营养活性物质的蛋白类载体研究进展

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摘 要: 营养活性物质因具有一系列调节人体生理机能的功能活性而备受关注。然而, 营养活性物质的低溶解性、化学不稳定性和低生物利用度极大地限制了它们在食品工业中的应用。基于营养活性物质的理化性质, 针对性地设计有效的载体体系对其进行包埋和保护已成为当前研究的热点。天然蛋白质因具有乳化、凝胶、配体结合和多糖复合等特性, 可制备生成诸如蛋白质复合物、微/纳米粒子、乳状液以及乳化凝胶等具有不同结构的组装体, 已被广泛的用作单一营养活性物质的载体, 并正在逐渐应用于多种营养活性物质的共包埋, 在功能性产品的开发中具有广阔的应用前景。本文概述了营养活性物质的分类和功能特性、以及基于蛋白质的无脂型和乳状液型载体的研究进展。

关键词: 营养活性物质; 蛋白质; 无脂型载体; 乳状液型载体

Research progress of protein-based carriers for nutraceuticals

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ABSTRACT: Nutraceuticals have attracted great attention due to their series of functional activities that regulate the physiological function of human body. However, the application of nutraceuticals in the food industry has been greatly limited by their low solubility, chemical instability and low bioavailability. It is interesting to contrapuntally design an effective carrier for the encapsulation and protection of nutraceuticals based on their physicochemical properties. Natural proteins have the characteristics of emulsification, gelation, ligand binding and polysaccharide complexation and can be used to prepare the assemblies with different structures, such as molecular complexes, micro/nano particles, emulsions, and emulsified gels, which have been widely used as carriers of a single nutraceutical and are being applied for the co-encapsulation of multiple nutraceuticals. Protein-based carriers have the potential for the application in the development of functional products. This review summarized the classification and functional properties of nutraceuticals, as well as the research progress of fat-free and emulsion-based carriers made of proteins.

KEY WORDS: nutraceutical; protein; fat-free carrier; emulsion-based carrier

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1 引 言

营养活性物质虽然不是维持生长发育所必需的营养素，但在调节生理机能、预防疾病、维护健康方面发挥重要的作用[1]。为合理地利用营养活性物质以充分发挥其功能活性，正在进行越来越多的尝试。值得注意的是，营养活性物质通常是环境敏感的，易于发生结构改变，降低或失去活性，且生物利用度较低，这些因素限制了它们的应用[2]。设计可食用载体体系对营养活性物质进行包埋和保护，是开发功能性产品的关键。

基于消费者对多种营养活性物质需求的增加，以及不同活性物质间的相互作用[3,4]，将多种营养活性物质共包埋于同一产品中也成为功能性食品开发的趋势，因而针对共包埋载体体系的研究日益增加。蛋白质为天然生物大分子，具有乳化、凝胶、配体结合、多糖复合等特性，已被开发诸如复合物、纳米/微米粒子、乳状液及凝胶等具有不同结构的组装体，被广泛用于单一营养活性物质的包埋，并正在逐渐应用于多种活性物质的共包埋[5,6]。本文概述了营养活性物质及其蛋白类载体的研究进展，以期为营养活性物质的应用提供参考。

2 营养活性物质的分类及功能特性

营养活性物质广泛存在于果蔬、坚果、海洋生物以及加工食品中，其中维生素和酚类物质多为生物体内通过各种代谢过程产生的相对分子质量较小的次级代谢产物。营养活性物质有多种分类方式，可以按其来源、生物活性、溶解性、口服生物利用度等进行分类[7]。表 1 列举不同溶解性营养活性物质的来源、生物活性及限制应用因素。根据营养活性物质在水相及油相中溶解度的不同，可以将其分为 3 类：即具有较好脂溶性而不溶于水相的亲脂性活性物质；在水相中具有良好溶解性的亲水性活性物质；在水相及油相中溶解性均较低，而在醇相中具有较好溶解性的活性物质，称其具有两亲性。基于递送源于设计(delivery by design, DbD)的理念，以营养活性物质的理化性质为基础，依据目标产品的需要，可针对性开发可食用载体体系[8]。

