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虾青素的生理功能及其在动物生产中的应用

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摘　要: 虾青素是一种脂溶性的类胡萝卜素,具有抗氧化、提高机体免疫力等功能。作为一种天然的饲料添加剂,虾青素在动物生产中有着良好的应用前景,具有提高动物免疫力、提升畜产品品质等作用。本文阐述了虾青素的生理功能及其作用机制,并综述了国内外学者在动物生产中应用虾青素的最新研究成果,以期为虾青素在动物生产中更好地应用提供参考。

关键词: 虾青素;生理功能;作用机制;动物生产;应用

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虾青素(astaxanthin)又名变胞藻黄素或虾红素,存在于各种微生物和海洋动物中如红法夫酵母、微藻、三文鱼、磷虾以及复杂植物和一些鸟类中[1-2],天然虾青素主要来源于海鲜的提取[3-4]。虾青素在1938年被德国化学家理查德·库恩首次从龙虾体内提取并被鉴定,其抗氧化活性远远优于其他类胡萝卜素,是维生素C的6 000倍,是辅酶Q10的800倍,是维生素E的550~1 000倍,是花青素的200倍,因此,被称为"抗氧化之王"[5]。随着抗生素禁用,虾青素凭借其天然、无残留、具有抗氧化及提高机体免疫功能的特点,成为一种具有潜力的绿色添加剂,但现阶段关于虾青素在动物生产中应用的研究较少。因此,本文阐述了虾青素的生理功能,总结了其在动物生产中的作用效果与可能的作用机制,旨在为虾青素开发和利用提供理论参考。

1　虾青素的化学结构和存在形式

1.1　虾青素的化学结构

虾青素(分子式$C_{40}H_{52}O_4$),即3,3′-二羟基-4,4,-二酮基-β,β′-胡萝卜素,熔点为224 ℃,不溶于水,易溶于有机溶剂[6],化学结构如图1所示。由于共轭双键的存在,虾青素容易发生顺反异构,生成大量的几何异构体,顺式异构体中氢原子有空间位阻,因此,虾青素主要以全反式异构体形式存在。图1-A中为虾青素立体异构体形式3S、3′S;图1-B和图1-C分别为单酯和双酯形式;图1-D和图1-E分别为立体异构体3R、3′S和3R、3′R。天然虾青素主要以3S、3′S和3R、3′R为主,而合成虾青素以3S、3′S,3R、3′S,3R、3′R的比值为1:2:1固定存在[1,7-8]。

1.2　虾青素的存在形式

由于共轭双键具有疏水性,虾青素在细胞膜中两端的紫罗兰酮环分别嵌入磷脂双分子层,连接细胞膜的内外[6]。自然界中的虾青素主要以游离态和酯化态2种形式存在,化学合成的虾青素均为3S、3′R的游离态。在生物体内天然虾青素主要以3S、3′S或3R、3′R的酯化形式存在,其中红法夫酵母中的虾青素主要以酯化的3R、3′R为主[9],雨生红球藻中的虾青素含5%游离酯、25%双酯和70%单酯[5],主要以3S、3′S为主。游离态的虾青素容易氧化,可与蛋白质和脂质结合,形成蓝灰色的复合物,在受到光和热等环境因素胁迫时发生游离现象,呈现出红色。

