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蓝藻多糖的食药特性和应用研究进展

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摘要:蓝藻是地球上最重要的初级生产者之一,也是重要的生物资源。有些蓝藻在我国具有悠久的食用历史,比如发状念珠藻。蓝藻能合成多种生物活性物质,具有抑菌、抗氧化、抗肿瘤、抗炎症、抗病毒和免疫调节等功能,并在食品、医药、农业、环保和化妆品领域具有广泛的应用。多糖是蓝藻最主要的代谢产物之一,它本身结构复杂、性质多样,决定了其具有多样化的功能。本文对蓝藻多糖的制备过程、生物活性以及应用研究的进展进行综述,以期更好地开发和利用其食药用价值。

关键词:蓝藻;多糖;食药特性;生物活性

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Edible and medicinal properties of cyanobacterial polysaccharides and the application research progress

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Abstract: Cyanobacteria are one of the most important primary producers on the earth and serve as important biological sources. Some cyanobacteria have a long history as edible foods in China, such as *Nostoc flagelliforme*. Cyanobacteria can synthesize a variety of bioactive substances, possessing multiple functions, such as bacteriostat, antioxidation, anti-tumor, anti-inflammation, anti-virus, and immunomodulation. These substances can be widely applied in the fields of food, medicine, agriculture, cosmetics and environmental protection. The polysaccharides are one of their main metabolites. The polysaccharide itself has complex structures and diverse properties, which determine its functional diversities. This review summarizes the preparation process, biological activity, and application research progress of cyanobacterial polysaccharides, with the aim to better exploit their edible and medicinal values.

Key words: cyanobacterium; polysaccharide; edible and medicinal property; biological activity

0　引　言

蓝藻,又称蓝绿藻、蓝细菌,是光合自养的原核藻类,广泛分布于地球多样化的环境中。蓝藻可通过光合作用释放氧气,有些蓝藻还具有固氮能力,可增加土壤肥力和促进农作物生长[1,2]。蓝藻含有丰富的营养成分,比如胞外多糖和蛋白质,古人早在《本草纲目》中就记载了蓝藻发菜和葛仙米的食用和药用方法[3]。蓝藻可合成各种代谢物来应对环境胁迫,例如紫外吸收物质——伪枝藻素和类菌胞素氨基酸、抗氧化蛋白和多不饱和脂肪酸[4,5]。作为主要代谢物的胞外多糖是蓝藻抵抗环境逆境胁迫的关键因子[4,6],同时环境条件可调节藻类多糖的含量和组成、进而影响其性质和生物活性[1,3]。

蓝藻多糖由于具有许多优良特性而具有广阔的应用前景。例如,多糖的流变性、乳化性、保湿性和絮凝性,使其适宜应用于食品和化工领域[1];多糖的天然、无毒害和抗氧化,使其适宜应用于食品和化妆

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Gao X, Yuan X L, An J, *et al*. Edible and medicinal properties of cyanobacterial polysaccharides and the application research progress [J]. Biotic Resources, 2021, 43(1): 34-41.

品[7];另外,多糖的抗氧化、抗肿瘤、抗炎症和免疫调节等生物活性,可应用于生物医药和保健品[7]。此外,多糖还具有治理环境的应用价值,如粘结土壤颗粒、促进植物种子萌发和吸附污水中重金属离子[3]。因此,多糖是蓝藻资源开发的重要方向。蓝藻多糖在食药用领域已取得许多重要进展,但其结构特征与生物活性的对应关系还需深入探究。

本综述主要对蓝藻多糖的制备过程、生物活性、合成过程以及应用研究进展进行归纳,其中也包含部分其它藻类多糖的研究进展,以期提高人们对蓝藻多糖食药用价值的认识,并促进其开发和利用。

