谢	[11]

表 2 枣多糖抗氧化活性研究

多糖来源	实验设计	结 果	文献
灵宝大枣、 新郑大枣	1, 1-二苯基-2-三硝基苯肼(DPPH)乙醇溶 液、铁氰化钾溶液、水杨酸-乙醇溶液	DPPH·、羟自由基(·OH)、超氧阴离子自由基(·O ₂ ⁻)的清除能力以 及总还原能力与浓度呈正相关;	[16]
酸枣果肉	维生素C溶液、DPPH乙醇溶液 水杨酸-乙醇溶液	酸枣多糖浓度1 mg/mL, DPPH·清除率达最大值19.12%, ·OH清除 率达32.99%;	[17]
金丝小枣	DPPH乙醇溶液、邻苯三酚溶液	金丝小枣多糖质量浓度2 mg/mL, DPPH·清除率达最大值58.9% 红枣多糖质量浓度2.5 mg/mL, ·O ₂ 清除率达76.13%;	[18]
红枣	模拟唾液、胃肠动态消化过程	唾液消化后DPPH·清除率提高1.69倍。模拟肠液消化2 h, 清除 DPPH·与·OH最佳为(57.08±0.76)%与(79.13±1.16)%。胃与小肠 反消化液反应3 h, 2,2-联氮-二(3-乙基-苯并噻唑-6-磺酸)二铵盐 (ABTS)自由基清除率达最大值(37.8±1.31)%和(25.03±0.93)%;	[19]
大枣	D-半乳糖诱导昆明小鼠衰老模型	超氧化物歧化酶(SOD)、谷胱甘肽过氧化物酶(GSH-Px)↑, 丙二 醛(MDA)水平↓;	[20]
黑枣	过氧化氢(H ₂ O ₂)诱导人脐静脉内皮细胞 HUVEC、MTT实验	细胞形态恢复, 存活率、细胞的荧光强度↑;	[21]
圆铃大枣	DPPH无水乙醇溶液、水杨酸-乙醇溶液、 FeSO ₄ 溶液	圆铃大枣多糖质量浓度1 mg/mL清除率: 33.417%(DPPH·), 11.905%(·O ₂ ⁻), 38.306%(·OH);	[22]
大枣	SD大鼠慢性疲劳综合征模型	高剂量组大鼠血清MDA含量↓;	[23]
大枣	小肠缺血再灌注兔模型	SOD、过氧化氢酶(CAT)、GSH-Px↑, 家兔肠组织MDA水平↓;	[24]
哈密大枣	MET诱导斑马鱼胚胎氧化损伤 H ₂ O ₂ 诱导人肝癌HepG2细胞氧化损伤	斑马鱼胚胎: 质量浓度5、25、50 μg/mL, HJP1-a保护作用最强。 多糖HJP-3、HJP-2浓度25 μg/mL, 胚胎存活率分别提高71.3%与 70.7%。HepG2细胞: HJP-1a、HJP-3、HJP-4组分多糖浓度与存活 率提高成正比, 100 μg/mL, HJP-3保护作用最强, 25 μg/mL, HJP- 2最强	[25]

