Comprehensive Review on Astaxanthin – Sources, Chemistry, Pharmacological Activities, Formulation Strategies, and Therapeutic Applications with marketed formulations:

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***Abstract*—The wide range of health benefits and variety of Pharacological activities of carotenoids have made them the focal point of industrial as well as academic research on a global scale. Astaxanthin, a xanthophyll carotenoid renowned for its exceptional antioxidant potency, has attracted widespread scientific and pharmaceutical interest due to its diverse therapeutic activities. This review provides a comprehensive overview of astaxanthin, beginning with its natural and synthetic sources, structural chemistry, and physicochemical properties that influence its biological behavior. The pharmacological profile of astaxanthin including its antioxidant, anti-inflammatory, cardioprotective, neuroprotective, hepatoprotective, ocular, and anticancer effects is critically examined. Special emphasis is placed on advanced formulation strategies such as nanoemulsions, liposomes, polymeric nanoparticles, nanostructured lipid carriers, and microencapsulation systems, which have been developed to overcome astaxanthin's inherent limitations related to poor aqueous solubility, instability, and low bioavailability. Furthermore, the review highlights recent progress in therapeutic applications, preclinical and clinical findings, and commercially available astaxanthin formulations currently marketed for health and wellness. Overall, this work consolidates current knowledge while identifying key research gaps, offering guidance for future development of astaxanthin-based nutraceuticals and pharmaceutical products.**

***Index Terms*—Astaxanthin, ROS. Photoprotection, Antioxidant, Beta carotene.**

I. INTRODUCTION

Astaxanthin (AXT) a non-vitamin A and a red-orange carotenoid is a member of the xanthophyll family as it contains oxygen with carbon and hydrogen atoms. It is safe for use and hence classified as "pure anti-oxidants" Astaxanthin is a xanthophyll carotenoid which is found in various microorganisms and marine animals[1].The natural astaxanthin are found more biological and pharmacological actives than synthesis one. It is more active as an anti-oxidant than canthaxanthin, zeaxanthin, lutein, vitamin C, vitamin E and β-carotene[4].The United States Food and Drug Administration (USFDA) has approved the use of astaxanthin as food colorant in animal and fish feed[2]. And also The European Commission considers natural astaxanthin as a food dye[3].This has adopted its consumption and nowadays, it is being widely used as a nutraceutical. Its global market demand is expanding and expected to reach $2.57 billion worldwide by 2025. Haematococcus pluvialis is a green microalga, which accumulates high astaxanthin content under stress conditions such as high salinity, nitrogen deficiency, high temperature and light[5-6].

The interest on natural pigments and high cost of synthetic pigments demand the isolation of astaxanthin from natural sources[7]. The use of astaxanthin as a nutritional supplement has expanded rapidly across foods, feeds, nutraceuticals, and pharmaceuticals. This review summarizes current knowledge on astaxanthin sources, extraction

techniques, Chemistry, Pharmcological and biological activities, Formulation, Therapeutic application and health benefits, as well as its applications in disease prevention and commercial products.

II. SOURCE OF ASTAXANTHIN

The natural sources of astaxanthin include algae, yeast, salmon, trout, krill, shrimp, and crayfish. Table 1 summarizes astaxanthin obtained from various microorganisms. Commercial production primarily relies on Phaffia yeast, Haematococcus, and chemically synthesized astaxanthin. Among these, Haematococcus pluvialis is considered one of the richest natural sources[8]. Farmed Atlantic salmon has been reported to contain 6–8 mg/kg of astaxanthin in its flesh. In large trout, astaxanthin levels available on the European and Japanese markets are approximately 6 mg/kg and 25 mg/kg of flesh, respectively. Shrimp, crab, and salmon also serve as important dietary sources of astaxanthin[9,10,11,12,13,14,15,16].

Table 1. Sources of astaxanthin.