营养活性物质(如维生素、多酚和黄酮类化合物)通常具有抗氧化、抗炎和抑菌等作用[4, 9]，其摄入对许多疾病如癌症[10]、糖尿病[11]、心血管疾病[12]及神经退行性疾病[13]有积极的影响。针对膳食中 β-胡萝卜素摄入量的研究表明，其可减少心血管疾病[14]；白藜芦醇通过调节血红素加氧酶的活性来抑制帕金森氏病和阿尔茨海默氏病[15]；姜黄素与儿茶素复合使用可有效抑制结肠癌的发生[16]。多种活性物质共同使用的效果不仅只是二者功效的简单相加[4]，还存在协同增效作用或拮抗现象。例如，番茄红素和叶黄素混合后与单一营养活性物质相比表现出更强的抗氧化活性，可有效避免多层脂质体的氧化损伤[17]。表没食子儿茶素没食子酸酯(epigallocatechin gallate, EGCG)与白藜芦醇和 γ-生育三烯酚组合协同抑制了乳腺癌细胞的增殖和基因的表达[18]。维生素 C 和 E 协同抑制了体内脂质的过氧化[19]。此外，维生素 C、茶多酚及白藜芦醇可以再生 α-生育酚，这种再生反应增强了 α-生育酚的抗氧化能力，在临床上维生素 C 多和 α-生育酚补充使用[20,21]。然而，研究还发现维生素 E 和 β-胡萝卜素以及阿魏酸混合时抗氧化性则表现为拮抗效应[22]。

营养活性物质的功能活性表达受多种因素的限制，不利于生物利用度的提高，通常需要较高剂量的摄入才能保证在体内发挥促进健康的作用；相反，长期摄入大剂量的活性物质也可能导致不良反应并降低功能响应性，限制了其在疾病预防中的应用[23]。研究证实，过量摄入富含类胡萝卜素的蔬菜可能会造成皮肤中橙黄色色素的沉积，即胡萝卜素过多症[24]。因此，营养活性物质摄入不足和过量均会导致生理变化，甚至可能产生病理影响，而在 2 种极端情况之间，存在一定浓度范围内最佳有益摄入量。每日推荐摄入量是为避免 97%的人口缺乏症状所需要的最低摄入量而建立，利于在整个生命周期中维持机体处于健康状态。然而，由于需要考虑各年龄段人群对活性物质的吸收消化情况，且营养活性物质的摄入不涉及明显的病理学，因而在某些情况下也面临最佳摄入量难以确定的问题[25]。

3 营养活性物质的蛋白类载体开发

如表 1 所示，营养活性物质多为环境敏感，往往在加工储藏过程中受光、氧、温度及 pH 等因素的影响，进而发生氧化、降解等结构变化，导致活性降低。此外，亲脂性及两亲性活性物质难相容于水相产品。而且，多数活性物质的体内吸收较差、生物利用度不高。这些因素限制了营养活性物质在功能性产品中的开发应用。针对食品的特殊性，可食用载体必须满足以下条件：无毒，通常认定为安全(generally recognized as safe, GRAS)级别；具有生物相容性和可降解性；物理稳定性强，可有效保护活性物质；对活性物质进行有效包埋，且包埋率较高；活性物质可控释放[48]。按含油脂与否，可食用载体可以分为无脂型和乳状液型两种类型[49]。

蛋白质具有高的营养价值，可生成不同结构的组装体，已被广泛的用作营养活性物质包埋和保护的有效载体[50]。蛋白质自身的生物活性和生物可降解性也分别有利于营养活性物质的保护和控释。目前，研究多集中于单一活性物质的包埋、保护和控制释放。随着多种活性物质间增效作用的不断报道、以及对具有多种健康效益的功能食品需求的增加，将多种活性物质强化于同一载体也成为食

品研发的一种趋势[51]。在富含ω-3 不饱和脂肪酸的奶酪中，酪蛋白酸钙乳状液包埋的维生素 E、维生素 A 和辅酶 Q10(coenzyme Q10, CoQ10)的添加可以抑制脂质氧化达 3 个月，由于 CoQ10 使得维生素 E 再生，维生素 E 通过 CoQ10 首先抵抗脂质氧化，而维生素 A 在维生素 E 和 CoQ10 后起抗氧化的作用[52]。在相同溶解性的活性物质的包埋研究后，具有不同溶解性的活性物质的共包埋正在引起越来越多的研究兴趣。