表 3 枣多糖抗肿瘤活性研究

多糖来源	实验设计	结 果	文献
若羌枣种子	宫颈癌细胞(HeLa) CCK-8检测细胞实验 荧光显微镜观察细胞形态 流式细胞仪	多糖剂量与孵育时间增加, 凋亡细胞、凋亡小体↑, 若羌枣多糖质量浓度400 μg/mL, 24 h与48 h抑制率: 63.37%、 67.64%;	[28]
狗头枣	人结肠癌细胞(LoVo)、巨噬细胞RAW 264.7、MTT法、流式细胞术、乳酸脱氢酶 LDH法	阻滞细胞G ₀ /G ₁ 期, 巨噬细胞存活率↑, 狗头枣多糖质量浓度400 μg/mL, 肿瘤细胞存活率↓, 刺激巨噬细胞产生培养上清抑制癌细胞, 最佳多糖浓度400 μg/mL;	[29]
若羌枣	人结肠癌细胞(SW620)、姜酚、流式细胞 术、CCK-8检测、荧光显微镜分析	若羌枣多糖与姜酚联合使用优于单独使用, 凋亡比例为 (60.2±2.6)%, 抑制集落形成。单独使用阻滞G ₂ /M期, 联合使用阻滞 G ₀ /G ₁ 期;	[30]
灰枣	HepG2、MTT实验、流式细胞术、划痕法、 Transwell法检测细胞增殖、Western blot(WB)法观测	凋亡相关蛋白(Bax, Caspase-3/-9等)↑, Bcl-2↓, Bax促进细胞色素C释放而诱导肿瘤细胞凋亡, 通过线粒体途径抑制 肿瘤细胞。灰枣多糖BJP-2质量浓度800 μg/mL, 40%以上的细胞进入 凋亡状态, 400 μg/mL与800 μg/mL细胞迁移率与侵袭数↓;	[31]
红枣	HepG2、MTT法、流式细胞术、PI染色法、 RT-PCR检测	细胞增殖水平、s周期分布、晚期细胞凋亡率↓, caspase-3 mRNA表达水平↑, 红枣多糖质量浓度40 mg/mL: 最大抑制率68.79%, 凋亡基因Bcl-2与多糖浓度成正比, caspase-3 mRNA成反比;	[32]
陕北滩枣	HepG2、荷瘤昆明小鼠模型(S ₁₈₀ 细胞)、 MTT法、流式细胞仪检测	肝癌细胞: 阻滞G ₀ /G ₁ 期, 增殖水平、诱导凋亡↓, 陕北滩枣多糖质量浓度400 mg/mL明显抑制S ₁₈₀ 肿瘤细胞白细胞、血 小板↑, 胸腺、脾脏指数↑	[33]

发现对宫颈癌、结肠癌、肝癌等多种肿瘤细胞具有抑制作用(表 3), 主要通过抑制肿瘤细胞增殖、调节细胞周期、免疫调节、诱导癌细胞凋亡、调节凋亡蛋白与凋亡基因等途径, 并且往往是多机制协同作用, 这也表明了其抗肿瘤机制的复杂性, 有望作为抗肿瘤药物研发的重要选择。而多糖的抗肿瘤机制与靶点密切相关, 如通过靶向半乳糖凝集素(Galectin-3)、受体 TLR-4、蛋白 VEGF 等发挥抑制血管生成、激发免疫等作用, 加强枣多糖靶向性的研究可为其成药性提供更多可能^[34,35]。

1.4 抑制肝损伤机制

目前大分子多糖保肝药物鲜有报道, 研究发现

表 4 枣多糖抑制肝损伤活性研究

多糖来源	实验设计	结果	文献
大枣	昆明小鼠、SD大鼠 四氯化碳(CCl ₄)所致肝损伤模型	最佳剂量: 100 mg/kg(大鼠), 200 mg/kg(小鼠), 血清ALT(谷丙转氨酶)↓, 大鼠: 肝窦恢复, 肝细胞再生, 炎细胞浸润、脂泡变性减轻 小鼠: 肝组织浑浊肿、空泡及脂肪变性减轻;	[36]
新疆大枣	ICR小鼠 CCl ₄ 所致肝损伤模型	与柴胡疏肝散联用, 小鼠血清ALT、AST(谷草转氨酶)、ALP(碱性磷酸酶)↓, SOD↑;	[37]
陕北滩枣	昆明小鼠 CCl ₄ 所致肝损伤模型	剂量400 mg/kg, ALT、AST、LDH↓, SOD、GSH-Px↑, MDA↓;	[38]
酸枣果肉	昆明小鼠 CCl ₄ 所致肝损伤模型	SOD、CAT、GSH↑, MDA↓, 蛋白表达(HO-1、GSTα、NQO1)↑, 增强肝组织Nrf2;	[39]
冬枣	昆明小鼠 CCl ₄ 所致肝损伤模型	肝脏组病理组织剂量依赖性改善, ALT、AST↓, 高剂量枣多糖保护正常肝脏结构, 无细胞坏死和炎症浸润;	[40]
黄河滩枣	昆明小鼠 CCl ₄ 与对乙酰氨基酚所致肝损伤模型	最佳剂量400 mg/kg, ALT、AST、LDH(乳酸脱氢酶)↓, SOD、GSH-Px↑, MDA↓, 脂肪变性、细胞坏死、炎症浸润↓	[41]

