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MINI REVIEW

The potential of astaxanthin as a natural compound for decelerating skin aging: an update review

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Abstract

Astaxanthin, a potent antioxidant found in natural sources such as algae, shrimp and salmon, is emerging as a promising agent for slowing skin aging. This review thoroughly examines the molecular mechanisms by which astaxanthin exerts its anti-aging effects. It is interesting to note that astaxanthin activates critical cellular pathways such as Nrf2/ARE, NF-κB and TGF-β. By enhancing the Nrf2/ARE pathway, astaxanthin increases the expression of antioxidant enzymes that protect skin proteins such as collagen and elastin from oxidative damage. In addition, astaxanthin suppresses the NF-κB pathway, thereby reducing inflammation, and promotes collagen synthesis by activating the TGF-β pathway. These effects inhibit collagen-degrading enzymes such as MMP-1, thereby preventing wrinkle formation. Astaxanthin also modulates the MAPK pathway, which is involved in several cellular processes, including the response to oxidative stress, inflammation, and cell proliferation. Numerous studies provide strong evidence for the benefits of astaxanthin in preventing and treating skin aging, inhibiting wrinkles, increasing skin elasticity, reducing IL-1α, TNF-α, IL-6, IL-8, MMP1, ROS activity, brightening skin, increasing collagen production, and maintaining overall skin health and beauty, as well as contributing to skin repair and regeneration. With its potent antioxidant, anti-inflammatory and collagen-stimulating properties, astaxanthin has significant potential as an ingredient in anti-aging and photoprotective skin care products. Understanding these mechanisms provides valuable insight into the role of astaxanthin in preventing aging and improving skin health.
Keywords: Anti-inflammation, antioxidant, collagen stimulation, skincare

Introduction

Skincare trends have gained significant traction recently, reflecting a growing focus on maintaining youthful, healthy skin. Advances in technology and scientific research have spurred innovation in anti-aging skincare products, making them a crucial part of the beauty and wellness industry. In 2021, the global anti-aging market was valued at approximately 62.6 billion USD, with an expected compound annual growth rate (CAGR) of around 7% between 2022 and 2027 [1]. Several factors, including increased skincare awareness [2], technological advancements in anti-aging products, and the rising population of elderly individuals worldwide, drive this rapid growth [1]. By 2050, the global population aged 60 years and older is projected to reach 1.6 billion, underscoring the increasing demand for effective anti-aging solutions [1]. Therefore, the anti-aging and aesthetics sector industry allows continuous innovation to develop new products and services attractive to consumers, thereby expanding the overall market for preventing aging [3].

Skin aging is a multifactorial process influenced by intrinsic factors such as genetics, hormonal changes, metabolism, and extrinsic factors, including ultraviolet (UV) exposure, pollution, and lifestyle [4, 5]. Intrinsic aging, driven by genetic and biological processes, results in the gradual loss of skin elasticity, hydration, and collagen over time [6]. Hormonal changes, particularly the decrease in estrogen in women and testosterone in men, contribute to thinning, dryness, and decreased skin elasticity [7, 8]. Meanwhile, extrinsic factors like UV radiation accelerate premature aging by damaging collagen and elastin fibers, leading to wrinkles, hyperpigmentation, and overall loss of skin integrity [5, 9, 10].

One of the most effective strategies to counteract skin aging, particularly from UV damage, is using antioxidants.

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Antioxidants can neutralize reactive oxygen species (ROS) generated by UV exposure, reducing oxidative stress and preventing cellular damage [11, 12]. Topical as well as oral antioxidants can support skin brightening, growth of extracellular matrix proteins, and anti-aging [13-15].

Among natural antioxidants, astaxanthin (3,3'-dihydroxy-β, β'-carotene-4,4'-dione), a xanthophyll carotenoid, has gained attention for its powerful antioxidant, anti-inflammatory, and photoprotective properties. Astaxanthin has demonstrated the ability to reduce oxidative stress, promote skin health, and protect against UV-induced damage, making it a promising compound in the anti-aging and skin care industries [16-19].

Astaxanthin not only protects against photoaging but also supports skin elasticity [20], hydration, and the reduction of wrinkles and fine lines. Several studies have highlighted astaxanthin's potential in improving skin texture, reducing hyperpigmentation, and enhancing wound healing [19, 21, 22]. Despite these benefits, comprehensive research on the specific mechanisms through which astaxanthin slows skin aging remains limited. This review aims to assess the potential of astaxanthin as a natural anti-aging agent, focusing on its role in preventing skin wrinkles and promoting overall skin health.

Skin aging and pathways involved in skin aging

Skin aging is a complex process characterized by a decline in skin quality due to the combined effects of chronological aging, hormonal deficiencies, premature aging, and environmental factors [5]. The factors contributing to skin aging are classified into two categories: intrinsic and extrinsic. Intrinsic factors, affecting cells throughout the body, include aging, genetics, metabolic processes, and hormonal changes. On the other hand, extrinsic factors encompass environmental and lifestyle influences such as exposure to ultraviolet (UV) radiation, pollution, and harmful chemicals [23].

Intrinsic aging is driven by several physiological changes, including hormone reduction, glycation, apoptosis, methylation, immune system decline, and the production of free radicals. Additionally, intrinsic aging involves the degeneration of extracellular matrix components such as elastin, collagen, and fibrillin, along with alterations in oligosaccharides. Conversely, extrinsic aging is primarily influenced by external factors like an unhealthy lifestyle, poor dietary habits, stress, and environmental exposure. Environmental factors such as UV radiation, pollution, and smoking particularly damage the skin [4].