SourceType	Specific Source	Notes / Characteristics
Microalgae	Haematococcus pluvialis	Richest natural source; contains highest astaxanthin concentration.
	Chlorella zofingiensis	Produces moderate levels; used in some supplements.
	Phaffia rhodozyma (yeast)	Yeast-based source; commonly used in aquaculture feed.
Bacteria	Paracoccus carotinifaciens	Used industrially; produces astaxanthin naturally.
Plants	Red yeast rice, certain algae-associated plants	Minor contributors; lower content compared to microalgae.
Marine Animals	Krill	Source of astaxanthin-rich oil used in supplements.
	Shrimp, crab, lobster (shells/exoskeleton)	Astaxanthin present in carapace; often extracted from processing waste.
	Salmon, trout	Accumulate astaxanthin from diet; give fish their pink color.
	Flamingos	Pink coloration due to astaxanthin intake from algae-fed crustaceans.
Synthetic	Laboratory-synthesized astaxanthin	Used widely in aquaculture; chemically identical but different isomer mix

III. CHEMISTRY OF ASTAXANTHIN

Astaxanthin is a member of the xanthophylls, because it contains not only carbon and hydrogen but also oxygen atoms (Figure 1). Astaxanthin consists of two terminal β-ionone rings connected by a polyene chain. The molecule contains two asymmetric carbons at the 3 and 3′ positions of the rings, each bearing a hydroxyl (-OH) group. Whereas esterification of both hydroxyl groups produces a diester. Astaxanthin occurs in several forms, including stereoisomers, geometric isomers, and both free and esterified states[17].All of these forms are found in natural sources. The stereoisomers (3S, 3′S) and (3R 3′R) are the most abundant in nature. Haematococcus biosynthesizes the (3S, 3′S)-isomer whereas yeast Xanthophyllomyces dendrorhous produces (3R, 3′R)-isomer[18].

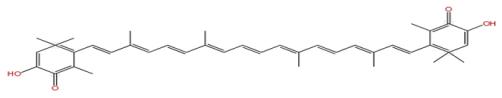

Fig. 01. Planner structure of astaxanthin

IV. PHARMACOLOGICAL ACTIVITIES AND THERAPEUTIC APPLICATION OF ASTAXANTHIN

4.1 Antioxidant Effects:

The presence of the hydroxyl (OH) and keto (C=O) moieties on each ionone ring explains some of its unique features, namely, a higher antioxidant activity. In recent years, a number of studies on astaxanthin have in vitro and in vivo demonstrated its antioxidant effect, for example, the quenching effect on singlet oxygen, a strong scavenging effect on superoxide, hydrogen peroxide and hydroxyl radicals and an inhibitory effect on lipid peroxidation[20-21]. An antioxidant is a molecule that inhibits oxidation. Oxidative damage is primarily caused by free radicals and reactive oxygen species (ROS), which are highly reactive molecules generated during normal aerobic metabolism. Excessive oxidative molecules can initiate chain reactions that damage proteins, lipids, and DNA, leading to various disorders. Such oxidative molecules can be neutralized by both endogenous and

exogenous antioxidants, including carotenoids. Carotenoids possess long polyene chains with conjugated double bonds, enabling them to exert antioxidant effects by quenching singlet oxygen and scavenging free radicals, thereby terminating chain reactions. Their biological benefits are largely attributed to these antioxidant properties and their physical and chemical interactions with cell membranes[19]. Feeding rats with Haematococcus biomass, a source of astaxanthin, resulted in elevated levels of antioxidant enzyme including catalase, superoxide dismutase, and peroxidas as well as increased thiobarbituric acid reactive substances (TBARS) in plasma and liver Antioxidant enzyme levels were increased when astaxanthin fed to ethanol-induced gastric ulcer rats [8].

4.2 Anti-Lipid Peroxidation Activity:

Astaxanthin has a unique molecular structure which enables it to stay both in and outside the cell membrane. β-Carotene and vitamin C can be incorporated into the lipid bilayer of cellular membranes, where they function as potent antioxidants. These compounds protect against oxidative damage through multiple mechanisms, including quenching singlet oxygen, scavenging free radicals to prevent propagation of chain reactions, maintaining membrane integrity by inhibiting lipid peroxidation, enhancing immune system function, and modulating gene expression. Astaxanthin and its esters have demonstrated significant antioxidant activity, showing up to 80% inhibition of lipid peroxidation in ethanol-induced gastric ulcer and skin cancer rat models. Furthermore, various studies have confirmed that astaxanthin effectively suppresses lipid peroxidation in diverse biological samples[4,22,23].