枣多糖具有良好保肝作用(表 4), 其抑制肝损伤主要通过直接减轻肝脏病理变化及促进修复再生、抑制肝脏内过氧化、降低转氨酶水平、调节氧化还原转录因子 Nrf2 通路。因此基于天然大分子枣多糖研发保肝药, 是拥有巨大开发潜力的新方向。而造成肝损伤的原因较为复杂, 如饮酒、肝炎、药物等, 在其他中药多糖中发现的不同作用机制是值得借鉴探索的, 如激活凋亡蛋白(Bcl-2、Bax、Caspase3)、激活蛋白受体 Notch 和蛋白激酶 Akt 通路等^[42]。

1.5 调节肠道菌群机制

肠道菌群及活性酶可参与碳水化合物的代谢, 进而增加有益菌群丰度和减少有害微生物数量, 故多糖具有较好益生元作用^[43-44]。研究表明(表 5), 枣多糖的调控机制与其本身可被分解利用、促进益生菌增殖等有关。此外, 还有研究发现灰枣多糖具有良好的益生元活性, 可提高发酵乳杆菌、植物乳杆菌、鼠李糖乳杆菌、嗜酸乳杆菌的增殖率^[49], 故枣多糖有望作为一种益生元制剂。

1.6 免疫调节机制

多糖是枣发挥免疫调节的重要活性成分(表 6),

既可直接作用于免疫细胞促进增殖和活化, 又能同时刺激免疫器官等从而触发多通道协同发挥调节作用, 其具体调节机制包括抑制补体的激活、促进巨噬细胞增殖、增强免疫器官脾脏与胸腺、调节淋巴细胞及细胞因子表达。但多糖进入细胞进行调节不仅需要激活细胞内信号通路, 还要与多种细胞表面受体(TLRs、Dectin-1、MR、CR3)结合, 进一步挖掘完整作用机制是必要的^[61,62]。

1.7 抗炎机制

传统小分子非甾体抗炎药具有肾毒性以及胃肠道刺激等副作用^[63-64], 故从天然产物中挖掘低毒、副作用小的抗炎物质极为必要。目前(表 7), 枣多糖抗炎主要与 I-κB/NF-κB 和 ERK/MAPK 信号通路, 调节 TNF-α、IL-1β、IL-6 和 IL-17 等炎症因子分泌有关。未来需要研究更多炎症相关的信号通路与靶蛋白, 如 Akt-mTOR、STAT 信号通路以及靶向 TLR2、TLR4、Dectin-1 受体^[69-71]。

1.8 其他活性

在吕梁木枣多糖、交城骏枣多糖^[72]、内黄大枣多糖^[73]研究中发现具有抗疲劳作用, 这与抗氧化、

表 5 枣多糖调节肠道菌群活性研究

多糖来源	实验设计	结果	文献
喀什骏枣	体外模拟消化与酵解	还原糖增加后减少, 酵解产物总糖、葡萄糖、pH↓, 多糖可被肠道微生物分解利用;	[45]
大枣	C57BL/6小鼠 氧化偶氮甲烷(AOM)联合葡聚糖硫酸钠(DSS)诱导	益生菌多样性↑, 乳杆菌科、拟杆菌科和德巴利菌科等↑;	[46]
木枣	C57BL/6小鼠 AOM/DSS诱导、采用16S rDNA 基因测序、靶向GC和非靶向UHPLC-MS方法	双歧杆菌、拟杆菌、乳酸杆菌、梭状芽孢杆菌↑;	[47]
金丝小枣	ICR小鼠免疫抑制模型	SCFA(乙酸、丙酸、异丁酸、异戊酸、戊酸)↑, 普雷沃菌科Alloprevotella↑, 脱硫弧菌丰度↓	[48]