1　多糖的提取与纯化

蓝藻多糖根据其在细胞中的分布分为储存多糖、释放多糖和胞外多糖三种类型。储存多糖存在于细胞内,释放多糖可释放到液体培养基中,胞外多糖存在于由胶鞘、荚膜或黏质组成的细胞外层[8]。储存多糖通过破碎细胞壁后提取获得;释放多糖可通过乙醇沉淀、离心获得;胞外多糖先通过水煮和搅拌、再乙醇沉淀提取。图1显示了蓝藻多糖的提取、纯化及开发流程。培养条件影响多糖的组成和性质,提取方法影响得率,纯化方法影响纯度。水提醇沉是提取多糖的经典方法,即热水浸提后用乙醇使多糖沉淀,提取温度、料液比、浸提时间和乙醇浓度是影响多糖得率的重要因素[9]。酶处理可提高多糖的释放量,例如木瓜蛋白酶,但耗时较长[10]。近年来,新的提取工艺如超声波处理,也被用于藻类胞外多糖的提取,其具备萃取时间短和萃取效率高的特点[11]。为提高多糖得率可采取碱酶复合处理,多糖得率高达48%[10]。酵母发酵法提取多糖是采取酵母利用提取液中还原糖和蛋白进行生长、但不利用多糖的特点,经酵母处理后获得的地木耳多糖纯度高达75.4%,分离的酵母可应用于生产,实现了资源的多元化利用,但多糖得率有待提高[12]。采用微滤和超滤耦合系统进行的切向流技术实现了葛仙米胞外多糖的规模化生产,这有利于提高葛仙米多糖的应用价值[13]。同样采用径向流色谱法或与切向流技术结合也可实现藻类胞外多糖的提取,这种方式对设备和技术要求较高[14,15]。为得到均一化的多糖,可采用Sevag法和透析法分别去除蛋白质和小分子杂质,然后通过离子交换树脂和凝胶层析纯化,树脂、型式和洗脱剂是提高多糖纯度的关键[16]。

2　多糖的组成和影响因素

蓝藻多糖的单糖组成包括已糖类(葡萄糖、果糖、半乳糖和甘露糖)、戊糖类(阿拉伯糖、核糖和木糖)、脱氧已糖类(岩藻糖和鼠李糖)和糖醛酸等,糖链上还含有修饰基团(如甲基化、硫酸化和乙酰化)[17]。除藻种因素外,培养条件可明显影响多糖合成和单糖组成。例如,氮源可调控发菜胞外多糖含量和组成[18],连续光照和高光强可提高多糖产量但对单糖组成未有显著影响[19,20],波长变化会对单糖组成产生影响[21],适当调节波长比例可提高胞外多糖含量[22]。有机碳源种类也明显影响多糖含量[23],调节葡萄糖和乙酸盐的比例会促进胞外多糖的合成[24],而无机碳源(如Na_2CO_3)则显著改变单糖组成[18]。Na_2CO_3和CO_2混合培养可促进葛仙米可溶性多糖的合成[25]。搅拌和盐胁迫也可促进发菜多糖的产量[26,27]。蓝藻的突变改造也是提高释放多糖的方式之一[28]。通过添加活性氧调节发菜细胞氧化还原水平也增加了胞外多糖的含量[29]。纳米材料接触藻细胞后也会引起胞外多糖含量和组成的变化,浓度越高,多糖含量越高[30~32]。

3　多糖的结构和生物合成

多糖结构的多样性决定了其性质和生物活性的多样性。由于多糖结构复杂,易被硫酸化和取代基(如乙酰基、甲基和丙酮基)取代,因此目前结构解析多集中在链接方式和单糖组成,对于侧链数量和相关基团报道较少。目前已有综述对蓝藻多糖的结构

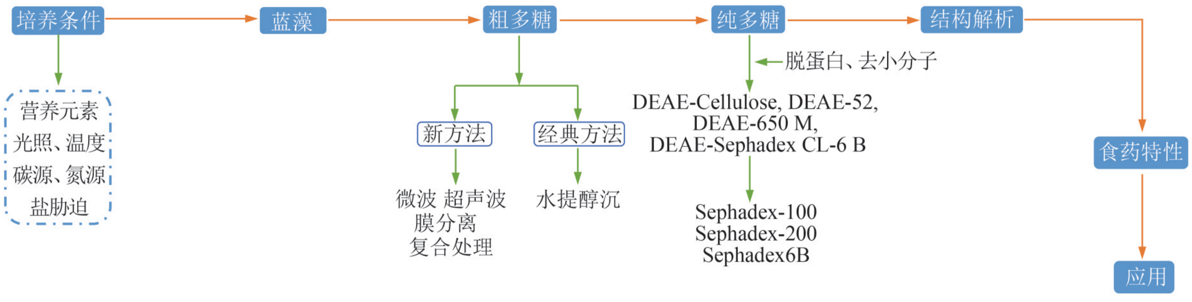

图1　蓝藻多糖的提取、纯化和开发流程

Fig. 1　Schematic diagram of the extraction, purification and exploitation of cyanobacterial polysaccharides