4.3 Anti-Inflammation activity:

In inflammation-associated clinical conditions, such as Crohn's disease, phagocytic leukocytes at the site of inflammation including the intestinal mucosa and lumen release reactive oxygen species (ROS). The concurrent accumulation of neutrophils further contributes to a pro-oxidative environment, resulting in depletion of antioxidant vitamins and elevated levels of oxidative stress markers and lipid peroxidation products[24]. Astaxanthin is a potent antioxidant that effectively mitigates the initiation and progression of inflammation in biological systems. It exhibits strong anti-inflammatory properties, reducing inflammatory responses at the cellular and tissue levels. Additionally, algal cell extracts from Haematococcus and Chlorococcum have been shown to significantly decrease bacterial load and attenuate gastric inflammation in Helicobacter pylori-infected murine models[25-26]. Administration of astaxanthin in combination with Ginkgo biloba extract and vitamin C has been reported to reduce inflammatory cell counts in bronchoalveolar lavage fluid and to increase cAMP and cGMP levels in lung tissues. In a separate study, astaxanthin esters and total carotenoids derived from Haematococcus exhibited a dose-dependent gastroprotective effect against acute gastric lesions in ethanol-induced ulcer models in rats. This protective effect is likely mediated through inhibition of H^+/K^+-ATPase activity, upregulation of mucin production, and enhancement of endogenous antioxidant defenses. The results also demonstrated that astaxanthin enhances neutrophil phagocytic and microbicidal functions while reducing the production of superoxide anions and hydrogen peroxide. These effects appear to be mediated by calcium release from intracellular stores and increased nitric oxide production, indicating a protective role of astaxanthin in modulating human neutrophil function. Immune cells are particularly susceptible to oxidative stress due to the high content of polyunsaturated fatty acids in their plasma membranes and their inherently elevated production of reactive oxygen species[28].

4.4. Anti-Diabetic Activity:

Oxidative stress is markedly elevated in patients with diabetes mellitus, primarily driven by hyperglycemia, pancreatic β-cell dysfunction, and consequent tissue damage. Astaxanthin has been shown to mitigate hyperglycemia-induced oxidative stress in pancreatic β-cells, while also improving glucose homeostasis and serum insulin levels. Astaxanthin can protect pancreatic β-cells against glucose toxicity. It was also shown to be a good immunological agent in the recovery of lymphocyte dysfunctions associated with diabetic rats[29-30]. Enhanced insulin sensitivity in both spontaneously hypertensive corpulent rats and mice on high fat plus high fructose diets was observed after feeding with astaxanthin. The urinary albumin level in astaxanthin treated diabetic mice was significantly lower than the control group[31].

4.5 Cardiovascular Disease Prevention:

Astaxanthin demonstrated cardioprotective effects by preventing isoproterenol-induced mitochondrial dysfunction in a rat model. Administration of astaxanthin significantly improved the function of respiratory chain complexes and ATP synthase, thereby enhancing mitochondrial respiratory performance in damaged cardiac tissue. Additionally, astaxanthin modulated cyclophilin D (CyP-D) activity and increased levels of adenine nucleotide translocase (ANT), contributing to the preservation of mitochondrial integrity and cardiac function[32].

In another study, astaxanthin was found to improve myocardial dysfunction by modulating the phosphorylation and acetylation status of receptor-regulated SMADs (R-SMADs). R-SMADs are transcription factors that mediate fibrosis through signaling of the TGF-β superfamily ligands. Astaxanthin ameliorated cardiac dysfunction by promoting deacetylation of R-SMADs via activation of the silent information regulator factor 2-related enzyme 1 (SIRT1), thereby attenuating fibrotic signaling pathways[33].