表 6 枣多糖免疫调节活性研究

多糖来源	实验设计	结 果	文献
木枣	THP-细胞诱导分化巨噬细胞 ELISA检测试剂盒 MTT细胞毒性实验	巨噬细胞与多糖共孵育24 h, 鸡红细胞的吞噬率、吞噬指数↑;	[50]
金丝小枣	昆明小鼠 不同浓度粗多糖经口给药 MTT法	金丝小枣粗多糖: 脾细胞增殖率、脾脏与胸腺指数、腹腔巨噬细胞↑, 纯化组分ZSP3、ZSP4: 诱导脾淋巴细胞增殖指数最高(200 g/mL);	[51]
大枣	BALB/c小鼠免疫模型 MTT法、ELISA法	大枣多糖质量浓度20~320 μg/mL, 淋巴细胞增殖↑, IL-2、IL-6、IL-10、IL-12、mRNA表达↑;	[52]
金丝小枣	昆明小鼠 4×4双因子实验设计、MTT法	枣多糖(0 ~ 150 μg/mL)协同LPS促进脾B淋巴细胞增殖;	[53]
新疆阿克苏灰枣	多糖100 mg/kg灌胃雄性小鼠7 d MTT法	多糖HP1与HP2组分, 均可显著提高小鼠免疫器官和巨噬细胞吞噬指数;	[54]
金昌枣	巨噬细胞RAW264.7、昆明小鼠 样品刺激淋巴细胞、MTT法	多糖JJC1与JJC2组分巨噬细胞吞噬功能↑, 脾细胞增殖↑, JJC2补体激活抑制作用: 经典途径(CH50:2.73 mg/mL)、替代途径(AP50:2.99 mg/mL);	[55]
酸枣仁	RAW264.7细胞 MTT法、Griess法、WB分析	酸枣多糖5、10、50 μg/mL, 增殖率分别为115%、147%、182%, 促进巨噬细胞NO的释放, 引起IκB-α和ERK的蛋白磷酸化;	[56]
酸枣仁	Caco-2细胞、LPS 诱导损伤 MTT法、WB分析、RT-PCR法	酸性多糖6.25、12.5、25 μg/mL, 细胞增殖↑, 细胞Occludin、ZO-1 蛋白表达量↑, 炎症因子IL-6、IL-8、IL-1β、TNF-α的mRNA转录表达↓;	[57]
酸枣仁	5 μg/mL多糖不同时间作用于 RAW264.7细胞、WB分析	诱导IκB-α和ERK蛋白磷酸化 激活IκB/NF-κB和ERK/MAPK信号通路;	[58]
红枣	Jurkat T(急性白血病T细胞) 多糖与细胞共培养	白细胞介素(IL)-2↓, 2.5 mg/mL红枣多糖抑制率达81.7%;	[59]
金丝小枣	绵羊红细胞	金丝小枣多糖ZSG4b浓度为210 μg/mL, 抗补体活性为90%	[60]

表 7 枣多糖抗炎活性研究

多糖来源	实验设计	结 果	文献
木枣	RAW264.7巨噬细胞 MTT法、Griess法测定NO产生、ELISA检测	木枣多糖ZMP处理(200~800 μg/mL)显著维持巨噬细胞活力↑, NO产生↓, TNF-α水平↓, 细胞因子IL-10↑; NO产生↓, 骏枣多糖浓度100 μg/mL, COX-2的表达显著降低↓,	[65]
骏枣	RAW264.7巨噬细胞 细胞活力测定、ELISA检测、WB分析	TNF-α、IFN-γ、IL-1, 剂量依赖性↓, 多糖浓度50 μg/mL、100 μg/mL, TNF-α、IL-17水平显著↓, 抑制NF-κB和p38/JNK MAPK信号传导发挥抗炎作用;	[66]
酸枣果肉	Caco-2、RAW264.7细胞 三硝基苯磺酸(TNBS)诱导SD 大鼠肠炎模型、 ELISA、MPO试剂盒、WB分析	多糖浓度100 μg/mL时, Caco-2细胞屏障保护作用最大, 紧密连接蛋白表达、AMPK活性↑, 大鼠结肠损伤↓, 血清与结肠组织TNF-α、IL-1β、IL-6表达↓;	[67]
酸枣仁	多糖喂养及TNBS诱导C57BL/6小鼠肠炎模型	水肿、坏死和炎细胞浸润↓;	[58]
酸枣仁	LPS诱导Caco-2细胞炎症模型 RNA、cDNA试剂盒	炎症细胞因子IL-6、IL-8、IL-1β和TNF-α的水平↓, 调节紧密连接蛋白(occludin、ZO-1)的表达↑	[68]