3.1　基于蛋白质的无脂型递送载体

蛋白质不但可以与营养活性物质结合生成复合物，而且可通过自聚集或静电复合等方式形成纳米/微米粒子，已广泛用于营养活性物质的包埋和保护。一方面，基于蛋白质的无脂型递送载体避免了油相的添加，符合“低脂”型饮食发展的趋势；另一方面，阐明这些蛋白质组装体对营养活性物质的包埋和保护机制是设计更复杂的共包埋载体体系的基础。

3.1.1　蛋白质复合物

蛋白质如β-乳球蛋白(β-lactoglobulin, β-LG)、牛血清白蛋白(bovine serum albumin, BSA)、α-乳白蛋白(α-lactalbumin, α-LA)具有天然的配体结合位点，它们和营养活性物质的相互作用以及生成的蛋白质-单配体复合物已经被广泛报道[53, 54]。天然蛋白质可在不同位点结合具有不同溶解性的营养活性物质，这使得制备蛋白质-多配体

表 1　营养活性物质的分类、来源、功能特性及影响因素和每日推荐摄入量

Table 1　Classification, source, functional characteristics, influencing factors and recommended daily intake for nutraceuticals

分类	名称	来源	功能特性	主要限制因素	每日推荐摄入量
亲脂性	α-生育酚[26,27] (α-tocopherol)	小麦胚芽、葵花籽、初榨橄榄油、花生油、大豆油	抗氧化、防止红细胞膜不饱和脂肪酸损伤、提高机体免疫力、促进机体性激素分泌	水溶性差，对光、热、氧敏感，生物利用度低	3~15 mg/d
	姜黄素[23,28] (curcumin)	姜黄	抗炎、抗氧化、抑制癌症如结肠癌和乳腺癌	水溶性差，生物利用度低	3 mg/kg 体重/d
	β-胡萝卜素[29,30] (β-carotene)	胡萝卜、枸杞子、菠菜、西兰花	抗氧化、降低与年龄有关的黄斑变性，癌症和心血管疾病的风险。	水溶性差，对光、热不稳定	5~6 mg/d
	虾青素[31,32] (astaxanthin)	南极磷虾、雨生红球藻、法夫酵母	抗氧化、抗衰老、抗肿瘤、预防心血管疾病	水溶性差，对光、氧及碱性环境敏感，易氧化降解	2 mg/d
	视黄醇[33,34] (retinol)	鱼肝油、动物肝脏	维护视觉正常、维持上皮组织细胞健康、促进免疫球蛋白合成	水溶性差；对光、热、氧气及酸性环境敏感，易氧化降解	700 μg/d
亲水性	叶酸[2,35] (folic acid)	绿色蔬菜、水果、谷物	缺乏将导致巨幼细胞性贫血、阿尔茨海默症、唐氏综合症、情绪障碍、动脉粥样硬化、妊娠并发症和男性不育	对光、热及酸性环境敏感，易氧化降解	400 μg/d
	表没食子儿茶素没食子酸酯[36,37](EGCG)	茶叶	抗氧化、延缓衰老、调节心脑血管、抗炎、预防癌症	对光、氧、热及中性碱性环境敏感，易氧化降解	300 mg/d
	抗坏血酸[38,39] (ascorbic acid)	柑橘类水果、蔬菜	抗氧化、预防癌症	在光、氧、热及碱性环境中易氧化降解	75 mg/d(女性) 90 mg/d(男性)
	花青素[40,41] (anthocyanin)	葡萄、蓝莓、紫甘薯、血橙	抗氧化、抗炎、抗癌及保护神经系统	对光、氧、热敏感	36 mg/d
两亲性	白藜芦醇[42,43] (resveratrol)	葡萄、花生、虎杖	抗氧化、抗炎、抗肿瘤、调节血脂	水溶性较差，对光、氧敏感易氧化异构化	5~10 mg/d
	柚皮素[44,45] (naringenin)	西柚、胡柚皮、柑桔、葡萄柚	抗氧化、抑菌作用、抗病毒、抗癌、肝保护作用、神经保护作用	水溶性较差，生物利用度低，味苦	6~12 mg/d
	槲皮素[46,47] (quercetin)	洋葱、苹果、葡萄酒	抗氧化、抗炎、抑制肥胖	水溶性较差，生物利用度低，对热和碱性环境敏感	6~18 mg/d