进行了较为详细的阐述[33],这里不做赘述。

蓝藻多糖的生物合成涉及装配、多聚化和运输等过程[1]。合成相关的基因类型包括:核苷酸糖(nucleotide sugar)合成,糖基转移酶(glycosyltransferase),寡糖和多糖加工相关基因。其生物合成的第一步在细胞质中进行,生成核苷酸糖,即活化的含糖基的单糖;第二步,在糖基转移酶的催化下,将糖基逐个地转移到质膜的特定载体分子上,形成寡糖单元;第三步,在周质空间(外膜与细胞膜之间的狭窄空间)里,寡糖被加工为多糖并分泌到胞外。蓝藻一般含有大量的糖基转移酶基因,与蓝藻产生丰富的多糖有关。在周质空间里,多糖的组装和分泌主要包括三个途径[33~35]:ABC(ATP-binding cassette)转运依赖途径、Wzx/Wzy蛋白依赖途径、合成酶依赖途径。第一种途径与荚膜多糖合成有关,其通过横跨内膜和周质空间的ABC转运蛋白和外膜转运蛋白KpsD来实现多糖合成与输出。第二种途径涉及Wzx、Wzy和Wza三种蛋白。膜蛋白Wzx负责跨内膜寡糖重复单元的翻转,Wzy催化周质空间中寡糖重复单元的聚合,Wza蛋白将多糖移位并输出至胞外。第三种途径是依赖合成酶的途径,其可形成多聚物,如透明质酸、纤维素和藻酸盐的复合物。此外,ExoD蛋白也参与多糖的合成过程,具体机制还不明了。

4 多糖的生物活性

4.1 抗氧化活性

活性氧自由基过量后会加速细胞衰老、诱发肿瘤和心血管等疾病,因此降低活性氧含量是防止细胞受损的关键,其中非化学合成的抗氧化剂越来越受到重视。藻类多糖在体外具有较强的抗氧化活性,对于预防生物体损伤有着重要作用[36]。地木耳多糖能显著清除DPPH(1,1-二苯基-2-三硝基苯肼),但对O_2^-、·OH清除活性弱[37],从葛仙米分离的多糖可显著清除O_2^-、·OH,并提高了体外培养的人类肾293细胞的存活率[38]。由此看出,不同蓝藻来源多糖的抗氧化活性或作用方式有所差异。糖醛酸含量的增加可提高发菜多糖的活性氧清除能力,如DPPH、·OH和$ABTS^+$[39],这可能与糖醛酸残基改变了与之相连的多糖复合物的物化性质和溶解性有关[40]。此外,多糖分子量和硫酸根含量也可影响多糖的体外抗氧化活性[41,42]。

4.2 抗病毒活性

蓝藻多糖对包膜病毒有明显的抑制作用,其阴离子基团可与糖蛋白的碱性氨基酸之间的离子相互作用,从而限制病毒的吸附[43]。发菜多糖可抑制单疱疹病毒与宿主细胞的结合,其结构的重复单元末端含有GlcA,葛仙米多糖也具有类似的结构,推测与抗病毒活性有关[44,45]。硫酸化多糖的抗病毒活性与分子量和硫酸化程度有关[46],其葡萄糖醛酸的羟基还原为葡萄糖后可引起抗病毒活性消失[47]。值得注意的是,许多抗病毒药物具有副作用,而海洋藻分泌的多糖具有低毒性和多功能的特点,正逐步成为抗病毒药物的新物质[48]。

4.3 抗肿瘤活性

藻类多糖也具有较强的抗肿瘤活性[49]。葛仙米水溶性多糖可抑制小鼠体内肿瘤细胞的生长[50]。发菜多糖具有抗突变的能力,可通过减少由丝裂霉素诱导微核的产生从而降低癌症发生的风险[51]。在小鼠大肠癌模型中注射地木耳多糖溶液,大肠癌的经典标志物表达明显下降,肠道中肿物显著减少[52];在体外实验中,地木耳多糖可阻止小细胞肺癌(small cell lung cancer, SCLC)的转移,通过还原p-JAK1来抑制与癌症形成和转移有关的JAK1途径,从而限制肺癌细胞的活动[53]。盐处理的发菜胞外多糖提高了体外培养的小鼠RAW 246.7巨噬细胞的免疫力,并增强了体外抑制人结肠癌细胞增殖的能力[54]。同时,多糖的分子大小、形式、支化程度和在水中的溶解度也会影响肿瘤细胞活性[46]。