降低乳酸等代谢产物积累有关。狗头枣多糖对口腔细菌病原体具有抑制作用, 通过生长抑制、调节炎症反应等途径^[74]。木枣多糖具有降血脂作用, 对脂质的抑制呈浓度依赖性^[75]。陕北滩枣多糖还能减少胰岛素抵抗与血脂异常^[76]。新疆若羌灰枣多糖可降血糖、降血脂, 以及通过抗氧化改善肝脏胰腺组织^[77]。沧州金丝小枣多糖体外试验发现具有

降血糖活性, 可通过激活 PI3K/Akt 通路缓解胰岛素抵抗^[78]。

2 结构分析

对枣多糖进行了结构特征总结(表 8), 结构特征主要集中在相对分子质量、糖苷键类型及连接方式、单糖组成等一级结构方面, 已被解析的结构类型

表 8 枣多糖一级结构

多糖来源	相对分子质量	糖苷键	单糖组成及物质的量比	生物活性	文献
骏枣	3.25×10 ⁴ D	α -吡喃葡萄糖苷骨架	Rha-Ara-Gal-Glc-Xyl-Man-GalA=(0.05:0.34:0.29:0.15:0.08:0.02:0.06)	抗氧化	[81]
板枣	-	α -糖苷键	GalA-Gal-Ara-Glc-Rha-Xyl-Man	抗氧化	[82]
木枣	89.90 kD	-	Ara-Gal-Glc-Rha-Man=(4.52:2.64:1.04:0.49:0.41)	抗炎	[65]
木枣	16.97 kD	(1,3,5)-Ara ₁ (1,3)-Ara ₁ (1,5)-Ara ₁ (1,4)-Gal ₁ (1)Ara ₁ (1)Glc	Ara-Gal-Glc-Man-Xyl=(17.36:3.29:2.68:1.05:1.0)	降血脂	[75]
木枣	28.94 kD	(1,2,4)-Rha ₁ (1,3,5)-Ara ₁ (1,4)-GalA ₁ (1)-Ara ₁ (1)-Rha(HG)	Rha-Ara-Xyl-Man-GalA=(1.0:0.9:0.05:0.07:28.9)	抗氧化	[83]
木枣	9.73 kD	(1,4)- α -GalA ₁ (1,3)- β -D-Gal ₁ (1,3,5)-Ara ₁ (1,2,4)- α -L-Rha ₁ (1)-Ara ₁ (1)-Rha ₁ (1)-Gal(HG)	Rha-Ara-Xyl-Man-Glc-Gal-GalA=(10.51:6.7:0.5:0.26:0.5:6.75:74.69)	抗氧化	[84]
木枣	59.1 kD	-	Rha-Ara-Xyl-Man-Glc-Gal-GalA=(2.3:19.7:1.2:1.0:2.6:8.3:13.2)	抗肿瘤	[85]
木枣	HJP1:6.762×10 ⁴ D HJP3:2.936×10 ⁴ D	HJP1:(1,3)-Rha ₁ (1)-Ara ₁ (1,5)-Ara ₁ (1,6)-Gal ₁ (1,4)-Gal ₁ (1,4)-GaA ₁ ;HJP3:(1)-Rha ₁ (1,5)-Ara ₁ (1,3,5)-Ara ₁ (1)-Gal ₁ (1,4)-GalA(RG- I)	Man-Rha-GalA-Glc-Gal-Ara HJP1=(1.3:27.6:6.7:3.7:13:47.6) HJP3=(0.6:16:16.7:6.5:21:39.2)	抗肿瘤	[86]
木枣	HJP1:6.762×10 ⁴ D HJP2:6.13×10 ⁴ D HJP3:2.936×10 ⁴ D	α 和 β 型糖苷键	Man-Rha-GalA-Glc-Gal-Ara HJP1=(4.3:16.4:1.28:7.9:21.8:48.4) HJP2=(2.44:4.06:1.42:3.41:55.4:33.3) HJP3=(0.69:22.5:6.14:1.68:29:40)	免疫调节 抗氧化	[50]
灰枣	6.42×10 ⁴ D	(1,5)- α -L-Ara ₁ (1,4)- β -D-Gal ₁ T- α -L-Ara ₁ (1,4)- β -D-Gal ₁ (1,4)- α -L-6MeGalA ₁ T- α -L-Ara ₁ T- β -D-Gal	GalA-Ara-Gal-Rha-Xyl-GlcA-Glc-Fuc-Man (39.78:31.93:16.86:6.43:1.86:1.28:1.02:0.61:0.23)	抗肿瘤	[31]