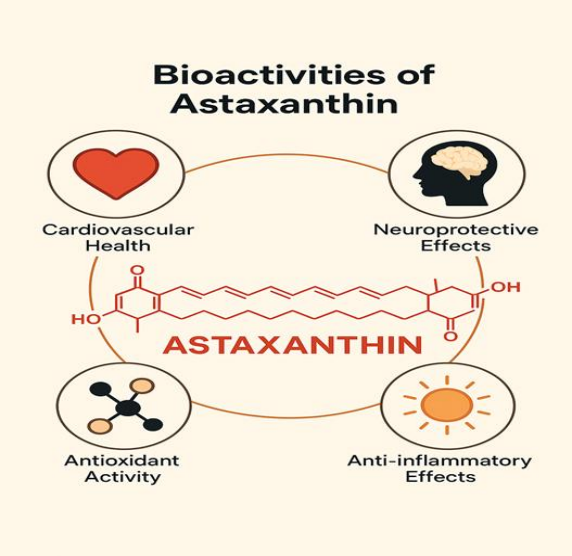

Fig. 02 Bioactivities of Astaxanthin.

4.5 Anti-cancer activity:

The anti-cancer potential of astaxanthin is well established. In a hamster buccal pouch (HBP) model, astaxanthin effectively suppressed tumor progression by inhibiting NF-κB and Wnt signaling pathways through downregulation of key regulatory enzymes such as IKKβ and GSK-3β. This inhibition may be attributed to astaxanthin's ability to block the upstream activation of signaling kinases, including Erk and Akt. Additionally, astaxanthin's anti-cancer activity is further supported by its capacity to induce mitochondria-mediated apoptosis, contributing to its overall chemopreventive and therapeutic efficacy[42]. The ability of astaxanthin to reverse mitomycin C (MMC)–induced cytotoxicity in non-small cell lung cancer (NSCLC) cell lines, such as A549 and H1703, has been linked to its inhibitory effects on Rad51 expression and phospho-AKT (Ser473) protein levels. These findings suggest that astaxanthin may modulate DNA repair pathways and survival signaling, thereby mitigating MMC-associated cellular damage[43].

V. FORMULATION STRATEGIES

Because of its poor solubility and low bioavailability, researchers have developed many advanced formulation strategies of astaxanthin. Although astaxanthin exhibits therapeutic potential across a range of diseases, its clinical utility is limited by several pharmacokinetic and stability challenges. Specifically, astaxanthin demonstrates poor oral bioavailability, primarily due to its slow dispersion in the bloodstream and limited cellular uptake. Moreover, the compound is chemically unstable under acidic conditions and is highly susceptible to oxidative degradation owing to its extensive conjugated double-bond structure. Even brief exposure to elevated temperatures can induce significant degradation, further compromising its stability and efficacy. While they are also controlled-released and site-specific for drug delivery [34].

5.1 Astaxanthin Nanoemulsion Formulations:

A nanoemulsion is a colloidal dispersion composed of two immiscible liquids oil-in-water (O/W), water-in-oil (W/O), or water-oil-water (W/O/W) stabilized by surfactants, with mean droplet sizes typically below 200 nm. Conventional emulsions generally consist of three fundamental components: the oil phase, the aqueous phase, and a surfactant. The nature of the surfactant dictates the continuous (external) phase of the emulsion: oil-soluble surfactants produce W/O emulsions, whereas water-soluble surfactants yield O/W emulsions. Nanoemulsions, as lipid-based nanocarriers, can be fabricated using high-energy methods such as high-pressure homogenization, ultrasonication, microfluidization, high-shear stirring, and membrane emulsification, or low-energy methods

including phase inversion temperature, emulsion inversion point, and spontaneous emulsification[35]. Although high-energy methods require greater energy input compared to low-energy approaches, they offer notable advantages, including the production of smaller droplet sizes, simpler preparation processes, and enhanced long-term stability. The choice of surfactant in nanoemulsion formulation is critical, as it not only dictates the continuous phase of the emulsion but also significantly influences its stability, biocompatibility, and safety[36].

Emulsifiers play a critical role in nanoemulsion stability by reducing surface tension, preventing droplet coalescence, and generating strong repulsive interactions between droplets. While synthetic emulsifiers are widely recognized for producing highly stable emulsions, there is growing interest in natural emulsifiers due to consumer health concerns, as excessive intake of synthetic emulsifiers may lead to gastrointestinal irritation. Therefore, it is essential to use the minimum effective concentration of emulsifier required to stabilize the nanoemulsion. Among emulsifiers, non-ionic types are generally considered safer than ionic emulsifiers and have gained popularity in recent research. Notably, astaxanthin nanoemulsions have been successfully formulated using natural emulsifiers, such as ginseng saponins, and have been thoroughly characterized for their physicochemical and functional properties[37].