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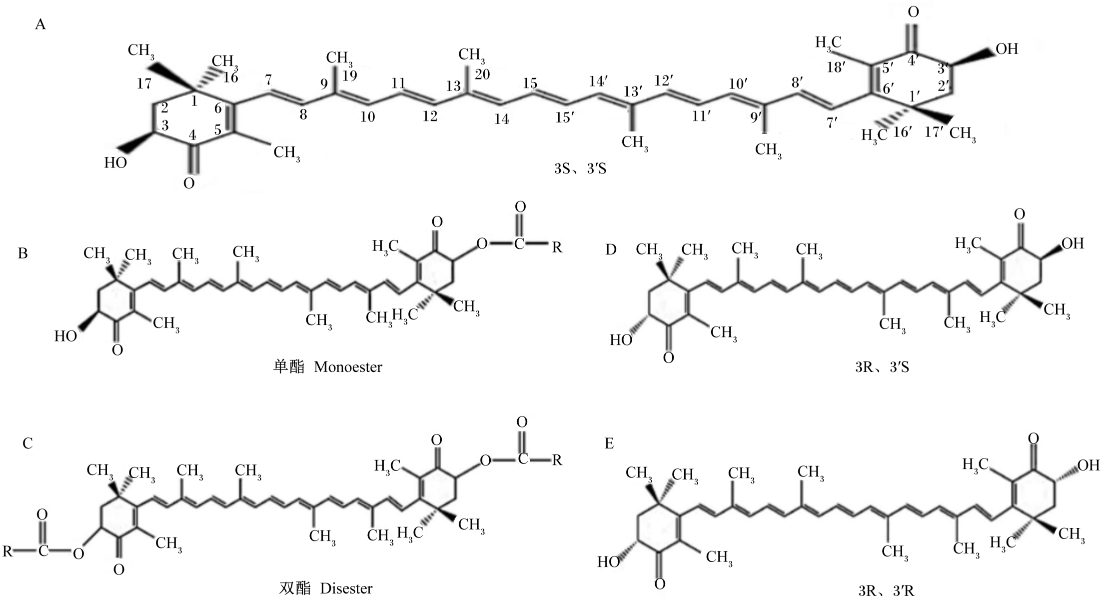

图 1　虾青素的化学结构

Fig.1　Chemical structure of astaxanthin

2　虾青素的吸收代谢机制

虾青素的生物利用率较低,主要是由于其水溶性和分散性差,因此,消化液中有限的溶解度会影响肠上皮细胞对虾青素的吸收,使其与乳糜微粒结合进入到淋巴中[3,10-11]。动物摄入的虾青素在小肠的混合胶束中发生溶解,这些胶束是胆汁酸、磷脂、胆固醇、脂肪酸和单酰基甘油的混合物。虾青素通过胞质膜磷脂双层膜的自由扩散从胶束转移到上皮细胞,被肠黏膜细胞部分吸收后与乳糜微粒结合,含有虾青素的乳糜微粒进入血液后被脂蛋白脂肪酶消化,储存在肝脏中,然后与极低密度脂蛋白(very low density lipoprotein,VLDL)、低密度脂蛋白(low density lipoprotein,LDL)和高密度脂蛋白(high density lipoprotein,HDL)结合,最终通过体循环运输到皮肤、肌肉和性腺等组织中。肝脏是类胡萝卜素的主要代谢器官,可将虾青素分解成其他色素或者不含色素的代谢物,并随胆汁分泌到肠道,进行重吸收,未被代谢的虾青素则被重新包装成 VLDL 重新进入肝脏,最后经肾脏排出。到达肌肉组织中的虾青素通过疏水键与肌动球蛋白结合形成复合物,沉积在肌节和结缔组织当中,在 VLDL 和 LDL 流经血液时,部分复合物被胆固醇酯转移蛋白(cholesterol ester transfer protein,CETP)转移到 HDL 中,运送至到皮肤和性腺,在性腺和卵细胞中,虾青素与卵黄脂蛋白可形成复合物并沉积[12]。虾青素酯在被吸收和转运前,需要被胆固醇酯酶水解[13],Coombes 等[14]发现人血液中游离的虾青素含量可达 0.19 μmol/L,说明游离态虾青素可能在人体循环中被优先吸收或选择性转运[15]。此外,动物试验也显示,虾青素的生物利用度受其酯化状态的影响[16],表明将其添加到食品、饮料和医药产品中时需使用表面活性剂和其他载体[17]。

由于人工合成的虾青素均为游离态,所以其稳定性低于天然虾青素,而且不能以酯化形式存在,产生多变的颜色,在体内的吸收率和沉积率均低于天然虾青素。人工合成虾青素可能因混入各种杂质或非天然副产物等引起生物利用安全性问题。

3　虾青素的主要生物学功能

3.1　着色功能

虾青素进入生物体后可以不经修饰或生物转化而直接贮存沉积在组织中,与肌红蛋白非特异性结合,呈现出红色[18]。虾青素的着色机制主要包括 2 种:第 1 种即蛋白质复合物中虾青素的物理排列,与游离的虾青素(双键角度约 50°)相比,虾

