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Astaxanthin and Cancer: A Comprehensive Review of Research

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ABSTRACT

Astaxanthin, a red carotenoid pigment abundantly present in seafood and microalgae, has garnered increasing attention for its potential therapeutic implications in cancer. This article delves into the scientific intricacies surrounding astaxanthin and its direct effects on cancer cells. Astaxanthin exhibits remarkable anti-cancer properties, including the inhibition of cancer cell proliferation, induction of apoptosis, and suppression of metastatic processes. At the molecular level, astaxanthin showcases anti-proliferative effects through modulation of cell cycle regulators, disrupting the uncontrolled growth of cancer cells. Additionally, its ability to induce apoptosis, a programmed cell death mechanism, presents a promising avenue for curtailing aberrant cell survival. Furthermore, astaxanthin exhibits a notable impact on metastasis, inhibiting the migration and invasion of cancer cells through interference with key signalling pathways involved in these processes. This article also outlines the natural sources of astaxanthin, predominantly derived from microalgae and seafood, emphasizing its bioavailability and potential for integration into cancer therapeutic strategies. The scientific insights presented here aim to contribute to the growing body of knowledge surrounding astaxanthin and its application as a natural compound with significant anti-cancer potential. As research progresses, astaxanthin holds promise as a candidate for novel therapeutic interventions in the ongoing battle against cancer.

1. Introduction

With an estimated 9.6 million deaths from cancer reported worldwide in 2020, cancer is still the second leading cause of death in the world. The continuous increase in recorded cases of cancer, which is predicted to reach 28.4 million new cases per year by 2040, has prompted efforts to discover different methods to combat this complex challenge (1). Over the years, considerable efforts have been made to discover new therapies that can reduce the incidence and progression of cancer (2–4). In this regard, natural compounds with strong antioxidant properties have emerged as promising options, and drugs such as taxol, vincristine, and vinblastine are widely available in cancer treatment centres (5). Among natural compounds, astaxanthin, a carotenoid pigment found naturally in microalgae, seafood, and certain plants, has attracted much attention for its unique antioxidant capabilities and potential health benefits .(6)

Astaxanthin is a red fat-soluble pigment that has the highest oxygen radical absorption capacity compared to other carotenoids (7). The molecular structure of astaxanthin enables this pigment to neutralize a wide range of free radicals and reactive oxygen species (ROS), thereby reducing oxidative stress as an indicator factor in the initiation and progression of cancer (8,9). These properties may also reduce oxidative stress-induced DNA damage and suppress chronic inflammation, both of which are known carcinogens (10). Preliminary research including in vitro studies, animal models and early clinical trials shows that astaxanthin has a promising role in inhibiting the proliferation of cancer cells, inducing apoptosis and reducing the risk of metastasis (11-14). Although detailed research and comprehensive clinical trials are necessary to determine the role of astaxanthin in cancer prevention and treatment, the unique molecular properties and physiological effects of this carotenoid provide a suitable avenue for continued exploration in the field of oncology.

The purpose of this review article is to comprehensively investigate the effect of astaxanthin on cancer. For this purpose, in this study, the main sources of astaxanthin production, its action mechanisms in biological systems and its potential impact on different types of cancer will be investigated. In this regard, evidence from in vitro studies, animal models, and clinical trials will be reviewed to evaluate the validity of claims related to the anticancer properties of astaxanthin.

2. Astaxanthin sources

Before investigating the bioactive properties of astaxanthin, it is necessary to discover its diverse sources in the natural world. There are generally two sources for astaxanthin: biological sources and synthetic synthesis. Natural astaxanthin has a trans structure, which gives the molecule a stable activity, while synthetic astaxanthin has a cis structure and thus has little bioavailability (15). Natural astaxanthin is synthesized and found in a variety of sources in aquatic and terrestrial ecosystems, including microbial, animal and plant sources (16,17). This ketocarotenoid is synthesized at the initial level of production in the food chain by microalgae or phytoplankton. Then it was consumed by zooplanktons or crustaceans and the astaxanthin received from them accumulates in the second level of the chain. In the next step, astaxanthin is transferred to the body of fish and thus accumulates along the food chain (18). Understanding the different sources of astaxanthin in the food chain provides valuable insights into the accessibility and importance of astaxanthin for various applications, including potential applications in cancer research and management.