5.2 Nanoparticles:

A nanoparticle is generally defined as a particulate entity with a diameter ranging from 1 to 100 nm. The term encompasses a broad spectrum of nanoparticle classes distinguished by their physical and chemical characteristics. Common examples include carbon-based, metal-based, ceramic-based, semiconductor-based, polymeric, and lipid-based nanoparticles. Owing to their unique structural, chemical, mechanical, magnetic, electrical, and biological properties, nanoparticles represent a highly versatile platform for the delivery of bioactive compounds, offering enhanced stability, targeted delivery, and improved therapeutic performance[38]. Nano-sized particles typically exhibit prolonged circulation times in the bloodstream, enable controlled and sustained release of bioactive compounds, and induce fewer adverse alterations in plasma components, thereby reducing potential systemic side effects[39].

Encapsulation of astaxanthin within liposomes (Ast-L) markedly enhances its physicochemical stability and membrane transport efficiency. The total transport time required for Ast-L to reach the cell cytoplasm was 6.00 hours, compared to 7.55 hours for free astaxanthin, indicating improved cellular uptake. Furthermore, Ast-L elicited significantly greater activation of key antioxidant enzymes superoxide dismutase, catalase, and glutathione S-transferase than free astaxanthin, demonstrating its superior antioxidant efficacy[40]. Astaxanthin-loaded liposomes formulated and stabilized with novel sea cucumber–derived sulfated sterols, instead of conventional cholesterol, exhibited markedly enhanced performance. These sterol-stabilized liposomes demonstrated prolonged physicochemical stability, greater antioxidant activity, and significantly improved bioavailability compared with traditional cholesterol-based liposomal systems[41].

Table 2: Marketed formulation of Astaxanthin product description.

Sr No	Product Name	Manufacturer/ Country	FormulationType	Description
1	AstaReal®Capsules/ Softgels	AstaReal AB,,Sweden/ Japan	Soft gelatin capsules	Contains natural AST (4-12mg) from H pluvialis oil, clinically validated for antioxidant and skin health benefit.
2	BioAstin® Hawaiian Astaxanthin	Nutrex Hawaii USA	Soft gelatin capsules	12 mg AST from algae, marketed for skin, eye and immune support.
3	AstaReal drink 10 mg	Fuji Chemical Industries, Japan	Ready to drink supplement	Water-dispersible beverage form of AST, claims skin moisture improvement.
4	OxyShield Tablets	GNC / USA	Tablet	AST 4 mg + Vit E + β-carotene, claims skin wellness.
5	AstaGlow Drink Mix	Yamada Bee CO, Japan	Effervescent powder drink	AST 6 mg + Vit C, improves skin hydration and skin tone.

VI. CONCLUSION

Astaxanthin exhibits potent antioxidant activity and has demonstrated significant therapeutic potential against a range of disorders, including hypertension, diabetes, and cancer. Its well-documented anti-inflammatory, wound-healing, cardioprotective, hepatoprotective, neuroprotective, and osteoprotective effects further support its relevance in pharmaceutical and nutraceutical applications. Natural astaxanthin, particularly in its esterified form, displays superior bioavailability and biological activity compared to synthetic and free-form counterparts. However, despite its broad health benefits, critical gaps remain in optimizing cost-effective, sustainable extraction methods and elucidating its molecular mechanisms of action. Continued research in these areas will be essential to fully harness astaxanthin's therapeutic potential and advance its development as a valuable nutraceutical agent. Continued interdisciplinary research is essential to optimize sustainable production methods, clarify molecular mechanisms of action, and design advanced delivery platforms capable of achieving consistent pharmacokinetic and therapeutic outcomes. Overall, astaxanthin holds considerable promise as a nutraceutical and pharmaceutical agent, and ongoing scientific progress is expected to further unlock its full therapeutic potential

REFERENCE:

[1] Yamashita, E. (2013). Astaxanthin as a medical food. Functional Foods in Health and Disease, 3(7), 254–258. https://doi.org/10.31989/ffhd.v3i7.49 Yang, L., Gu, J., Luan, T., Qiao, X., Cao, Y., Xue, C., et al. (2021). Influence of oil matrixes on stability, antioxidant activity, bioaccessibility and bioavailability of astaxanthin.