狗头枣	-	β -吡喃糖苷	Man-Rha-GlcA-Glc-Gal-Ara=(1.5:0.7:3.7:64.4:7.8:21.9)	抗肿瘤	[29]
黄河滩枣	-	-	Man-Rha-GalA-Glc-Gal-Ara=(2.62:14.3:8.40:5.29:32.9:36.4)	抑制肝损伤	[41]
陕北滩枣	-	-	Man-Rib-Rha-GlcA-GalA-Glc-Xyl-Gal-Ara=(2.8:1.8:6.6:2.6:10.9:5.3:3.4:16.5:50.2)	抑制肝损伤	[38]
灰枣	HP1:6.87×10 ⁴ D HP2:1.11×10 ⁵ D	-	Rha-Ara-Man-Glc-Gal HP1=(1.0:2.43:3.01:7.28:7.11) HP2=(1.0:3.28:1.89:0.48:2.28)	免疫调节	[54]
灰枣	JP-UD:72.99 kD	(1,5)- α -L-Ara ₁ (1,3)- α -L-Ara ₁ (1,3)- β -L-Gal ₁ (1,4)- β -L-GalA ₁ (1,4)- α -L-GalA ₁ T- β -D-Gal	Man-GlcA-Rha-GalA-Glc-Gal-Xyl-Ara (1.17:2.64:1.02:60.46:2.02:13.26:0.59:18.84)	益生元	[49]
哈密大枣	HJP-2:4.590×10 ⁴ D HJP-3:6.986×10 ⁴ D HJP-4:1.951×10 ⁵ D	HJP-2:D-吡喃葡萄糖环 HJP-3/HJP-4: α 型糖苷键 HJP-3:T- α -L-Ara ₁ (1,5)- α -L-Ara ₁ (1,4)- β -D-GalA ₁ T- β -D-Gal ₁ (1,2,4)- α -L-Rha(RG- I)	Rha-Ara-Gal-Glc-Man-Xyl-Fru-GalA HJP-2=(0.56:16.52:10.74:0.49:0.26:0.25:0.82:70.36) HJP-3=(9.81:24.15:10.97:0.2:0.24:0.83:0:53.8) HJP-4=(2.24:30.91:7.60:0.29:0:0.19:1.78:56.98)	抗氧化	[25]
若羌枣	115 kD	α 和 β 构型共存	ZJPs-II-Ara-Rha-Glc-Xyl-Gal=(26.31:8.62:18.35:15.72:5.52)	抗肿瘤 抗氧化	[30]
金昌枣	JCS-1:71.75 kD JCS-2:357.39 kD	α 构型糖苷键	GalA-Gal-AraJCS-1=(39.04:1.26:1.39) GalA-Man-Rha-Ara-GalJCS-2=(19.87:2.07:1.77:1.65:1.16)	免疫调节 抗凝血	[87]
哈密大枣(黑枣)	1.24×10 ⁵ D	BJP-4:(1,4)- α -L-GalA ₁ (1,5)- α -L-Ara ₁ (1,4)- β -D-Gal ₁ (1,3)-GlcA ₁ T- α -L-Ara ₁ T- β -D-GalA	GalA-Ara-Gal-Glc (49.40:33.54:7.71:7.19)	调节肠道菌群 抗炎	[88]
阜平大枣(婆枣)	JP-1:1.637×10 ³ D JP-2:1.799×10 ³ D JP-3:2.047×10 ³ D	α 和 β 型糖苷键连接	GalA-Ara JP-1=(4.18:2.06) GalA-Glu-Gal-Ara JP-2=(8.1:1.97:3.37:3.88) GalA-Gal-Ara JP-3=(6.41:1.61:3.4)	免疫调节 调节肠道菌群	[89]
大枣	89.90 kD	-	Ara-Gal-Glc-Rha-Man=(49.67:29.01:11.43:5.38:4.51)	调节肠道菌群	[46]