Astaxanthin has been found and identified in many microorganisms including microalgae Haematococcus pluvialis, Chlorella zofingiensis and Chlorococcum sp., red yeast or Phaffa rhodozyma, and marine bacterium Agrobacterium auraniacum (19-21). Under environmental

stress conditions, microorganisms produce astaxanthin as a protective mechanism against UV radiation, high temperatures, and nutrient deficiency.(22)

The first strain used in the industrial production of astaxanthin is Xantholomyces dendrorhous. This yeast is one of the important astaxanthin-producing microorganisms and contains approximately 0.2-0.5 mg/g of dry cell weight of carotenoids, of which 40-95% is astaxanthin (23). Green microalgae H. pluvialis is one of the best microbial sources of natural astaxanthin, which can convert 4-5% of its dry weight into astaxanthin. This microalgae belongs to the chlorophyte branch and is the main producer of astaxanthin on an industrial scale (24). Various studies have shown that H. pluvialis can produce more astaxanthin than other known industrial strains such as Chromochloris zofigensis and Chlorococcum sp. (25) It has also been determined that the antioxidant capacity of natural astaxanthin produced by H. pluvialis is ten times higher than other carotenoids, including beta-carotene, lutein and canthaxanthin, and a hundred times higher than alpha-tocopherol.(26) .

Astaxanthin enters the food chain through the consumption of microalgae by marine organisms. For example, aquatic zooplankton that feed on seaweed (rich in beta-carotene, fucoxanthin, and diatoxanthin) can accumulate large amounts of astaxanthin in their tissues (17). The study of Caramujo et al. in 2012 determined that Amphiascoides atopus species contain the highest amount of astaxanthin among myobenthic pinnipeds (27). Zooplankton is ingested by marine fish (e.g. salmonids) and crustaceans (e.g. shrimp, crab, king prawn, lobster, lobster, and krill) at higher dietary levels (16). The pinkish-red colour of the flesh of these creatures is due to the accumulation of astaxanthin in their tissues and has turned them into important sources of edible astaxanthin for humans.(28)

Among crustaceans, shrimps have a high ability to store astaxanthin, and for this reason, they have been studied by several researchers (29-31). The astaxanthin content of green tiger shrimp (Penaeus semisulcatus) muscles is reported to be 1.41 mg per 100 grams of tissue (29). Depending on the processing technique, krill oil also contains a significant amount of astaxanthin (0.1-15 mg/g) (32). High levels of astaxanthin (27 µg/mg) have been reported in the eggs and gonads of the sea urchin Arabica ligula, which is responsible for the specific colour of these eggs.(33)

While astaxanthin is less abundant in terrestrial plants compared to aquatic sources, some plant species contain this carotenoid in lower amounts. For example, astaxanthin has been detected in red-pigmented fruits and vegetables such as red peppers and strawberries, albeit at lower levels than in algae and seafood (Deis). Many flowering plants in the Adonis genus also contain astaxanthin, and their bright colours help attract pollinators.(34)

Knowledge of these natural sources provides valuable insight into diet and bioavailability for individuals seeking to incorporate astaxanthin into their diet, either for general health or as a potential adjunct in cancer management.

3. Mechanism of action of astaxanthin

Astaxanthin, 3,3´dihydroxy-β,β-carotene-4,4´-dione, belongs to the family of xanthophylls, including oxygenated carotenoid derivatives, and as mentioned before, due to its strong antioxidant properties and its ability to influence cellular mechanisms. It is famous (35). The biological activity of astaxanthin in the body will lead to various benefits, including anticancer effects (Figure 1). Understanding the mechanism of action of astaxanthin in biological systems is very important in clarifying the effect of this substance on cancer prevention and treatment.

