

韩吉平,江 宁,诸永志,等.天然虾青素的制备和功能研究进展[J].江苏农业科学,2021,49(8):56-60.

doi:10.15889/j.issn.1002-1302.2021.08.009

天然虾青素的制备和功能研究进展

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摘要:虾青素属于类胡萝卜素家族的重要成员,是一种天然抗氧化剂,具有良好的清除自由基和屏蔽紫外光的能力。综述了天然虾青素的制备方法,并对不同制备方法的优缺点进行比较与总结。近年研究发现,虾青素具有广泛的生物学效应,本文对天然虾青素在药用和营养方面的潜在应用进行了综述。

关键词:虾青素;制备;功能

中图分类号: TS254.1 **文献标志码:** A **文章编号:** 1002-1302(2021)08-0056-05

虾青素(astaxanthin)是一种脂溶性色素^[1],呈橙红色,广泛存在于虾、蟹等甲壳类动物体内,同时也是一种类胡萝卜素的含氧衍生物^[2]。一般特殊的结构容易产生特殊的生物功能。大量研究表明,虾青素具有许多生理活性,如有效清除体内自由基、抗衰老^[3]、抗肿瘤^[4]、预防心脑血管疾病^[5]、心血管疾病^[6]、保护肝脏^[7]、抗糖尿病^[8]等。此外,虾青素是一类能穿透血脑、血视网膜屏障的类胡萝卜素,对改善中枢神经系统和脑功能有积极作用^[9]。

1 天然虾青素的制备方法

1.1 有机溶剂萃取法

大量研究表明,丙酮对虾青素的提取效果较

好,这是因为其含有与虾青素高度相似的羰基。相较于甲醇、乙醇、乙腈等有机溶剂,丙酮提取的虾青素回收率最高^[10]。此外,Sachindra 等研究发现,与较单一的有机溶剂相比,混合溶剂(异丙醇:己烷体积比=1:1)对虾青素的提取率更高^[11]。然而,丙酮等有机溶剂具有沸点低、易挥发、中等毒性等特点,在食品加工中可能存在食品安全隐患。

1.2 微波辅助萃取法

微波辅助萃取技术是在传统有机溶剂萃取基础上发展起来的一种新型萃取技术。研究表明,利用微波辅助萃取技术从雨生红球藻中提取虾青素是一种经济有效的方法。微波能通过微藻生物质传递,增加细胞内动能,引起液体颗粒振动。随后细胞温度的升高和细胞壁压力的增加导致细胞分裂。此外,微波辅助过程通过打破萃取溶剂分子间的化学键,促进溶解离子通过细胞基质孔隙,达到缩短提取时间的作用^[12]。微波辅助技术不仅可以提高虾青素的萃取效率,而且可以提高提取率。

收稿日期:2020-07-21

基金项目:江苏现代农业产业技术体系项目(编号:JATS[2019]415)。

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Reports,2016,6:25107.

[57] Yang X Y,Zeng Z H,Yan J Y,et al. Association of specific pectin methyltransferases with Al³⁺-induced root elongation inhibition in rice [J]. *Physiologia Plantarum*,2013,148(4):502-511.

[58] Zhu C Q,Cao X C,Bai Z G,et al. Putrescine alleviates aluminum toxicity in rice (*Oryza sativa*) by reducing cell wall Al contents in an ethylene-dependent manner[J]. *Physiologia Plantarum*,2019,167(4):471-487.

[59] Yang W,Ruan M,Xiang M,et al. Overexpression of a pectin methyltransferase gene PtoPME35 from *Populus tomentosa* influences

stomatal function and drought tolerance in *Arabidopsis thaliana* [J]. *Biochemical and Biophysical Research Communications*,2020,523(2):416-422.

[60] Chung D,Pattathil S,Biswal A K,et al. Deletion of a gene cluster encoding pectin degrading enzymes in *Caldicellulosiruptor bescii* reveals an important role for pectin in plant biomass recalcitrance [J]. *Biotechnology for Biofuels*,2014,7(1):147.