复合物成为可能。BSA 是由 3 个同源结构域(I-III)组成, 每个域包含 2 个子域(A 和 B), 组装成圆柱状结构, 主要配体结合位点分别位于子结构域 IIA 和 IIIA 的疏水腔中, 即位点 I 和位点 II[55]。β-LG 是由 8 条反平行的 β-折叠链组成内包含花萼状疏水孔穴的 β-桶型结构, 外部有一α-螺旋, 具有多个潜在的配体结合位点: β-桶的内腔、Trp19-Arg124 附近的外表面、α-螺旋与 β-桶间凹槽状的疏水口袋、靠近 β-桶孔的位置、以及二聚体中单体-单体界面处[56]。这些蛋白质可以结合金属离子、脂肪酸、维生素和多酚化合物等活性物质, 改善它们的水溶性和化学稳定性。在此基础上, 研究发现, β-LG 可同时结合α-生育酚、白藜芦醇和叶酸生成蛋白质-三配体复合物[56]; BSA 结合视黄醇、EGCG 和白藜芦醇生成四元复合物[55]。然而, 天然蛋白质的配体结合位点是溶剂可及的, 通常不能达到长期有效的保护作用。β-乳球蛋白和视黄醇、白藜芦醇和叶酸生成复合物后, 进一步和果胶复合生成纳米粒子, 可以抵抗蛋白质对白藜芦醇储藏稳定性的负作用[57]。因此, 利用蛋白质的配体结合特性, 再组装制备复杂的组装体系, 将有可能实现对不同溶解性的活性物质的共包埋和保护。

3.1.2 基于蛋白质的纳米/微米粒子

蛋白质是环境敏感的, 通过热处理、pH 循环、反溶剂沉淀等方法可制备自组装纳米/微米粒子。热变性的β-LG 可与 EGCG 反应生成纳米粒子, 改善 EGCG 的氧化稳定性[58]。酪蛋白具有解离和再缔合特性, 通过 pH 循环法, 将姜黄素包埋在酪蛋白纳米颗粒中, 在碱性条件下抑制了姜黄素的降解, 显著地改善其细胞摄取情况[59]。在通过反溶剂沉淀法制备的玉米蛋白纳米粒子中, α-生育酚主要包埋在疏水内核, 而白藜芦醇则更接近于粒子的表面[60]。将 α-生育酚掺入大麦蛋白纳米颗粒以隔离内部水相和外部环境, 降低了内部维生素 B_{12} 的泄露而显著地提高了包埋率[61]。另外, 利用带相反电荷的蛋白质间通过静电吸引组装成微球结构, β-LG 与蛋清溶菌酶可包埋 90.8%的维生素 D_3[62]。

蛋白质可与多糖反应生成复合粒子, 与单独蛋白或多糖相比, 复合粒子具有显著的优势。在蛋白载体具有较高包埋率的基础上, 多糖复合可提高颗粒的分散性, 同时可对复合粒子的结构进行调控, 针对性地定制载体体系[63]。研究发现, 将果胶静电吸附在酪蛋白酸钠/玉米醇溶蛋白颗粒上, 不仅改善了纳米颗粒的理化稳定性, 显著地提高纳米颗粒对姜黄素的包埋率, 并使得姜黄素可在胃肠道条件下持续释放[64]。包埋白藜芦醇的大豆蛋白纳米颗粒对环境压力(如 pH 值、离子强度和紫外线)不稳定, 通过静电作用复合海藻酸钠, 纳米颗粒稳定性得到改善的同时提高了白藜芦醇的光稳定性[65]。利用层层组装技术制备透明质酸涂层的玉米蛋白粒子, 将姜黄素包埋在玉米蛋白内核, 将槲皮素包埋于玉米蛋白和透明质酸壳层间, 改善了 2 种活性物质的长程物理稳定性, 并延缓了它们在胃肠条件下的释放[66]。蛋白质/多糖复合物取代脂质载体可制备低脂型食品, 有助于降低肥胖引起的动脉硬化、高血压、糖尿病和癌症的发病率。