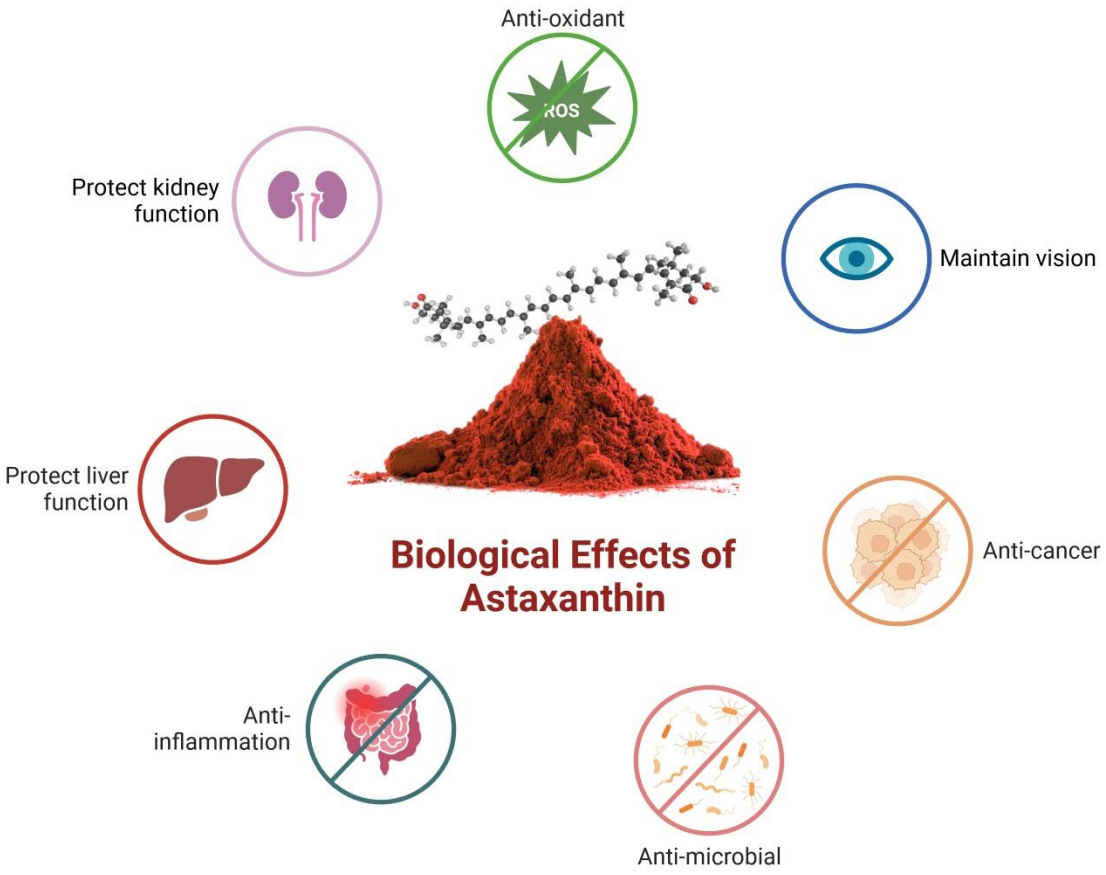

Figure 1. Some biological effects of astaxanthin on the body. The figure was prepared using the website www.biorender.com.

The unique molecular structure of astaxanthin has given it unique chemical properties. Astaxanthin has two carbonyl groups, two hydroxy groups and eleven conjugated ethylene double bonds. The polyene system gives astaxanthin its distinct molecular structure, chemical properties, and light-absorbing properties (36). In the molecular structure of astaxanthin, each double bond in the polyene chain can exist in two configurations as cis or trans geometric isomers. Natural all-trans astaxanthin is easily isomerized to cis-trans mixtures, especially the cis-9 and cis-13 isomers, due to environmental reasons such as high temperature, exposure to light, or the presence of acid (37). The presence of hydroxyl and keto groups in each ionone ring explains some of the unique properties of astaxanthin, such as the ability to esterify higher antioxidant activity and a more polar nature than other carotenoids (38). As a powerful antioxidant, astaxanthin can donate electrons to free radicals and convert them into more stable products (39). This ability allows astaxanthin to neutralize oxidative stress, which is a key factor in DNA damage, mutation, and initiation of carcinogenesis (40). Astaxanthin can reduce oxidative stress, one of the main drivers of cancer.(12)

In addition to direct antioxidant activity, astaxanthin exhibits anti-inflammatory properties that are increasingly important in cancer biology (41,42). Chronic inflammation is closely related to cancer progression because it fosters a microenvironment that leads to tumour growth and invasion. Astaxanthin has been found to reduce intracellular and mitochondrial reactive oxygen species (ROS) levels and interleukin-8 expression in gastric epithelial cells by activating PPAR-γ and catalase (42,43). Therefore, it is possible that astaxanthin can indirectly prevent cancer progression by reducing inflammation.

Astaxanthin also affects gene expression and signal transmission pathways. This molecule can modulate the activity of transcription factors involved in cell proliferation and survival, such

as nuclear factor NF-κB, nuclear factor erythroid-related factor 2 (Nrf2) and activating protein APA-1. These transcription factors play an important role in coordinating cellular responses to inflammation and oxidative stress, thus linking astaxanthin to cancer research (44).