[61] Biswal A K,Atmodjo M A,Li M,et al. Sugar release and growth of biofuel crops are improved by downregulation of pectin biosynthesis [J]. *Nature Biotechnology*,2018,36(3):249-257.

1.3 超声波辅助萃取法

超声波辅助提取技术是一种高效回收雨生红球藻虾青素的现代技术。超声波对虾青素的提取是通过空化作用,细胞壁被快速破坏,从而增强萃取剂在细胞基质中的传递^[13]。超声波的功率、温度和溶液浓度是虾青素提取的关键参数。Zou 等通过在超声功率 200 W,溶液浓度 48% 乙醇/乙酸乙酯(液固比为 20 : 1),温度 41.1 °C,提取时间 16.0 min 的试验条件下的超声辅助萃取,实现雨生红球藻生物量的虾青素产量达 27.58 mg/g^[14]。

1.4 酶解法

天然虾青素以游离虾青素、虾青素单酯和二酯 3 种形式存在,其中主要存在形式是较稳定的虾青素酯,即虾青素单酯和虾青素二酯^[15-16]。虾青素酯的脱酯方法分为皂化法和酶解法。为了评估酶解和皂化作用对天然虾青素酯的去酯化相对效率,Su 等发现使用胆固醇酯酶可以使虾青素酯完全水解,其降解和异构化作用显著减弱^[17]。

1.5 超临界流体萃取法

超临界流体萃取是指将超临界状态的 CO₂ 流体作为萃取溶剂与含有虾青素的原料接触,通过调节不同提取参数(温度、时间、压力、添加物等)得到萃取虾青素的最佳条件。利用超临界 CO₂ 萃取法可以最大程度地保持虾青素的生物活性,且可将萃取和分离合二为一。

超临界流体是物质的一种特殊的流体状态,是指在温度和压力高于临界点的情况下,其可以像气体一样从固体中渗出,像液体一样溶解物质。超临界流体萃取是一种环境友好的萃取方法,因为当 CO₂ 作为超临界流体时,可以实现无溶剂萃取。同时,在系统中加入乙醇或甲醇等碳氢化合物和天然油,会增加 CO₂ 对不同溶质的亲和力,从而提高虾青素的提取率^[18]。Cheng 等在微流反应器中对破裂的血球菌进行低压超临界 CO₂ 萃取,并通过光学通道实时监控萃取过程,使用超临界流体萃取法和乙醇助溶剂在 30 s 内快速提取约 98% 的虾青素^[19]。

1.6 油提法

油提法通常用于提取天然虾青素,葵花籽油和椰子油对虾青素的提取率分别可达 26.3 μg/g 和 24.7 μg/g^[20]。温度对亚麻籽油提取虾青素具有显著影响,在高温(60 ~ 90 °C)下,油提法可以获得较高的虾青素回收率;但温度越高,虾青素的稳定性

越差,易发生降解,因此选择合适的提取温度至关重要;此外,当亚麻籽油中含有虾青素时,虾青素的强抗氧化作用可以显著降低亚麻籽油的氧化速率^[21]。

2 天然虾青素的功能研究

虾青素因具有特殊的分子结构,其表现出包括抗氧化、抗衰老和抑制化学物质诱变等生物活性。大量研究表明,虾青素在预防和治疗肿瘤、糖尿病、心血管疾病、眼病、皮肤病、运动疲劳和增强免疫力等方面具有潜在的有益作用^[22-58]。

2.1 降血压

据统计,高血压是全球疾病负担和全球死亡率的最大单一贡献者。虾青素可以通过抑制血管平滑肌细胞增殖和恢复线粒体功能来有效治疗血管重构。在体外,虾青素可减轻血管平滑肌细胞的增殖和迁移,降低细胞中活性氧的含量水平,并平衡与活性氧相关的酶的活性,包括还原型辅酶 II (NADPH) 氧化酶、黄嘌呤氧化酶和超氧化物歧化酶。Chen 等通过血清学试验,发现虾青素可降低自发性高血压大鼠的血压并减轻血管重构^[22]。添加虾青素的饮食通过降低血压、改善心血管重塑和氧化应激状态,有治疗高血压的作用^[23]。