(Continued)					
多糖来源	相对分子质量	糖苷键	单糖组成及物质的量比	生物活性	文献
大枣	-	存在(1,3),(1,2),(1,6)糖苷键	Ara-Xyl-Glc-Gal-Man-Rha	抗衰老 抗氧化	[20]
骏枣	153.3 kD	1,4- α -D-GalA(HG)	GalA	抗炎	[66]
大枣	-	-	Man-Rib-GlcA-GalA-Glu-Xyl-Gal-Ara= (5.3: 3.1: 3.6: 11.4: 13.4: 14.5: 23.4: 25.1)	免疫调节	[90]
红枣	143 108/67 633 D	-	Rha-Ara-Xyl-Man-Glc-Gal=(2.2: 7.8: 1.2: 0.2: 1.4: 3.8)	免疫调节 抗炎	[59]
冬枣	45.3 kD	(1,4)- α -L-GalA,(1,4)- α -L- GalA6Me(HG)	GalA	抑制肝损伤	[40]
金丝小枣	1.4×10 ⁵ D	-	Rha-Ara-Man-Gal=(13.8: 4: 3: 8)	抗补体	[60]
金丝小枣	JP:2.75×10 ⁵ D Ac-JP:3.38×10 ⁵ D	-	Rha-Ara-Xyl-Man-Glc-Gal JP=(105: 100: 161: 5: 10: 7) Ac-JP=(39: 100: 121: 2: 5: 10)	免疫调节 调节肠道菌群	[48]
酸枣果肉	-	β -糖苷键	Man-Rha-GlcA-GalA-Glc-Xyl-Gal-Ara (2.03: 3.74: 1.05: 17.64: 38.59: 3.36: 10.44: 23.16)	抑制肝损伤	[39]
酸枣仁	UAE/ZSS: 10 000/2.34 kD HWE/ZSS: 9 550 /3.16 kD	主要由 α -构型组成 鼠李糖残基 含有 o -乙酰基	GlcA-Man-Rha-Glc-Gal-Xyl UAE=(0.89: 15.42: 18.36: 0.2: 35.49: 29.33) HWEI=(4.15: 11.91: 20.74: 0.48: 23.25: 39.47)	免疫调节	[91]
酸枣仁	ZY-2:7.76 kD ZY-3:10.71 kD ZY-4:8.31 kD	α 与 β 构型糖苷键	Man-Rha-GlcA-GalA-Glc-Gal-Xyl-Ara ZY-2=(7.22: 8.54: 3.89: 2.32: 4.89: 20.56: 39.67: 6.34) ZY-3=(6.11: 7.32: 2.22: 4.15: 7.18: 35: 28: 54.17: 10) ZY-4=(7.28: 7.47: 3.89: 5.15: 10: 16: 18.89: 44.66: 5)	抗炎	[68]

Glc: 葡萄糖; Gal: 半乳糖; Ara: 阿拉伯糖; Man: 甘露糖; Rha: 鼠李糖; Xyl: 木糖; GlcA: 葡萄糖醛酸; GalA: 半乳糖醛酸; Rib: 核糖; Fru: 果糖; Fuc: 岩藻糖