青素的 C6－C7 键的扭曲角度大大降低，形成6－S－反式构象，呈现出蓝灰色。此外，在甲壳素中配对的虾青素之间通过激子偶联，端环与蛋白质结合形成的多烯链共面，并沿复合形式的共轭阵列增强重叠，从而使甲壳类动物的壳呈现出红色[19-20]。第2种涉及虾青素在络合过程中发生的可逆电离，被认为是 α－羟基环己酮残基去质子化和质子转移的结果。虾青素在酸和碱诱导下，与去质子化的蛋白质结合形成烯醇化物，一端与3号氧原子和组氨酸之间的氢键结合，另一端与4号氧原子和水－酪氨酸对之间的氢键结合，高温条件会导致氢键断裂，呈现出由蓝灰色至红色的变化[21]。

3.2 抗氧化功能

活性氧簇（reactive oxygen species，ROS）过量是导致机体氧化损伤的主要因素。机体内过量的 ROS 通过链式反应与蛋白质、脂质、碳水化合物及核酸生成不同氧化产物，造成氧化损伤。虾青素具有诱捕活性氧、增强细胞阻断氧化应激的能力[22]，通过清除过量的 ROS 以终止链式反应，发挥其抗氧化功能[23]。虾青素有比胡萝卜素更长的共轭体系，较长的共轭体系使得虾青素分子可以更强、更活跃地吸收单线态氧的能量，并将吸收的能量以热能的形式耗散。其抗氧化功能主要源于其分子结构，通过两端极性紫罗兰酮环和磷脂双分子层融合，以自由扩散的方式穿过细胞膜[24]，虾青素可以存在于细胞膜和脂蛋白中，不改变双层膜的结构完整性或电子密度，其多烯链能捕获细胞膜中的自由基，末端环可以清除细胞膜外部和内部的自由基[18]。最新研究发现，幽门螺旋杆菌会导致线粒体中 ROS 水平上升，使胃肠上皮细胞中超氧化物歧化酶的活性降低，而用5 μmol/L虾青素预处理胃肠上皮细胞后，其超氧化物歧化酶的活性不会受到幽门螺旋杆菌的影响，说明虾青素可能对线粒体具有保护作用[25]。

3.3 免疫功能

炎症的特点是血浆和细胞产生促炎因子的能力增强，其中，巨噬细胞产生 ROS 是引发机体产生炎症反应的关键潜在因素[26-27]。有研究表明，虾青素能减少巨噬细胞中 ROS 的积累，抑制核因子－κB（nuclear factor-kappaB，NF-κB）诱导的炎性介质的产生[28-30]。核因子 E2 相关因子 2（nuclear factor erythroid-2-related factor2，Nrf2）通过增加抗氧化酶的产生和抑制 NF-κB 信号通路使机体抗炎功能增强[31-32]。虾青素除在抑制核因子－κB p65（p65 nuclear factor-kappaB，NF-κB p65）易位方面发挥作用外，还通过激活 Nrf2 通路，限制炎性介质产生[33]。此外，虾青素能阻断 Toll 样受体 4 的表达，抑制 NF-κB p65 的磷酸化和 NF-κB 的降解[34]，达到抗炎效果。Han 等[35]发现虾青素抑制了信号转导和转录激活因子 3 的 DNA 结合活性，从而抑制脂多糖诱导的氧化反应、神经炎症反应和淀粉样蛋白形成。Park 等[36]发现虾青素通过抑制 NF-κB 抑制蛋白的降解，进而抑制 NF-κB 的活化，抑制了炎性细胞因子如前列腺素 E2（prostaglandin E2，*PGE*2）、肿瘤坏死因子（tumor necrosis factor，*TNF*）、白细胞介素－1β（interleukin-1β，*IL*-1*β*）、诱导性一氧化氮合酶（inducible nitric oxide synthase，*iNOS*）、环氧合酶 2（cyclooxygenase 2，*COX*2）的表达，以及减少一氧化氮（nitric oxide，NO）的产生。因此，虾青素主要通过抑制巨噬细胞中 ROS 的积累和下调促炎因子途径提高机体免疫的功能。