In summary, astaxanthin's multifaceted mechanisms of action include antioxidant, anti-inflammatory, and gene-regulatory activities. These features determine the position of astaxanthin as a compound with the potential to impact the complex landscape of cancer biology. In the next parts of this review, the experimental evidence from laboratory and animal studies will be examined in depth to determine the practical consequences of these mechanisms in the field of cancer prevention and treatment.

4. Direct effect of astaxanthin on cancer

Evidence shows that astaxanthin has anticancer effects in various types of cancer, including oral, prostate, colon, and liver cancer (45–48). Probably, the structure of long conjugated chains, unsaturated ketone (C = O) and α-hydroxy ketones contribute to the anticancer effects of astaxanthin stereoisomers (32). Studies have shown that astaxanthin has the potential to prevent cancer progression through mechanisms such as induction of apoptosis, inhibition of uncontrolled cell proliferation, and suppression of tumour cell migration and invasion (Figure 2). These effects are especially important in preventing the uncontrolled growth and spread of cancer cells, thus introducing astaxanthin as a promising candidate in efforts to prevent and treat cancer. While more research is needed to fully understand the extent of astaxanthin's effectiveness in different types of cancer, these findings provide a compelling reason to continue research into the therapeutic potential of astaxanthin in Cancer Management.

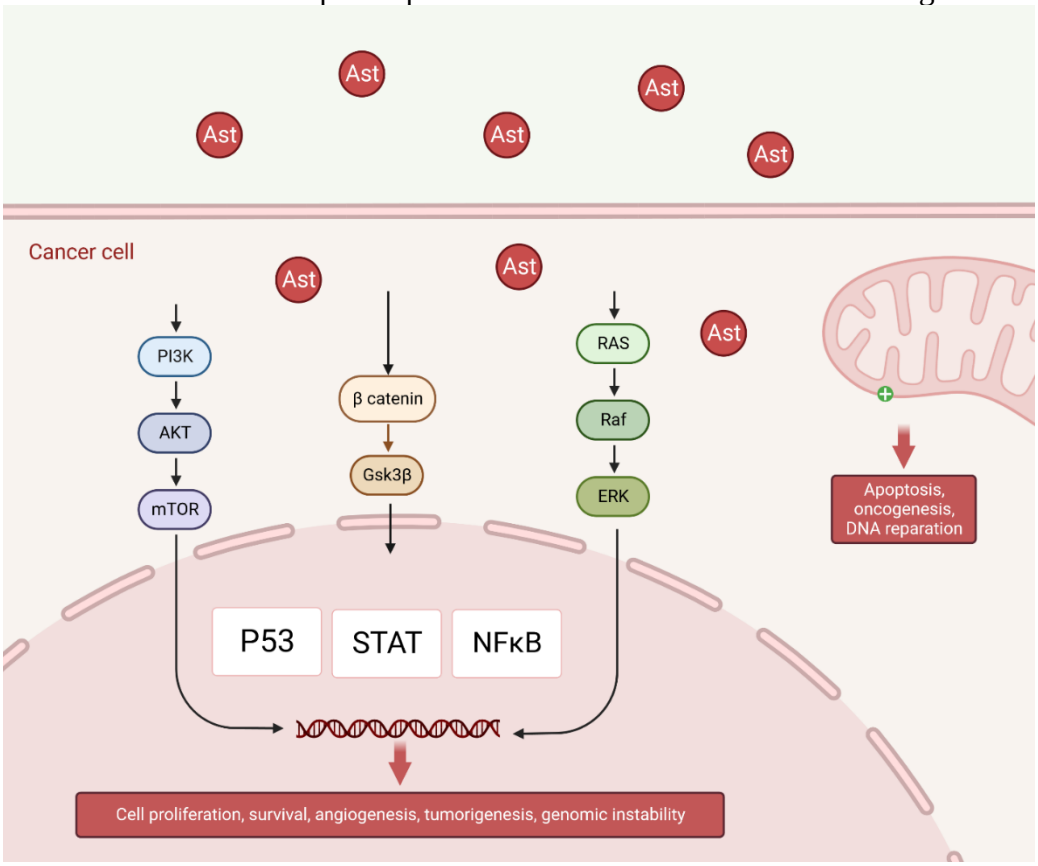

Figure 2. Molecular mechanisms of the effect of astaxanthin on cancer cells. AST: astaxanthin. The figure was prepared by the website www.biorender.com.