[2] Capelli, B., Bagchi, D., & Cysewski, G. R. (2013). Synthetic astaxanthin is significantly inferior to algal-based astaxanthin as an antioxidant and may not be suitable as a human nutraceutical supplement. Nutrafoods, 12(4), 145–152.

[3] Roche, F. Astaxanthin: Human food safety summary. In Astaxanthin As a Pigmenter in Salmon Feed, Color Additive Petition 7C02 1 1, United States Food and Drug Administration; Hoffman-La Roche Ltd.: Basel, Switzerland, 1987; p. 43.

[4] Rao, A. R., Sindhuja, H. N., Dharmesh, S. M., Sankar, K. U., Sarada, R., & Ravishankar, G. A. (2013). Effective inhibition of skin cancer, tyrosinase, and antioxidative properties by astaxanthin and astaxanthin esters from the green alga Haematococcus pluvialis. Journal of Agricultural and Food Chemistry, 61(16), 3842–3851.

[5] Sarada, R.; Tripathi, U.; Ravishankar, G.A. Influence of stress on astaxanthin production in Haematococcus pluvialis grown under different culture conditions. Process Biochem. 2002, 37, 623–627.

[6] Sarada, R.; Ranga Rao, A.; Sandesh, B.K.; Dayananda, C.; Anila, N.; Chauhan, V.S.; Ravishankar, G.A. Influence of different culture conditions on yield of biomass and value-added products in microalgae. Dyn. Biochem. Proc. Biotechnol. Mol. Biol. 2012, 6, 77–85.

[7] Ambati, R. R., Moi, P. S., Ravi, S., & Aswathanarayana, R. G. (2014). Astaxanthin: Sources, extraction, stability, biological activities and its commercial applications - a review. Marine Drugs, 12(1), 128–152. https://doi.org/10.3390/md12010128.

[8] Ranga Rao, A.; Raghunath Reddy, R.L.; Baskaran, V.; Sarada, R.; Ravishankar, G.A. Characterization of microalgal carotenoids by mass spectrometry and their bioavailability and antioxidant properties elucidated in rat model. J. Agric. Food Chem. 2010, 58, 8553–8559.

[9] EFSA (European Food Safety Authority). Opinion of the scientific panel on additives and products or substances used in animal feed on the request from the European commission on the safety of use of colouring agents in animal human nutrition. EFSA J. 2005, 291, 1–40.

[10] Ranga Rao, A.; Raghunath Reddy, R.L.; Baskaran, V.; Sarada, R.; Ravishankar, G.A. Characterization of microalgal carotenoids by mass spectrometry and their bioavailability and antioxidant properties elucidated in rat model. J. Agric. Food Chem. 2010, 58, 8553–8559.

[11] Ranga Rao, A.; Sarada, R.; Baskaran, V.; Ravishankar, G.A. Identification of carotenoids from green alga Haematococcus pluvialis by

HPLC and LC-MS (APCI) and their antioxidant properties. J. Microbiol. Biotechnol. 2009, 19, 1333–1341.

[12] Lorenz, R.T. A Technical Review of Haematococcus Algae; NatuRose™ Technical Bulletin #060; Cyanotech Corporation: Kailua-Kona, HI, USA, 1999; pp. 1–12.

[13] EFSA (European Food Safety Authority). Opinion of the scientific panel on additives and products or substances used in animal feed on the request from the European commission on the safety of use of colouring agents in animal human nutrition. EFSA J. 2005, 291, 1–40.

[14] Iwamoto, T.; Hosoda, K.; Hirano, R.; Kurata, H.; Matsumoto, A.; Miki, W.; Kamiyama, M.; Itakura, H.; Yamamoto, S.; Kondo, K. Inhibition of low-density lipoprotein oxidation by astaxanthin. J. Atheroscler. Thromb. 2000, 7, 216–222.