2.2 抗衰老

紫外线老化是导致衰老的重要因素。紫外线到达人体皮肤后会产生活性氧和基质金属蛋白酶,破坏胶原蛋白和弹性蛋白,导致黑色素沉积和产生皮肤皱纹^[24]。据报道,虾青素可以阻止皮肤增厚和胶原蛋白减少,以对抗紫外线引起的皮肤损伤^[25-27],减缓紫外老化引起的生理功能变化^[28]。据报道,膳食中加入虾青素可改善紫外光老化引起的面部皮肤屏障受损和缺乏弹性,且耐受性良好^[29]。

2.3 抗疲劳

抗疲劳作用包括延缓疲劳产生和加速疲劳消除^[30]。天然虾青素由于特殊的分子结构,在清除自由基、降低过氧化物水平、强化机体抗氧化系统等方面有显著功效^[31]。虾青素可以跨越血脑屏障,保护大脑免受急性损伤和慢性神经退行性变^[32]。虾青素的神经保护特性源于其抗氧化、抗凋亡和抗炎作用^[33-34]。

在剧烈运动引起的氧化应激情况下,天然虾青素具有对抗自由基产生并加速自由基清除的作用,显示出卓越的抗氧化功效。通过抗氧化与抗疲劳

效果的相关性分析发现,抗氧化能力的提高可以增强抗疲劳能力,两者相辅相成。膳食中补充虾青素可改善脂质代谢、碳水化合物代谢和氨基酸代谢,对清除自由基和减轻肌肉损伤有显著作用^[35]。

2.4 护眼

研究表明,虾青素可以通过其抗氧化作用减少大鼠视网膜中视网膜蛋白氧化物的含量,抑制缺血诱导的视网膜细胞死亡,并降低高血压引起的视网膜细胞凋亡,在修复视网膜损伤中具有关键作用^[36]。因此,虾青素可在多种眼部疾病中发挥有益作用,包括延缓代谢性白内障发展^[37]、提高改善干眼症患者泪液稳定性、缓解眼睛疲劳^[38]。

虾青素的神经保护作用也可用于青光眼的治疗,眼压升高会导致筛板变形并引起血流紊乱,从而导致轴突丢失和视网膜神经节细胞凋亡,并伴有典型的视神经损伤^[39]。此外,虾青素具有良好的安全性,在临床研究中均无任何不良事件的报告^[40-41]。

2.5 增强免疫力

免疫系统对自由基引起的损伤高度敏感。虾青素不仅能为自由基提供电子,还能与自由基结合生成无害的化合物,从而清除自由基或者终止自由基的链式反应,并恢复免疫系统的防御机制。为了研究虾青素对免疫系统的作用, Park 等将雌性家猫设为模型动物,研究表明,饲喂虾青素的猫外周血单个核细胞的增殖和自然杀伤细胞活性增加^[42]。Zhu 等指出日粮中添加虾青素可以提高生长性能,提高抗氧化和免疫反应,调节相对炎症相关基因的表达^[43]。Jeong 等的研究结果证实了虾青素对免疫细胞的成熟诱导和功能调节活性,这表明在癌症治疗中虾青素的抗氧化作用可增强免疫系统功能^[44]。

2.6 抗糖尿病活性

糖尿病与氧化应激密切相关,氧化应激可能是自由基增加、抗氧化防御能力降低或两者共同产生的结果。一般来说,糖尿病患者的氧化应激水平非常高。它是由高血糖、胰岛 B 细胞功能紊乱和组织损伤引起^[45]。虾青素可降低血浆中葡萄糖和胰岛素水平,并改善全身胰岛素敏感性和胰岛素刺激的葡萄糖摄取。

虾青素治疗可显著提高葡萄糖耐受性和缓解胰岛 B 细胞功能不全,抑制血脂异常和氧化应激,增加抗氧化酶的活性,并最终改善生殖结果^[46]。在糖尿病大鼠淋巴细胞的功能障碍恢复中,虾青素也是一种良好的免疫制剂^[47]。添加虾青素可显著降