1. 4. Anticancer effects of astaxanthin through inhibition of uncontrolled cell proliferation

Tumor formation is characterized by the abnormal proliferation of cancer cells. Proliferation

of cancer cells increases its aggressive power, the cell migrates and sticks to the target tissue. These steps allow the tumour cell to acquire a metastatic phenotype (49). Cell proliferation depends on signals transmitted by growth factors and adhesion proteins and is usually regulated by signalling pathways such as mitogen-activated protein kinase (MAPK) and phosphatidyl-inositol 3-kinases (PI-3K) (50). The effect of astaxanthin on cell proliferation in cancer cells has been investigated by many researchers. For example, the antiproliferative effects of astaxanthin on some human and mouse strains such as CBRH7919 (rat liver cancer strain) and SHZ88 (rat breast cancer strain) have been investigated by Song et al. in 2011 (51). The results of this study show the antiproliferative effects of astaxanthin on these cell lines, and among them, the CBRH-7919 cell line showed the highest sensitivity to astaxanthin (IC50=39 micromolar). In another study, Sun et al in 2020 investigated the growth inhibitory effect of astaxanthin on the invasive cell line DU145 (prostate cancer). These researchers stated that astaxanthin exerts its anticancer effects by inhibiting the proliferation of DU145 cells as well as reducing the expression of STAT3 mRNA and protein (45). In addition, it has been found that astaxanthin induces and inhibits the growth and proliferation of the LS-180 (colorectal adenocarcinoma) cell line by increasing the expression of Bax and Caspase3 and decreasing the expression of Bcl2 (52). The antiproliferative effect of astaxanthin on the SKBR3 breast cancer cell line has also been investigated. Researchers in this study showed that astaxanthin inhibits cell cycle progression in the G0/G1 phase in a dose-dependent manner, cell proliferation and induces apoptosis in cells.(52)

The interesting thing about astaxanthin is that the results of some studies have shown that the anti-proliferative effects of astaxanthin are more effective on cancer cells and normal cells are less affected. For example, a 2018 study by McCall et al showed that astaxanthin significantly reduced the proliferation and migration of breast cancer cells (MCF-7) compared to normal cells.(12)

2. 4. Anticancer effects of astaxanthin through induction of apoptosis

Apoptosis, often referred to as programmed cell death, is a critical mechanism for regulating growth, maintaining healthy cells, and eliminating damaged or cancerous cells (53). The role of astaxanthin in this process is related to its ability to modulate different signalling pathways involved in apoptosis, including the regulation of pro-apoptotic and anti-apoptotic proteins (54).

It has been found that astaxanthin induces apoptosis through the mitochondrial pathway of apoptosis in the human ovarian cancer cell line (SKOV3) by increasing Bcl-2/Bax expression and caspase-3 activation. The researchers of this study have shown that the inactivation of NF-kB and the activation of p53 and MAPK signalling pathways were among the simultaneous effects of astaxanthin on these cells (Su, Chen). Increased expression of apoptotic proteins such as Bax/Bad, caspase-3 and Bcl-2 in laryngeal squamous epithelial cell carcinoma cells (LS-180) has been observed after treatment with astaxanthin (52). The effect of astaxanthin on an oral cancer model was investigated by Kavitha et al. and it was found that astaxanthin decreased the expression of anti-apoptotic Bcl-2, death promoter associated with p-Bcl2 (Bad) and survivin, as well as increased the expression of pro-apoptotic Bax and Bad. The entry of cytochrome c into the cytosol, as well as the cleavage of poly-ADP ribose polymerase (PARP), induces the process of mitochondrial apoptosis.(55)

Taken together, these data show that astaxanthin can induce apoptosis in cancer cells through the mitochondrial pathway (intrinsic pathway). Contrary to the research done on the expression changes of the proteins involved in the process of mitochondrial apoptosis, according to the available information, no research has been done on the effect of astaxanthin on the external pathway of cell death (death receptor pathway). Therefore, more research is needed to determine whether astaxanthin can also induce apoptosis in target cells through the CD95 (Fas)

receptor.

An interesting (and controversial) point is the existence of evidence for the anti-apoptotic properties of astaxanthin. For example, astaxanthin can attenuate aflatoxin-induced cytochrome c entry, Bax/Bcl-2 ratio, caspase-9, and caspase-3 and prevent apoptosis in aflatoxin-treated IPEC-J2 cells. It has been found that astaxanthin exerts such effects through the Nrf2 signalling pathway and increases the expression of HSP70, NQO-1 and HO-1 genes (56). The reason for this could be the different effects of astaxanthin on different cell lines.