[15] Aflalo, C.; Meshulam, Y.; Zarka, A.; Boussiba, S. On the relative efficiency of two- vs. one-stage production of astaxanthin by the green alga Haematococcus pluvialis. Biotechnol. Bioeng. 2007, 98, 300–305.

[16] Torzillo, G.; Goksan, T.; Faraloni, C.; Kopecky, J.; Masojídek, J. Interplay between photochemical activities and pigment composition in an outdoor culture of Haematococcus pluvialis during the shift from the green to red stage. J. Appl. Phycol. 2003, 15, 127–136.

[17] Higuera-Ciapara, I.; Felix-Valenzuela, L.; Goycoolea, F.M. Astaxanthin: A review of its chemistry and applications. Crit. Rev. Food Sci. Nutr. 2006, 46, 185–196.

[18] Hussein, G.; Sankawa, U.; Goto, H.; Matsumoto, K.; Watanabe, H. Astaxanthin, a carotenoid with potential in human health and nutrition. J. Nat. Prod. 2006, 69, 443–449.

[19] Naguib, Y.M.A. Antioxidant activities of astaxanthin and related carotenoids. J. Agric. Food Chem. 2000, 48, 1150–1154.

[20] Miki. W: Biological functions and activities of animal carotenoids. Pure Appl. Chem. 1991;63(1):141-146.

[21] Palozza, P and Krinsky, N I: Astaxanthin and canthaxanthin are potent antioxidants in a membrane model. Arch. Biochem. Biophys 1992; 297:291-295.

[22] Kamath, B.S.; Srikanta, B.M.; Dharmesh, S.M.; Sarada, R.; Ravishankar, G.A. Ulcer preventive and antioxidative properties of astaxanthin from Haematococcus pluvialis. Eur. J. Pharmacol. 2008, 590, 387–395.

[23] Goto, S.; Kogure, K.; Abe, K.; Kimata, Y.; Yamashita, E.; Terada, H. Efficient radical trapping at the surface and inside the phospholipid membrane is responsible for highly potent antiperoxidative activity of the carotenoid astaxanthin. Biochim. Biophys. Acta 2001, 1512, 251–258.

[24] Aghdassi E and Allard J P: Breath alkanes as a marker of oxidative stress in different clinical conditions. Free Radic. Biol. Med. 2000; 28:880–886.

[25] Liu, B.H.; Lee, Y.K. Effect of total secondary carotenoids extracts from Chlorococcum sp. on Helicobacter pylori infected BALB/c mice. Int. Immunopharmacol. 2003, 3, 979–986.

[26] Bennedsen, M.; Wang, X.; Willen, R.; Wadstrom, T.; Andersen, L.P. Treatment of H. pylori infected mice with antioxidant astaxanthin reduces gastric inflammation, bacterial load and modulates cytokine release by splenocytes. Immunol. Lett. 1999, 70, 185–189.

[27] Kamath, B.S.; Srikanta, B.M.; Dharmesh, S.M.; Sarada, R.; Ravishankar, G.A. Ulcer preventive and antioxidative properties of astaxanthin from Haematococcus pluvialis. Eur. J. Pharmacol. 2008, 590, 387–395.

[28] Park J S, Chyun J H, Kim Y K, Line L L, Chew B P: Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans. Nutr. Metab. 2010; 7: 18-22.

[29] Uchiyama, K.; Naito, Y.; Hasegawa, G.; Nakamura, N.; Takahashi, J.; Yoshikawa, T. Astaxanthin protects β-cells against glucose toxicity in diabetic db/db mice. Redox Rep. 2002, 7, 290–293.

[30] Otton, R.; Marin, D.P.; Bolin, A.P.; Santos, R.C.; Polotow, T.G.; Sampaio, S.C.; De Barros, M.P. Astaxanthin ameliorates the redox imbalance in lymphocytes of experimental diabetic rats. Chem. Biol. Interact. 2010, 186, 306–315.

[31] Uchiyama, K.; Naito, Y.; Hasegawa, G.; Nakamura, N.; Takahashi, J.; Yoshikawa, T.

Astaxanthin protects β-cells against glucose toxicity in diabetic db/db mice. Redox Rep. 2002, 7, 290–293.