3.4 预防心血管疾病

氧化应激和炎症是动脉粥样硬化性心血管疾病的病理生理特征。虾青素是一种潜在的治疗动脉粥样硬化性心血管疾病的药物[37-38]，对心肌[39-40]、脑[41]、肝脏[42]、肾脏[43]等不同缺血再灌注损伤体内模型具有保护作用。此外，虾青素能降低高脂饮食引起的高脂血症大鼠的凝血、血小板聚集和纤溶活性，这些作用与虾青素降低血脂和脂蛋白含量、产生抗氧化剂和保护内皮细胞有关[44]。临床研究也发现，虾青素具有轻微的降血糖作用[45]。然而，关于虾青素的代谢和药代动力学等方面的认识还有待进一步研究。

3.5 抗癌作用

虾青素对不同类型的癌症都具有抑制作用，包括口腔癌[46]、膀胱癌[47]、结肠癌[48-49]、白血病[50]和肝细胞癌[51]、肺癌[52]和乳腺癌[53]等。其抗癌作用归因于其具有选择性抑制细胞增殖和调节细胞凋亡的功能[54-55]。此外，虾青素的抗癌机制与细胞膜的稳定性和膜蛋白基因表达有关，它通过改变膜稳定性和基因表达量来调节细胞间物质交换，维持细胞的正常功能[56-57]。

3.6 保护神经系统

虾青素被认为是一种潜在的神经保护剂，因

为它能够跨越脑血屏障,保护大脑免受急性损伤和慢性神经退行性病变的伤害[58]。有研究表明,虾青素具有促进或维持神经可塑性的潜力,可以通过促进神经发生和促进神经功能的增强而增强认知功能[59],Lobos 等[60]发现,淀粉样蛋白 β 肽寡聚体会促使神经元线粒体产生过量的 ROS,导致神经元损伤,而虾青素能够通过钙神经素/活化 T 细胞核因子(nuclear factors of activated T cells,NFAT)阻止淀粉样蛋白 β 肽寡聚体对突触的毒性作用。此外,虾青素对帕金森病诱导的神经衰退过程具有抑制作用[61],Lee 等[62]研究表明,虾青素对 1-甲基-4-苯基-1,2,3,6-四氢吡啶(MPTP)诱导的帕金森病(idiopathic Parkinson's disease,PD)小鼠模型中黑质神经元凋亡具有缓解作用,这种作用可归因于 B 淋巴细胞瘤-2(B-cell lymphoma-2,Bcl-2)蛋白表达的上调和促凋亡基因 Bax(Bcl-associated x protein,*Bax*)的表达降低,从而抑制半胱氨酸天冬氨酸蛋白酶 3 的活化。Altunrende 等[63]研究表明,虾青素对钙离子稳态具有保护作用,而钙离子能调节神经元中的许多细胞过程,通过调节突触处谷氨酸的释放量保护神经元功能的正常发挥。

4 虾青素在动物生产中的应用

4.1 虾青素在猪生产中的应用

Do 等[64]研究表明,饲粮中添加 0.5 mg/kg 虾青素促进了热应激下母猪卵母细胞的成熟,进而可提高其受精率及胚胎存活率,使热应激下母猪繁殖性能提高,这可能是虾青素缓解了高温对猪卵母细胞减数分裂的负面影响。Basioura 等[65]和 Lee 等[66]发现,虾青素对公猪精液质量具有保护作用,可能是虾青素降低了精液中 ROS 的含量,从而提高了精子的寿命。林建坤等[67]研究表明,饲粮中添加 4 400 mg/kg 虾青素和双乙酸钠的混合制剂能够显著提高 28 日龄三元杂交断奶仔猪血清和空肠黏膜超氧化物歧化酶、谷胱甘肽过氧化物酶的活性,提高了机体抗氧化能力,促进空肠细胞结构和功能的完整性,提高肠道对养分的消化能力,从而提高了生长性能。此外,由于肌肉中的不饱和脂肪酸和蛋白质分子与空气中的氧气结合形成过氧化物,会导致脂质分解和多肽链断裂,使肌肉的持水性和风味下降[68],虾青素具有强大的抗氧化功能和着色功能,可通过其在肌肉中的沉积,降低肌肉的脂质和蛋白质氧化速度,有望提高肉品质。