4 .3. Anticancer effects of astaxanthin through inhibition of cell invasion and migration

Invasion and migration of malignant cells are among the main signs of cancer progression and metastasis phenotype (57). Cancer cells need extracellular matrix remodelling to invade the surrounding tissue and metastasize. During this process, some proteins of the extracellular matrix are broken down, and the cancer cell can leave the tumour site and migrate to other parts of the body through the lymphatic system, blood flow, or by direct spread (58). Matrix metalloproteinases (MMPs) are a group of zinc-containing endopeptidases that can degrade and model extracellular matrix proteins and thereby facilitate the process of migration and invasion of cancer cells (59). Therefore, one of the usual strategies in the fight against cancer progression is to use inhibitors of matrix metalloproteinases or reduce their expression, thereby preventing the invasion and migration of cancer cells.

It has been found that astaxanthin reduces the expression of matrix metalloproteinases 7 and 10 (MMP-7, MMP-10) by suppressing the activation of PI3K/AKT/mTOR and NF-κB signalling pathways in gastric epithelial cells (60). Kowishk et al also showed in a study on the hamster model of oral cancer that dietary astaxanthin can reduce the expression of MMP-9 and MMP-2 by affecting the JAK-2/STAT-3 signalling pathway (47). Also, in another study, it was found that the expression level of matrix metalloproteinases 1, 2 and 9 in melanoma cell lines (A375 and A20558) decreased significantly after treatment with astaxanthin (14). Overall, this evidence shows that astaxanthin can prevent cancer progression and metastasis phenotypes by inhibiting the migration and invasion of malignant cells .

5. Indirect effect of astaxanthin on cancer

Inflammation and oxidative stress are among the vital factors affecting the development and progression of cancer (61). Astaxanthin exerts its indirect effects on cancer mainly through its anti-inflammatory and antioxidant properties. It is known that chronic inflammation creates a favourable environment for the growth of cancer cells and promotes tumour growth and metastasis (62). Astaxanthin's ability to suppress inflammation helps reduce these precancerous effects. In addition, the strong antioxidant activity of astaxanthin makes it possible to neutralize free radicals and reduce oxidative stress, thereby protecting cells from DNA damage and mutation (including factors involved in the initiation of cancer) (54). Evidence related to these two important properties of astaxanthin will be presented below.

5 .1. Antioxidant activity of astaxanthin

Oxidative stress, characterized by an increase in free radicals and reactive oxygen species (ROS), can cause DNA damage, protein oxidation, and lipid peroxidation in cells. This cell damage can cause the transformation of normal cells into cancer cells (63). With its strong antioxidant activity, astaxanthin acts as one of the strong defence mechanisms of living organisms against environmental oxidative stress. By neutralizing free radicals and ROS, astaxanthin can limit their destructive effects and thus their potential contribution to carcinogenesis (12).

Various comparative studies have shown that astaxanthin has higher antioxidant activity than other carotenoids. For example, it has been found that the antioxidant activity of astaxanthin is up to 10 times higher compared to different carotenoids such as lycopene, lutein, and beta-

carotene, and up to 100 times higher compared to alpha-tocopherol (26). Astaxanthin reduces the O2- level in the LPS-stimulated promonocytic human myeloid leukaemia cell line (U937). Treatment of these cells with astaxanthin will lead to the restoration of antioxidant function by catalase and superoxide dismutase, which affects the expression and activity of co-oxygenase 1 (HO-1) by inhibiting the nuclear transfer of Nrf2 (64). In another study, astaxanthin induced apoptosis, inhibited proliferation, and disrupted cell cycle progression by activating the Nrf2 antioxidant pathway in the K562 leukaemia cell line (65). In an experimental study, it was found that astaxanthin can increase the level of apoptosis by increasing the activity of antioxidant enzymes such as glutathione peroxidase, catalase and superoxide dismutase in LS-180 cells.(52)

The results of a new study have shown that nanocapsules prepared from astaxanthin and 5-fluorouracil (the main drug in the treatment of colorectal cancer) increase the activity of antioxidant enzymes such as catalase, superoxide dismutase, and glutathione peroxidase, as well as induce apoptosis in the HCT116 cell line. The results of this research have indicated an increase in the effectiveness of the drug due to the synergistic effects of astaxanthin and fluoroacyl.(66)

2. 5. Anti-inflammatory activity of astaxanthin

Chronic inflammation creates favourable conditions for cancer progression by encouraging cell proliferation, angiogenesis, and tissue remodelling (62). The anti-inflammatory properties of astaxanthin are revealed through the modulation of key signalling pathways related to inflammation and suppression of pro-inflammatory cytokines. These actions help maintain a balanced inflammatory response, potentially preventing precancerous cells from progressing to malignant tumours.(67)