3.2 基于蛋白质的乳状液型载体

蛋白质具有良好的乳化和凝胶等功能特性, 但利用单一特性制备的组装体通常体不能完全满足有效载体体系的要求。通过对蛋白质结构和功能特性关系的研究, 联合不同功能特性, 设计具有新颖结构的组装体, 将有利于开发可食用共包埋载体体系。

3.2.1 蛋白质乳状液

蛋白质具有两亲性, 可以用作乳化剂及稳定剂, 利用静电排斥和空间位阻效用使热力学不稳定的油-水两相趋于稳定[67]。蛋白质稳定的水包油(O/W)型乳状液已被广泛地应用于疏水性活性物质的包埋, 对番茄红素[68]、β-胡萝卜素[69]和维生素 D[70]等活性物质有较好的保护效果。抗氧化剂的加入已被报道可以改善乳状液内部油相或溶解于油相的活性物质的稳定性。根据“极性矛盾”理论, 疏水性和两亲性抗氧剂由于对油-水界面具有更高的亲和力而具有更好的保护效果。通过大豆分离蛋白与白藜芦醇间结合, 两者复合物直接可用作乳化剂, 改善 O/W 型乳状液的氧化稳定性[71]。基于乳清蛋白的配体结合特性, 白藜芦醇在葵花籽油表面的吸附率只有约 50%; 在此基础上, 利用 WPI 微凝胶稳定葵花籽油乳状液, 随着钙离子浓度增加, 白藜芦醇在油-水界面含量增加, 但其储藏稳定性反而降低, 进一步加入阿拉伯胶则可以抵抗钙离子对白藜芦醇稳定性的负作用[72-74]。随着蛋白质粒子稳定的乳状液的不断报道, 进一步扩展了单重乳状液在亲脂性和两亲性活性物质共包埋中的应用[75,76]。

3.2.2 蛋白质乳化凝胶

蛋白质在变性后结构展开, 分子间发生交联聚集, 当吸引力和排斥力达到平衡时生成具有三维网络结构的凝胶, 根据处理方式不同可以分为热致凝胶和冷致凝胶[77]。冷致凝胶包括酸致凝胶、酶促凝胶、金属离子交联凝胶, 可用于热敏性活性物质的递送。视黄醇在 WPI 冷凝胶中的包埋率可达 80%, 具有良好的保护效果[78]。明胶-果胶复合凝胶可有效包埋虾废料中含虾青素的脂质提取物, 抑制虾青素的氧化降解, 将其应用于酸奶体系, 可产生颜色均匀的产品, 提高了脂质提取物的着色性[79]。乳状液凝胶(又称乳化凝胶)是一种含有乳化油滴的凝胶体系, 通过液滴高度聚集使连续相凝胶化而形成。联合 WPI 的乳化和冷致凝胶特性已制备内嵌油脂球的自支撑凝胶, 将 α-生育酚包埋于内部葵花籽油滴中, 将白藜芦醇包埋于蛋白相, 两种活性物质均可以达到 100%包埋[80]。

利用水包油包水(W/O/W)型双重乳状液可以将亲水性活性物质包埋于内部水相, 亲脂性活性物质则溶于油相中, 实现对 2 种不同溶解性的活性物质的共包埋[81,82]。然

而, 采用简单方法难以获得高稳定性的双重乳状液。利用蛋白质的凝胶特性, 在双重乳状液的内水相中加入明胶作为胶凝剂, 以麦胶蛋白作为外水相乳化剂并酸致凝胶, 制备 W/OW 型乳化凝胶, 将 65.5%的 EGCG 和 97.2%的槲皮素分别包埋在内水相和油相, 改善了它们的生物可及性[83]。

4 展　望

营养活性物质载体体系的研究是目前科学研究的热点之一, 共包埋技术可同时实现多种活性物质的功能表达, 因而受到越来越多的关注。共包埋营养活性物质的选取需要关注它们间相互作用, 根据表现的特性设计载体体系。另外, 有效共包埋载体的开发及其在更加复杂的食品体系中的应用还有待进一步系统地研究。在阐明单一营养活性物质包埋和保护机制的基础上, 研究不同活性物质在载体体系中共存和可能的竞争, 将对营养活性物质的利用和功能性产品的开发具有指导意义。

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