主要为同聚半乳糖醛酸(HG)、鼠李半乳糖醛酸聚糖(RG), 具有活性的多糖主要为含有糖醛酸的酸性糖。对于枣多糖精细结构的解析, 还可采用酶解、部分酸水解确定多糖主链与支链, 核磁共振 HSQC 谱以及 HMBC 谱等确定糖残基连接顺序^[79-80]。

3 结构改造

改变枣多糖化学结构, 进行化学修饰也是阐明多糖构效关系的一个方向。羧甲基化后的金丝小枣多糖与酸枣多糖取代度分别为 0.24 和 0.76, 二者均提高了清除 DPPH· 和 ·OH 的能力, 对鼠李糖乳杆菌与嗜酸乳杆菌促生长效果增加^[92]。取代度为 0.092 的磷酸化若羌灰枣多糖自由基清除率提高^[93], 取代度为 0.846 的硫酸化红枣多糖对 DPPH· 和 ABTS 的清除力增强^[94]。硫酸化修饰的枣多糖显著刺激淋巴细胞增殖, 增强枣多糖的抗凝血活性和免疫活性, 硫酸化度越高活性越好^[87,95]。硒化内黄大枣多糖(Se-ZJP)中高剂量组显著升高小鼠肌糖原和肝糖原含量, 抗疲劳作用更强, 硒含量为 2.53%^[73]。乙酰化金丝小枣多糖(Ac-JP)较原糖(JP)

的水溶性增加且糖醛酸含量降低, 相对分子质量分别为 2.75×10⁵ 和 3.38×10⁵ D, 乙酰基含量为 19%, Ac-JP 可促进短链脂肪酸的生成, 增加有益菌群丰度, 促进免疫细胞因子 IFN- γ 、IL-4 和免疫球蛋白 A(Ig-A)、G(Ig-G)、M(Ig-M) 的产生^[48]。羧甲基化的酸枣多糖取代度为 0.76, 修饰后溶解度提高、黏度降低, 显著促进嗜酸乳杆菌和鼠李糖乳杆菌生长^[96]。初步的结构修饰研究表明, 取代基有利于生物活性的提高, 改变枣多糖的理化性质, 进一步发掘确切取代位点、不同取代度对活性的影响, 这将有助于枣多糖的深入开发利用。

4 结论与展望

目前, 对枣多糖已进行广泛的生物活性研究及机制探索, 如促造血、抗氧化、免疫调节、抗炎、抗肿瘤、降血脂、抗疲劳、抗补体、降血糖等。对活性多糖的初级结构进行了大量表征, 已被解析的枣多糖精细结构主要为果胶类构型, 硫酸化、乙酰化等结构改造修饰会对活性产生影响。所报道的枣多糖来源主要来自中国北方地区, 其中以大枣栽培变种报

道最多,酸枣、冬枣最少,针对枣的果肉、果仁都进行了详细的研究。但枣类品种诸多,研究空间巨大,还存在一些问题需要提高:(1)酸枣多糖研究报道较少,酸枣以酸枣仁入药为大宗常用中药材,加强对果肉与果仁多糖的研究,有利于减少果肉的浪费和酸枣资源的合理利用;(2)枣多糖具有抗肿瘤、抗炎等多种药理活性,但其多糖靶标分子的发现研究报道较少,活性多糖的临床药理安全性和有效性评估有待完善;(3)枣类多糖产品缺乏,其易提取、低毒且枣类果实药食两用,在食品、饲料等方面有着巨大潜在开发应用价值。若面对未来枣多糖产品工业化、商业化,提取纯化工艺需进一步改善,保证高效多产;(4)获取的活性多糖受品种多样、产地来源不同而存在一定差异,可根据地区资源分布特点,加强对品种的溯源考证,广泛挖掘不同品种枣提取得到的多糖其特性,有针对性的开发利用;(5)结构研究侧重于一级结构,精细结构解析较少,还需加强高级结构如构象的研究。同时利用表面等离子共振技术,探索发挥活性作用的结构靶点与靶分子作用机制,提高枣多糖研究的创新性与深度,从构效关系及靶向性进行剖析应是未来研究重点。

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