Research has shown that astaxanthin can help reduce inflammation by suppressing the nuclear factor NF-κB signalling pathway, a central factor in inflammation and cancer, and the expression of inflammatory mediators in RAW264 cells stimulated with lipopolysaccharide (68). NF-κB activity is mainly observed in cancer cells and is associated with increased cell proliferation and resistance to apoptosis. The protective effect of astaxanthin and metformin in the liver of polycystic ovary syndrome model rats has been investigated in a new study. The results of this research showed that astaxanthin returned the levels of malondialdehyde (MDA) to normal levels and reduced the levels of caspase-3 and NF-κB in the liver of rats. These results indicate the antioxidant and anti-inflammatory effects of astaxanthin in this disease model (69).

The effects of astaxanthin extend to other inflammation-related molecules, such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), both of which are involved in cancer development (70). The results of studies have shown that the concentration of 10 μM astaxanthin can reduce the expression of pro-inflammatory markers such as interleukin-1 beta, interleukin-6, tumour necrosis factor-alpha (TNF-α), COX-2 and iNOS (71). It has also been found that the treatment of the THP-1 macrophage line with this concentration of astaxanthin leads to a decrease in the expression of CD-36 and SR-A receptors (72). These results show the anti-inflammatory effect of astaxanthin on the expression of pro-inflammatory molecules in macrophages and other cells.

In summary, the dual role of astaxanthin as an antioxidant and anti-inflammatory agent is a significant point in the field of cancer. The ability of this carotenoid to combat oxidative stress and modulate inflammatory responses provides a multifaceted approach to preventing the initiation and progression of cancer. In the following sections, we will talk about the safety and toxicity of astaxanthin and the possibility of using this substance in the treatment and prevention of cancer.

6. Safety and toxicity of astaxanthin

Assessment of safety and toxicity is an important aspect of evaluating any potential option for cancer (73). Therefore, understanding the safety profile of astaxanthin is of great importance for the development of cancer treatment or prevention research.

Extensive studies have been conducted to investigate the possible toxic or harmful effects of astaxanthin. For example, the harmful effects of astaxanthin have been investigated in two separate sub-chronic studies in rats. Ono et al.'s study (1999) on the treatment of F344 rats for 90 days with concentrations of 0.25% astaxanthin (equivalent to 125 mg/kg/day) did not report any toxicological changes (74). In the next study, it was found that long-term treatment of rats with a maximum dose of 50 mg/kg/day of astaxanthin did not cause adverse effects in them. However, these two studies faced problems due to the use of very low doses and the use of the gavage method to receive astaxanthin in the second study. For this reason, Stewart et al. in 2008 evaluated the acute and subchronic toxicity of Haematococcus pluvialis biomass as a source of astaxanthin in rats. The results of this study showed that the treatment of Wistar rats for 90 days with maximum doses of 465 and 557 mg of astaxanthin/kg/day, respectively, did not cause any toxicity for male and female rats.(75)

In human clinical trials, astaxanthin has shown a favourable safety profile. For example, it has been found that doses of 6 mg per day for eight weeks or 20 mg per day for four weeks do not cause any significant changes in blood parameters in adults. The results of another trial showed that the daily consumption of 8 mg of astaxanthin for three months did not cause any digestive discomfort (32). It has also been found that taking a higher dose of astaxanthin at the rate of 40 mg daily in patients with indigestion for four weeks did not have any side effects (76).

So far, the safety profile of astaxanthin appears to be excellent based on the available evidence. However, it is important to acknowledge that the long-term safety of astaxanthin, especially at high doses, is an area that requires further research. Longitudinal studies and post-market surveillance are necessary to comprehensively assess any potential risks associated with the long-term use of astaxanthin. Future research should continue to investigate the safety of this compound in different patient populations and under different conditions, paving the way for the use of astaxanthin in cancer prevention and treatment strategies.

7. Challenges and limitations

While research on the potential role of astaxanthin in cancer prevention and treatment is promising, it is not without challenges and limitations. One of the main challenges is the diversity of different research designs and methods. This heterogeneity makes definitive conclusions and comparisons between studies challenging (77). Furthermore, the lack of standardized drug regimens and treatment durations in both animal and clinical studies complicates the evaluation of the true efficacy of astaxanthin.