4.4 抗炎活性

机体受到刺激后会产生一系列炎症反应,如毛细管扩张和通透性增加。研究发现,在小鼠炎症模型中,中剂量的发菜胞外多糖显著缓解小鼠耳部和足部肿胀程度[55]。地木耳多糖能缓解脂多糖对人单核细胞THP-1活力的抑制,并通过抑制细胞相关激酶的磷酸化,从而减少促炎因子的分泌[56]。在大鼠腹膜炎模型中,海藻硫酸化多糖和褐藻多糖可抑制白细胞向炎症部位迁移,减少白细胞在腹腔中聚集[57]。在炎症形成过程中,选择素和组织降解酶在其中起着重要作用,海藻硫酸化多糖和褐藻多糖可通过削弱选择素的聚集和抑制组织降解酶来达到抗炎的效果。

4.5 免疫调节活性

免疫调节是天然多糖包括蓝藻多糖在内的重要生物学功能[49]。多糖实现免疫调节的主要方式是激活宿主免疫应答[58]。在体内实验中,地木耳多糖可通过调节白化豚鼠的巨噬细胞的吞噬能力和NK细胞活性来实现非特异性免疫,还可通过增加溶血素抗体含量和提高淋巴细胞增殖能力来实现白化豚鼠的特异性免疫[59]。通过测定小鼠相关免疫指标表

明，发菜胞外多糖可提高小鼠的体内免疫能力[60]。藻类多糖可与吞噬细胞上的模式识别受体(PRR)——甘露糖受体和Toll受体结合进而调节天然免疫，例如，λ-卡拉胶结合Toll受体4刺激小鼠T细胞，产生T辅助蛋白1进而提高免疫能力[61]。

4.6 抑菌性及对肠道菌群的影响

在培养细菌的培养基添加一定量的多糖溶液后可对微生物生长产生较强抑制，其抑菌过程可能涉及细胞壁和细胞质膜的相互作用[62]。膳食多糖可调节降解多糖的细菌组成，丁酸是膳食多糖的主要代谢物，在结肠上皮细胞中发挥重要作用[61]。葛仙米活性多糖可对小鼠大肠癌原位模型中肠道菌群产生影响，活性多糖可促进产丁酸盐类群增加、减少有害菌类群，能有效抑制肿瘤的发生[63]。肠道菌群的作用一直是食品和医药领域研究的热点，目前关于蓝藻多糖在肠道菌群的影响报道较少，其调节机制需要进一步研究。

5 多糖的应用

蓝藻多糖具有独特的理化性质和生物活性，因此具有多种重要的开发和利用价值(图2)。

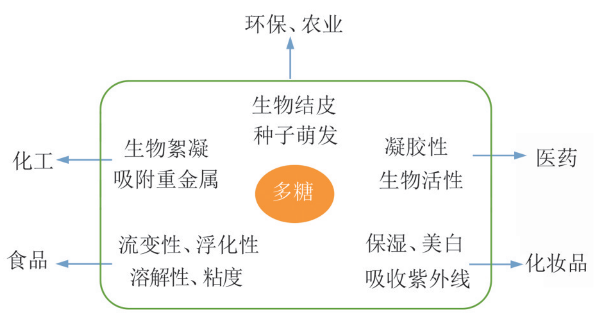

图2 蓝藻多糖的应用

Fig. 2 The application of cyanobacterial polysaccharides

5.1 食品领域

微生物多糖黄原胶是食品中常用的添加剂，具有粘度高、热稳定性强和相容性好的特点，而蓝藻多糖携带的基团也赋予自身良好的物理特性，如乙酰基团、缩氨酸部分和脱氧糖等[64]。在一定浓度下，葛仙米多糖粘度与黄原胶几乎相同[65]。发菜多糖的粘度、乳化性和流变性高于黄原胶，对豆油和花生油乳化性能可达70%以上[66]。因此蓝藻多糖可作为黄原胶的补充剂应用于饮料、蛋糕和调味品。