低小鼠因高脂、高果糖饮食所致的血糖和提高胰岛素水平^[48]。

2.7 抗肿瘤

虾青素可以通过自身的抗氧化特性,抑制应激诱导的自然杀伤细胞的肿瘤活性,虾青素有效改善了应激诱导的免疫功能障碍,甚至可以调节部分基因的活性,抑制恶性肿瘤的转移^[49]。Faraone 等研究指出,虾青素诱导下肿瘤细胞的细胞周期停滞、可抑制肿瘤扩散、增强肿瘤细胞对化疗的敏感性,并限制其不良反应^[50]。虽然虾青素、角黄素和 β -胡萝卜素均具有抑制肿瘤生长的作用,但虾青素的抗肿瘤活性最高^[51]。

虾青素调节免疫反应,抑制癌细胞生长,减少细菌负荷和缓解胃黏膜炎症,并防止紫外线引起的氧化应激^[52]。Zhang 等研究表明,虾青素可以抑制白血病细胞的增殖和生长^[53]。Yasui 等研究显示,虾青素分泌的促肿瘤坏死因子和抗炎因子能有效抑制结肠癌细胞的生长以及诱导癌细胞的凋亡^[54]。此外,虾青素还能有效预防胃癌、膀胱癌^[55],以及有效清除体内由光辐射产生的自由基,减少光化学对皮肤造成的损伤,阻碍皮肤癌的发生。消炎是预防和治疗癌症的有效手段。以这种方式,抑制炎症细胞因子的表达导致癌变过程停止^[56]。研究表明,虾青素对多种癌细胞有显著的抑制作用,可能是由于它们具有抗炎作用^[57-58]。

3 展望

综上所述,虾青素属于类胡萝卜素,是一种天然抗氧化剂,具有良好的清除自由基能力。天然虾青素卓越的生物活性使其具有广泛的应用前景和巨大的市场潜力,特别是在医药、化妆品、保健品、水产养殖、饲料添加剂等领域均具有很大的利用价值。目前,对虾青素与人体营养健康的相关研究起步较晚,且主要是集中在体外或临床前水平。因此,亟待深入研究虾青素对人体营养健康的作用机制,开发相关功能性食品、保健化妆品、宠物饲料等,扩大天然虾青素的应用范围和市场。

参考文献:

- [1] Ambati R R, Phang S M, Ravi S, et al. Astaxanthin: sources, extraction, stability, biological activities and its commercial applications - a review [J]. *Marine Drugs*, 2014, 12: 128 - 152.
- [2] Liu X B, Osawa T. *Cis* astaxanthin and especially 9 - *cis* astaxanthin exhibits a higher antioxidant activity *in vitro* compared to the all -