Another limitation is the relatively small number of clinical trials that have been conducted to date. As of 2010, 34 clinical studies have been reported on the use of astaxanthin, 22 of which have been completed so far. Astaxanthin has been tested mainly as a dietary supplement alone or in combination with other molecules in terms of safety and pharmacokinetic information or various injuries (78). The important point is that until the writing of this article, no clinical trial has been conducted on the effects of astaxanthin and cancer. It is necessary to carry out clinical research in this field to collect stronger evidence regarding the effect of astaxanthin on different types of cancer and patient profiles.

Furthermore, the long-term safety of astaxanthin remains an unanswered question. Although preliminary findings suggest overall safety and tolerability, research is needed to assess any potential risks associated with widespread astaxanthin administration (73). Overall, while astaxanthin shows great promise as a complementary approach to cancer prevention and treatment, addressing these challenges and limitations will be critical in advancing our understanding of its true potential.

8. Results and prospects

Overall, the discovery of the potential of astaxanthin in cancer prevention and treatment represents a fascinating journey at the intersection of biochemistry, cancer biology and nutrition. The significant anticancer, antioxidant and anti-inflammatory properties of this carotenoid, as well as its favourable safety profile, have created a lot of interest among researchers and healthcare professionals. The findings from laboratory and animal studies are promising and the selection of clinical trials has brought encouraging results. However, it is important to understand the complexity of cancer as a multifaceted disease with various factors involved. As such, astaxanthin should not be considered a stand-alone miracle cure but should be considered as part of a comprehensive approach to cancer care.

In the future perspective, the area of research on the effect of astaxanthin in the treatment and prevention of cancer has significant potential. Future studies should aim to address the gaps in current knowledge by conducting comprehensive trials including different types of cancer and large patient populations. Standardized drug regimens and duration of treatment should be established to facilitate meaningful comparisons across studies. Additionally, exploring the potential of astaxanthin with other therapeutic agents, lifestyle modifications, or conventional cancer treatments provides exciting avenues for further research. Also, continuous monitoring and evaluation of the long-term safety of astaxanthin intake in cancer management strategies will be essential.

In short, astaxanthin's journey from laboratory discovery to potential cancer treatment is a testament to the scientific community's dedication to improving cancer care. While much progress has been made, the road ahead is filled with opportunities for rigorous and innovative research, offering hope for improving outcomes and increasing the quality of life for cancer patients in the future.

9. Recommendations and consequences

Emerging research on the potential of astaxanthin in cancer prevention and treatment offers several important recommendations and implications for both healthcare professionals and individuals concerned about cancer risk. While more research is needed to solidify the role of this carotenoid, some important points can guide practical considerations:

First, it is recommended that clinicians be aware of the evolving landscape of astaxanthin research. This knowledge enables them to engage in informed discussions with patients about potential complementary strategies to manage cancer risk or support conventional cancer treatments. However, physicians should emphasize that astaxanthin should not replace established treatments but should be used as a complementary option.

For people interested in using astaxanthin in their health regimen, it is important to prioritize quality and safety. High-quality astaxanthin supplements from reputable sources should be sought, and the dosage should be in line with existing recommendations. According to the new food regulations of the European Union No. 2283/2015, the daily consumption of 8 mg of astaxanthin from the source of H. pluvialis is allowed for humans. Also, according to the license of the US Food and Drug Administration (FDA), the use of oral supplements of astaxanthin from the source of H. pluvialis with daily doses of 2-12 mg is allowed (78). Additionally, individuals should consult a healthcare professional before adding any dietary supplement, including astaxanthin, to their routine, especially if they have preexisting medical conditions or are taking medications.

Conclusion

In summary, the investigation of the bioactive properties of astaxanthin in the field of cancer treatment sheds light on a different and promising path for this red carotenoid pigment. Investigating the direct effect of astaxanthin on cancer cells includes a range of anticancer effects, including antiproliferative properties, induction of apoptosis, and interference in

metastasis processes. The complex molecular mechanisms underlying these phenomena make astaxanthin a significant candidate for ongoing scientific investigation and potential integration into cancer management protocols. The natural origin of astaxanthin, which is mainly obtained from microalgae and seafood, results in greater bioavailability and fewer side effects. While the intricacies of specific signalling pathways, optimal doses, and possible synergies require further elucidation, the documented anticancer properties of astaxanthin support further research on this natural compound as an adjunct in therapeutic strategies. Envisioning the future landscape of cancer research, astaxanthin emerges not only as a pigment but also as a bioactive compound with implications for cancer. Of course, in this direction, the need for more in vivo research as well as clinical trials on a wide scale is strongly felt.

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