5.2 医药领域

利用地木耳胞外多糖制备的可逆弹性凝胶具有良好的物理和化学凝胶特性，可用于制备新型水凝胶用于药物控制[67]。蓝藻分泌的硫酸化多糖可干扰病毒和宿主细胞结合以及转录过程，不过其有抗凝血性现象[68]，而发菜的非硫酸化多糖可弥补这种不足[44]。以地木耳多糖为原料制备的生物聚合物薄膜具有良好的机械性能，在开发新的生物聚合物材料方面具有不错的潜力[69]。念珠藻(*Nostoc* sp.)菌株Hindak胞外多糖可缓解豚鼠咳嗽并呈现剂量相关性，起效速度与沙丁胺醇相同，止咳效果可达5 h[70]。

5.3 环保和农业领域

胞外多糖可通过粘结土壤颗粒形成结皮，从而防止土壤水分和养分的流失[71]。螺旋藻属、念珠藻属和微囊藻属可减少除草剂草甘膦对土壤的污染[72]。在生物结皮中，蓝藻，如，具鞘微鞘藻、眼点伪枝藻和地木耳的胞外多糖可促进荒漠种子萌发，可提高荒漠中植被的覆盖率[73]。蓝藻多糖对多种农作物种子萌发有促进作用，这有利于农作物生长，但不同种子发芽所需处理浓度不同[3]。蓝藻多糖在环保和农业领域的应用价值有待被进一步发掘。

5.4 化工领域

絮凝剂已被广泛应用于食品工业和废水处理中，生物絮凝剂由于其无毒害、可降解等特点备受青睐[1]，其絮凝效果受到微生物和絮凝环境的影响[74]。研究表明，多种蓝藻多糖具有良好的生物絮凝性[75]。在一定范围内，蓝藻胞外多糖絮凝率高于黄原胶，当浓度为0.5 mg/L时，发菜胞外多糖对高岭土絮凝率高达93.5%，浓度为5 mg/L时对MgO絮凝率为86.1%[66]。这是由于多糖中带负电的糖醛酸与带正电荷的金属离子相结合[76]。将微藻和细菌的聚集体(MABA)应用于废水处理是一项新兴的技术，去除废水中有机物和营养的同时可收获相关代谢产物，并且多糖在维持MABA的稳定中起着关键作用[77]。

5.5 化妆品领域

化学合成的护肤品会引起皮肤过敏和泛油等现象，因此寻找天然的保湿剂和美白剂是研究方向之一。研究证实，蓝藻多糖保湿和美白的能力在化妆品领域具有较大应用潜力[7]。培养条件会提高蓝藻分泌多糖的吸湿和保湿能力，如葡萄糖和盐胁迫[78]。地木耳多糖可抑制酪氨酸酶活性阻止黑色素的形成，其制成的护肤产品具有美白、保湿、抗氧化和防晒等功效[79]。水前寺紫菜的多糖可用作保湿剂[7]。此外，蓝藻产生的紫外线吸收色素分子——类菌胞氨基酸和伪枝藻素，也可用作化妆品添加剂[7]，可减少对皮肤的伤害。多糖本身在对抗紫外辐射方面也有一定作用，如葛仙米多糖对UV-A的吸收率可达38%[80]。蓝藻多糖的优势突出，其相关产品有望应

用于市场。

6　结论与展望

蓝藻多糖的食药特性在医药、食品、化妆品、化工、环保和农业领域具有重要的应用前景,通过改善培养条件和添加外源物质可改变多糖的组成和化学特性、进而提高其生物活性。新兴提取方法如超声波、膜分离技术和复合处理的应用进一步提高了蓝藻多糖的提取、分离和纯化效率,但目前蓝藻规模化培养技术有待提高,多糖的开发成本较高。因此,经济高效地获取蓝藻多糖仍是一项基础性的研究工作。蓝藻多糖具有一定的絮凝性,细菌与蓝藻形成的聚集体可进一步提高絮凝能力,因此寻找合适的菌藻组合应用于污水处理是重要的探索方向。值得注意的是,多糖结构的复杂性使得其结构与生物活性对应关系的研究仍然面临巨大挑战,采取先进的技术手段准确解析多糖的结构是重要的突破口之一。在蓝藻多糖的食药特性方面,多糖的体外实验结果不一定能完全反映体内的实际效果,因此还需开展大量的体内和临床实验,进而在市场上规模化应用。综上所述,蓝藻多糖具有重要的食药用特性和开发价值,仍将是今后的热门研究方向。

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