- trans* isomer [J]. Biochemical and Biophysical Research Communications, 2007, 357(1): 187 – 193.
- [3] Peng J, Yuan J P, Wang J H. Effect of diets supplemented with different sources of astaxanthin on the gonad of the sea urchin *Anthodiaris crassispina* [J]. Nutrients, 2012, 4(12): 922 – 934.
- [4] Nagendraprabhu P, Sudhandiran G. Astaxanthin inhibits tumor invasion by decreasing extracellular matrix production and induces apoptosis in experimental rat colon carcinogenesis by modulating the expressions of ERK – 2, NF κ B and COX – 2 [J]. Investigational New Drugs, 2011, 29(2): 207 – 224.
- [5] Pashkow F J, Watumull D G, Campbell C L. Astaxanthin; a novel potential treatment for oxidative stress and inflammation in cardiovascular disease [J]. American Journal of Cardiology, 2008, 101(10A): 58D – 68D.
- [6] Fassett R G, Coombes J S. Astaxanthin in cardiovascular health and disease [J]. Molecules, 2012, 17: 2030 – 2048.
- [7] Visioli F, Artaria C. Astaxanthin in cardiovascular health and disease; mechanisms of action, therapeutic merits, and knowledge gaps [J]. Food & Function, 2016, 8(1): 39 – 63.
- [8] Uchiyama K, Naito Y, Hasegawa G, et al. Astaxanthin protects β – cells against glucose toxicity in diabetic db/db mice [J]. Redox Report, 2002, 7(5): 290 – 293.
- [9] Jyonouchi H, Sun S, Iijima K, et al. Antitumor activity of astaxanthin and its mode of action [J]. Nutrition and Cancer, 2000, 36(1): 59 – 65.
- [10] Ruen – ngam D, Shotipruk A, Pavasant P. Comparison of extraction methods for recovery of astaxanthin from *Haematococcus pluvialis* [J]. Separation Science and Technology, 2010, 46(1): 64 – 70.
- [11] Sachindra N M, Bhaskar N, Mahendrakar N S. Recovery of carotenoids from shrimp waste in organic solvents [J]. Waste Management, 2006, 26(10): 1092 – 1098.
- [12] Saini R K, Keum Y S. Carotenoid extraction methods; a review of recent developments [J]. Food Chemistry, 2017, 240: 90 – 103.
- [13] Rammuni M N, Ariyadasa T U, Nimarshana P H V, et al. Comparative assessment on the extraction of carotenoids from microalgal sources; astaxanthin from *H. pluvialis* and β – carotene from *D. salina* [J]. Food Chemistry, 2019, 277: 128 – 134.
- [14] Zou T B, Jia Q, Li H W, et al. Response surface methodology for ultrasound – assisted extraction of astaxanthin from *Haematococcus pluvialis* [J]. Marine Drugs, 2013, 11(5): 1644 – 1655.
- [15] Rao A R, Sarada R, Shylaja M D, et al. Evaluation of hepatoprotective and antioxidant activity of astaxanthin and astaxanthin esters from microalga – *Haematococcus pluvialis* [J]. Journal of Food Science and Technology, 2015, 52(10): 6703 – 6710.
- [16] Holtin K, Kuehnle M, Rehbein J, et al. Determination of astaxanthin and astaxanthin esters in the microalgae *Haematococcus pluvialis* by LC – (APCI) MS and characterization of predominant carotenoid isomers by NMR spectroscopy [J]. Analytical and Bioanalytical Chemistry, 2009, 395(6): 1613 – 1622.