4.2 虾青素在禽类生产中的应用

虾青素具有提高肉鸡生长性能、改善肉品质的作用。付兴周等[69]研究发现,肉鸡饲粮中添加 1%虾青素复合添加剂,其平均日增重和饲料转化率显著提高,宰后肌肉的 pH 下降速度显著降低。Perenlei 等[70]研究表明,饲粮中添加 20 mg/kg 含虾青素的酵母粉可显著增加肉鸡屠宰后肌肉的红度(a^*)和黄度(b^*)值,降低烹饪损失,且 120 h 时虾青素组的总游离氨基酸含量显著高于对照组。Inoue 等[71]也发现,饲粮中添加 0.15%富含虾青素的干细胞粉可显著增加肉鸡肌肉的红度和黄度。究其原因,虾青素可以在血浆、肝脏、性腺和大腿肌肉中富集,一方面由于其着色功能增加了胸肌和腿部肌肉的红度和黄度值,另一方面降低了热应激状态下肌肉中丙二醛(MDA)的含量,提高了肌肉的抗氧化能力。

在蛋鸡方面,吴斯诺等[72]发现,饲粮中添加 80 mg/kg 虾青素显著提高了太行鸡的生产性能,降低了料蛋比,同时改善了蛋黄颜色和哈氏单位。王钧艺等[73]研究表明,蛋黄颜色在一定范围内随着虾青素复合添加剂含量的增加而加深。这是由于蛋黄颜色是蛋形成过程中,虾青素与脂蛋白结合,通过体循环进入到蛋黄中,转化成棕油酸二酯在蛋黄内沉积,使蛋黄的黄色加深或呈现出红色[74]。

4.3 虾青素在水产养殖中的应用

饲料中添加一定量的虾青素可以提高大黄鱼幼鱼[75]和锦鲤[76]的生长性能、凡纳滨对虾[77]等水产品的存活率,其原因是虾青素可以增强鱼虾的免疫力,提高对高氮、低氧环境的耐受力[78-79]。虾青素还显著提高了水产品的色素沉积,对于甲壳类动物,如蟹、虾等,色素沉积主要在壳、性腺和肝胰腺上,而对肉色无显著影响;就鱼类而言,鱼体颜色鲜艳,而鱼肉却是白色。李小兵等[80]通过向金曼龙饲料中添加 200 mg/kg 的虾青素发现,在第 15 天时鱼体、鱼鳞、鱼鳍、鱼皮中色素沉积量达最高值,且不同组织部位的含量从高至低依次为鱼皮、鱼鳍、鱼鳞、鱼体、鱼头、鱼肉,体现了虾青素在不同部位沉积能力的差异。虾青素的作用效果与添加量有关,但其含量沉积过高会对机体产生额外的代谢,因此,多余的虾青素会通过代谢排出体外。

5 小 结

综上所述,虾青素具有多种生理功能,作为饲料添加剂在动物生产中具有提高动物的免疫力和产品品质的功能,但目前在动物生产应用方面的研究较少,且作用机制尚不清楚。因此,需要进一步深入研究虾青素在动物生产中的适宜添加量、作用效果和作用机制,为虾青素在动物生产中的利用提供数据参考。此外,最新研究表明,利用聚合物[81-82]、脂质[83-84]和环糊精体系[85]对虾青素的溶解度和稳定性均有改善,但对于包被后虾青素的抗氧化能力尚缺乏评估,因此,需深入研究来确定虾青素载体系统的生物学效价,以期为虾青素在动物生产中更好的应用提供理论依据。

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Physiological Function of Astaxanthin and Its Application in Animal Production

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Abstract: Astaxanthin is a fat-soluble carotenoid with strong antioxidant activity, which has been widely used in the food, cosmetics and health care products industry. As a natural feed additive, astaxanthin has a good application prospect in animal production, and can improve animal immunity and product quality. This paper aimed to illustrate the physiological functions and mechanism of astaxanthin and reviewed the latest research findings on the application in animal production, which could be regarded as a reference for application of astaxanthin. [***Chinese Journal of Animal Nutrition*, 2019, 31(11): 4986-4994**]

Key words: astaxanthin; physiological function; mechanism of action; animal production; application

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