[32] Krestinina, O., Baburina, Y., Krestinin, R., Odinokova, I., Fadeeva, I., & Sotnikova, L. (2020). Astaxanthin prevents mitochondrial impairment induced by isoproterenol in isolated rat heart mitochondria. Antioxidants, 9(3), 262. https://doi.org/10.3390/antiox9030262.

[33] Jingyao, Z., Zhang, S., Bi, J., Gu, J., Deng, Y., & Liu, C. (2017). Astaxanthin pretreatment attenuates acetaminophen-induced liver injury in mice. International Immunopharmacology, 45, 26–33. https://doi.org/10.1016/j.intimp.2017.01.028.

[34] Takeungwongtrakul S., Benjakul S., "Astaxanthin degradation and lipid oxidation of Pacific white shrimp oil: Kinetics study and stability as affected by storage conditions," International Aquatic Research, vol. 8, no. 1, pp. 15–27, 2016, doi: 10.1007/s40071-015-0120-z.

[35] Jaiswal M., Dudhe R., Sharma P. K., "Nanoemulsion: An advanced mode of drug delivery system," 3 Biotech, vol. 5, no. 2, pp. 123–127, 2015, doi: 10.1007/s13205-014-0214-0.

[36] Kumar-Narendra, Mandal A., "Surfactant stabilized oil-in-water nanoemulsion: Stability, interfacial tension, and rheology study for enhanced oil recovery application," Energy and Fuels, vol. 32, no. 6, pp. 6452–6466, 2018, doi: 10.1021/acs.energyfuels.8b00043.

[37] Shu G., Khalid N., Chen Z., Neves M. A., Barrow C. J., Nakajima M., "Formulation and characterization of astaxanthin-enriched nanoemulsions stabilized using ginseng saponins as natural emulsifiers," Food Chemistry, vol. 255, no. 2018, pp. 67–74, 2018, doi: 10.1016/j.foodchem.2018.02.062.

[38] Patra J. K., Das G., Fraceto L. F., Campos E. V. R., Rodriguez-Torres M. D. P., Acosta-Torres L. S., Diaz-Torres L. A., Grillo R., Swamy M. K., Sharma S., Habtemariam S., Shin H. S., "Nano based drug delivery systems: Recent developments and future prospects," Journal of Nanobiotechnology, vol. 16, no. 1, pp. 1–33, 2018, doi: 10.1186/s12951-018-0392-8.

[39] Emeje M. O., Obidike I. C., Akpabio E. I., Ofoefule S. I., "Nanotechnology in drug delivery," in Recent Advances in Novel Drug Carrier Systems, vol. 3, London: IntechOpen, 2012, pp. 69–106.

[40] Peng C. H., Chang C. H., Peng R. Y., Chyau C. C., "Improved membrane transport of astaxanthine by liposomal encapsulation," European Journal of Pharmaceutics and Biopharmaceutics, vol. 75, no. 2, pp. 154–161, 2010, doi: 10.1016/j.ejpb.2010.03.004.

[41] Srihera N., Li Y., Zhang T. T., Wang Y. M., Yanagita T., Waiprib Y., Xue C. H., "Preparation and characterization of astaxanthin loaded liposomes stabilized by sea cucumber sulfated sterols instead of cholesterol," Journal of Oleo Science, vol. 71, no. 3, pp. 401–410, 2022, doi: 10.5650/jos.ess21233.

[42] Kavitha, K., Kowshik, J., Kishore, T. K. K., Baba, A. B., & Nagini, S. (2013). Astaxanthin inhibits NF-κB and Wnt/β-catenin signaling pathways via inactivation of Erk/MAPK and PI3K/Akt to induce intrinsic apoptosis in a hamster model of oral cancer. Biochimica et Biophysica Acta (BBA) - General Subjects, 1830(10), 4433–4444. https://doi.org/10.1016/j.bbagen.2013.05.032.

[43] Ko, J. C., Chen, J. C., Wang, T. J., Zheng, H. Y., Chen, W. C., Chang, P. Y., et al. (2016). Astaxanthin down-regulates Rad51 expression via inactivation of AKT kinase to enhance mitomycin C-induced cytotoxicity in human non-small cell lung cancer cells. Biochemical.