- [17] Su F, Xu H R, Yang N, et al. Hydrolytic efficiency and isomerization during de – esterification of natural astaxanthin esters by saponification and enzymolysis [J]. Electronic Journal of Biotechnology, 2018, 34: 37 – 42.
- [18] Slack G C, McNair H M, Hawthorne S B, et al. Coupled solid phase extraction – supercritical fluid extraction on – line gas chromatography of explosives from water [J]. Journal of Separation Science, 2015, 16(8): 473 – 478.
- [19] Cheng X, Qi Z B, Burdyny T, et al. Low pressure supercritical CO₂ extraction of astaxanthin from *Haematococcus pluvialis* demonstrated on a microfluidic chip [J]. Bioresource Technology, 2018, 250: 481 – 485.
- [20] Sachindra N M, Mahendrakar N S. Process optimization for extraction of carotenoids from shrimp waste with vegetable oils [J]. Bioresource Technology, 2005, 96(10): 1195 – 1200.
- [21] Pu J N, Bechtel P J, Sathivel S. Extraction of shrimp astaxanthin with flaxseed oil; effects on lipid oxidation and astaxanthin degradation rates [J]. Biosystems Engineering, 2010, 107: 364 – 371.
- [22] Chen Y Q, Li S, Guo Y X, et al. Astaxanthin attenuates hypertensive vascular remodeling by protecting vascular smooth muscle cells from oxidative stress – induced mitochondrial dysfunction [J]. Oxidative Medicine and Cellular Longevity, 2020, 2020: 1 – 19.
- [23] Monroy – Ruiz J, Sevilla M, Carrón R, et al. Astaxanthin – enriched – diet reduces blood pressure and improves cardiovascular parameters in spontaneously hypertensive rats [J]. Pharmacological Research, 2011, 63(1): 44 – 50.
- [24] Yi X W, Xu W, Zhou H H, et al. Effects of dietary astaxanthin and xanthophylls on the growth and skin pigmentation of large yellow croaker *Larimichthys croceus* [J]. Aquaculture, 2014, 433: 377 – 383.
- [25] Liu X J, Chen X F, Liu H, et al. Antioxidation and anti – aging activities of astaxanthin geometrical isomers and molecular mechanism involved in *Caenorhabditis elegans* [J]. Journal of Functional Foods, 2018, 44: 127 – 136.
- [26] Rao A R, Sindhuja H N, Dharmesh S M, et al. Effective inhibition of skin cancer, tyrosinase, and antioxidative properties by astaxanthin and astaxanthin esters from the green alga *Haematococcus pluvialis* [J]. Journal of Agricultural and Food Chemistry, 2013, 61(16): 3842 – 3851.
- [27] Hama S, Takahashi K, Inai Y, et al. Protective effects of topical application of a poorly soluble antioxidant astaxanthin liposomal formulation on ultraviolet – induced skin damage [J]. Journal of Pharmaceutical Sciences, 2012, 101(8): 2909 – 2916.
- [28] Santos S D, Cahú T B, Firmino G O, et al. Shrimp waste extract and astaxanthin; rat alveolar macrophage, oxidative stress and inflammation [J]. Journal of Food Science, 2012, 77(7): H141 – H146.
- [29] Yoon H S, Cho H H, Cho S, et al. Supplementing with dietary astaxanthin combined with collagen hydrolysate improves facial elasticity and decreases matrix metalloproteinase – 1 and – 12 expression; a comparative study with placebo [J]. Journal of

- Medicinal Food,2014,17(7):810–816.
- [30] Jin H M, Wei P. Anti – fatigue properties of tartary buckwheat extracts in mice[J]. International Journal of Molecular Sciences, 2011,12:4770–4780.
- [31] Lorenz R T, Cysewski G R. Commercial potential for *Haematococcus* microalgae as a natural source of astaxanthin [J]. Trends in Biotechnology,2000,18(4):160–167.
- [32] Shen H, Kuo C C, Chou J, et al. Astaxanthin reduces ischemic brain injury in adult rats[J]. Faseb Journal,2009,23(6):1958–1968.
- [33] Zhang X S, Zhang X, Wu Q, et al. Astaxanthin offers neuroprotection and reduces neuroinflammation in experimental subarachnoid hemorrhage [J]. The Journal of Surgical Research, 2014,192(1):206–213.
- [34] Zhang X S, Zhang X, Zhou M L, et al. Amelioration of oxidative stress and protection against early brain injury by astaxanthin after experimental subarachnoid hemorrhage [J]. Journal of Neurosurgery,2014,121(1):42–54.
- [35] Polotow T G, Vardaris C V, Mihaliuc A R, et al. Astaxanthin supplementation delays physical exhaustion and prevents redox imbalances in plasma and soleus muscles of wistar rats [J]. Nutrients,2014,6:5819–5838.
- [36] Cort A, Ozturk N, Akpinar D, et al. Suppressive effect of astaxanthin on retinal injury induced by elevated intraocular pressure [J]. Regulatory Toxicology and Pharmacology,2010,58(1):121–130.
- [37] Yang M, Chen Y, Zhao T, et al. Effect of astaxanthin on metabolic cataract in rats with type 1 diabetes mellitus[J]. Experimental and Molecular Pathology,2020,113:104372.
- [38] Giannaccare G, Pellegrini M, Senni C, et al. Clinical applications of astaxanthin in the treatment of ocular diseases: emerging insights [J]. Marine Drugs,2020,18(5):239.
- [39] Floriani I, Quaranta L, Rulli E, et al. Health – related quality of life in patients with primary open – angle glaucoma. An Italian multicentre observational study[J]. Acta Ophthalmologica,2016,94(5):e278–e286.
- [40] Davinelli S, Nielsen M E, Scapagnini G. Astaxanthin in skin health, repair, and disease: a comprehensive review[J]. Nutrients,2018,10(4):522.
- [41] Higuera – Ciapara I, Félix – Valenzuela L, Goycoolea F M. Astaxanthin: a review of its chemistry and applications[J]. Critical Reviews in Food Science and Nutrition,2006,46(2):185–196.
- [42] Park J S, Mathison B D, Hayek M G, et al. Astaxanthin stimulates cell – mediated and humoral immune responses in cats [J]. Veterinary Immunology and Immunopathology, 2011, 144 (3/4): 455–461.
- [43] Zhu X M, Li M Y, Liu X Y, et al. Effects of dietary astaxanthin on growth, blood biochemistry, antioxidant, immune and inflammatory response in lipopolysaccharide – challenged *Channa argus* [J]. Aquaculture Research,2020,51(5):1980–1991.
- [44] Jeong S M, Kim Y J. Astaxanthin treatment induces maturation and functional change of myeloid – derived suppressor cells in tumor – bearing mice[J]. Antioxidants,2020,9:350.
- [45] Leite M F, de Lima A, Massuyama M M, et al. *In vivo* astaxanthin treatment partially prevents antioxidant alterations in dental pulp from alloxan – induced diabetic rats [J]. International Endodontic Journal,2010,43(11):959–967.
- [46] Chen Y Y, Tang J C, Zhang Y H, et al. Astaxanthin alleviates gestational diabetes mellitus in mice through suppression of oxidative stress[J]. Naunyn – Schmiedeberg’s Archives of Pharmacology, 2020,393:2517–2527.
- [47] Otton R, Marin D P, Bolin A P, et al. Astaxanthin ameliorates the redox imbalance in lymphocytes of experimental diabetic rats[J]. Chemico – Biological Interactions,2010,186(3):306–315.
- [48] Bhuvanewari S, Arunkumar E, Viswanathan P, et al. Astaxanthin restricts weight gain, promotes insulin sensitivity and curtails fatty liver disease in mice fed an obesity – promoting diet[J]. Process Biochemistry,2010,45(8):1406–1414.
- [49] Kurihara H, Koda H, Asami S, et al. Contribution of the antioxidative property of astaxanthin to its protective effect on the promotion of cancer metastasis in mice treated with restraint stress [J]. Life Sciences,2002,70(21):2509–2520.
- [50] Faraone I, Sinisgalli C, Ostuni A, et al. Astaxanthin anticancer effects are mediated through multiple molecular mechanisms: a systematic review [J]. Pharmacological Research, 2020, 155:104689.
- [51] Palozza P, Torelli C, Boninsegna A, et al. Growth – inhibitory effects of the astaxanthin – rich alga *Haematococcus pluvialis* in human colon cancer cells[J]. Cancer Letters,2009,283(1):108–117.
- [52] Park J S, Chyun J H, Kim Y K, et al. Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans[J]. Nutrition & Metabolism,2010,7:18.
- [53] Zhang X, Zhao W E, Hu L Q, et al. Carotenoids inhibit proliferation and regulate expression of peroxisome proliferators – activated receptor gamma (PPAR γ) in K562 cancer cells [J]. Archives of Biochemistry and Biophysics,2011,512(1):96–106.
- [54] Yasui Y, Hosokawa M, Mikami N, et al. Dietary astaxanthin inhibits colitis and colitis – associated colon carcinogenesis in mice via modulation of the inflammatory cytokines[J]. Chemico – Biological Interactions,2011,193(1):79–87.
- [55] Bowen J, Soutar C, Serwata R D, et al. Utilization of (3S,3’S) – astaxanthin acyl esters in pigmentation of rainbow trout (*Oncorhynchus mykiss*) [J]. Aquaculture Nutrition,2002,8(1):59–68.
- [56] Zare M, Roshan Z N, Assadpour E, et al. Improving the cancer prevention/treatment role of carotenoids through various nano – delivery systems [J]. Critical Reviews in Food Science and Nutrition,2021,61(3):522–534.
- [57] Gong X M, Smith J R, Swanson H M, et al. Carotenoid lutein selectively inhibits breast cancer cell growth and potentiates the effect of chemotherapeutic agents through ROS – mediated mechanisms[J]. Molecules,2018,23(4):905.
- [58] Tanaka T, Shnimizu M, Moriwaki H. Cancer chemoprevention by carotenoids[J]. Molecules,2012,17(3):3202–3242.