UV radiation, a major contributor to skin aging, induces oxidative stress. Oxidative stress is an imbalance between ROS formed and antioxidant defense mechanisms. ROS are reactive oxygen compounds and secondary products of aerobic metabolism. ROS imbalance is caused by increased ROS production, reduced antioxidant production, or both. Oxidative stress causes oxidative damage to various cell components, disrupts communication processes between cells, stimulates apoptosis, and is involved in various diseases associated with aging. Oxidative stress damages the skin's natural renewal and repair processes and damages DNA directly, causing cell mutations and premature aging. This oxidative stress is the leading cause of photoaging and premature skin aging. Both ultraviolet B (UVB) and ultraviolet A (UVA) can damage the skin. UVB is the main skin stress trigger that can damage escDNA and UVA increases the production of DNA toxic ROS [4].

ROS are unstable free radicals because they have unpaired electrons in the outer orbit. These compounds attract electrons from surrounding molecules to complete the electrons in the outer orbit and produce a very dangerous free radical chain reaction. Such free radicals are superoxide anion (O_2^-), hydroxyl radical (-OH), and peroxynitrate ($ONOO^-$). Hydrogen peroxide (H_2O_2) and nitric oxide (NO) are not free radicals, but are classified as ROS, because they trigger oxidation-reduction reactions and form free radicals. ROS plays a role in causing skin aging through cellular oxidation processes, activation of nuclear factor kappa B [23], activation of mitogen-activated pathway (MAP) kinase, and stimulation of pro-inflammatory cytokines. Increased ROS will damage proteins, lipids, and cell DNA, resulting in skin aging [4].

Intrinsic aging is associated with a reduction in transforming growth factor-beta (TGF-β) levels and ROS accumulation. In contrast, extrinsic aging, primarily caused by UV exposure, increases ROS in the dermal layer, initiating a cascade of molecular reactions. ROS activates the transcription factor AP-1, which, in turn, stimulates the expression of matrix metalloproteinase (MMP) enzymes, particularly collagenase-1 (MMP-1). These enzymes degrade collagen, contributing to skin aging [4].

Several molecular pathways are involved in the skin aging process, including the Nrf2/ARE, NF-κB, TGF-β, MAPK, Wnt/β-catenin, RAGE (Receptor for Advanced Glycation End Products), and p53 pathways [22, 24, 25]. The Nrf2/ARE pathway plays a crucial role in antioxidant defense and detoxification processes, while NF-κB regulates inflammatory and immune responses. Activation of the NF-κB pathway leads to the production of pro-inflammatory cytokines, promoting inflammation and tissue damage [26].

The TGF-β pathway is often dysregulated during aging, resulting in reduced collagen production, increased activity of extracellular matrix-degrading enzymes, and impaired cell regeneration. Similarly, the MAPK pathway mediates cellular responses to oxidative stress, inflammation, and proliferation. The Wnt/β-catenin pathway, essential for cell proliferation, differentiation, and tissue regeneration, also becomes less active with age, leading to decreased skin regeneration and collagen synthesis. Furthermore, the RAGE pathway, which is involved in the accumulation of advanced glycation end products (AGEs), exacerbates the formation of wrinkles and skin elasticity loss when overactivated. Finally, the p53 protein, which regulates apoptosis and cell proliferation, becomes more active with age, further reducing the skin's regenerative capacity [25].

The potential of astaxanthin in decelerating skin aging

Natural sources of astaxanthin

For decades, natural products have been researched for a wide range of uses in health due to their adaptability, safety, and cost-effectiveness [27]. There is also a continuous increase in the research involving the use of natural bioactive in cosmetics due to the increasing health and environmental concerns.

Green algae, especially *Haematococcus pluvialis*, are rich natural sources of astaxanthin with carotenoid pigments that have strong antioxidant properties. Due to its ability to produce astaxanthin in large quantities, *Haematococcus pluvialis* has become an important research subject in the fields of biotechnology and nutrition [28]. Astaxanthin extracted from *Haematococcus pluvialis* is used as a food supplement, an additional ingredient in food and beverage products, as well as in various skincare and health products. Astaxanthin is the most potent natural antioxidant [29] which comes from green algae [30-41], red algae [15], shrimp [41-48], crayfish [49], trout [50-56], krill [57-59], salmon [54, 56, 60-64], and yeast [65, 66] which has several essential biological functions including reducing pigmentation and protecting skin wrinkles against the effects of UV light. Even though it is contained in many natural sources, green algae is the largest producer of astaxanthin [67].

Mechanism of astaxanthin to prevent skin aging

Astaxanthin exerts its anti-aging effects primarily by modulating several key cellular pathways, including the Nrf2/ARE, NF-κB, and TGF-β pathways [22, 24]. One of its primary actions is enhancing the activity of the Nrf2/ARE pathway, which is critical for the cellular antioxidant defense system. When astaxanthin activates this pathway, it leads to the upregulation of antioxidant genes and detoxification enzymes, such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) [68]. These enzymes play a crucial role in neutralizing reactive oxygen species (ROS) and combating oxidative stress, a major contributor to skin aging. By increasing the cell's capacity to counter oxidative damage, astaxanthin helps protect essential structural proteins in the skin, such as collagen and elastin, from degradation caused by free radicals generated during UV exposure. Moreover, astaxanthin has been shown to reduce the activity of matrix metalloproteinase-1 (MMP-1), an enzyme responsible for collagen breakdown, significantly contributing to wrinkle formation [36, 69, 70].

In addition to its antioxidant properties, astaxanthin can suppress the activation of the NF-κB pathway, a signal-

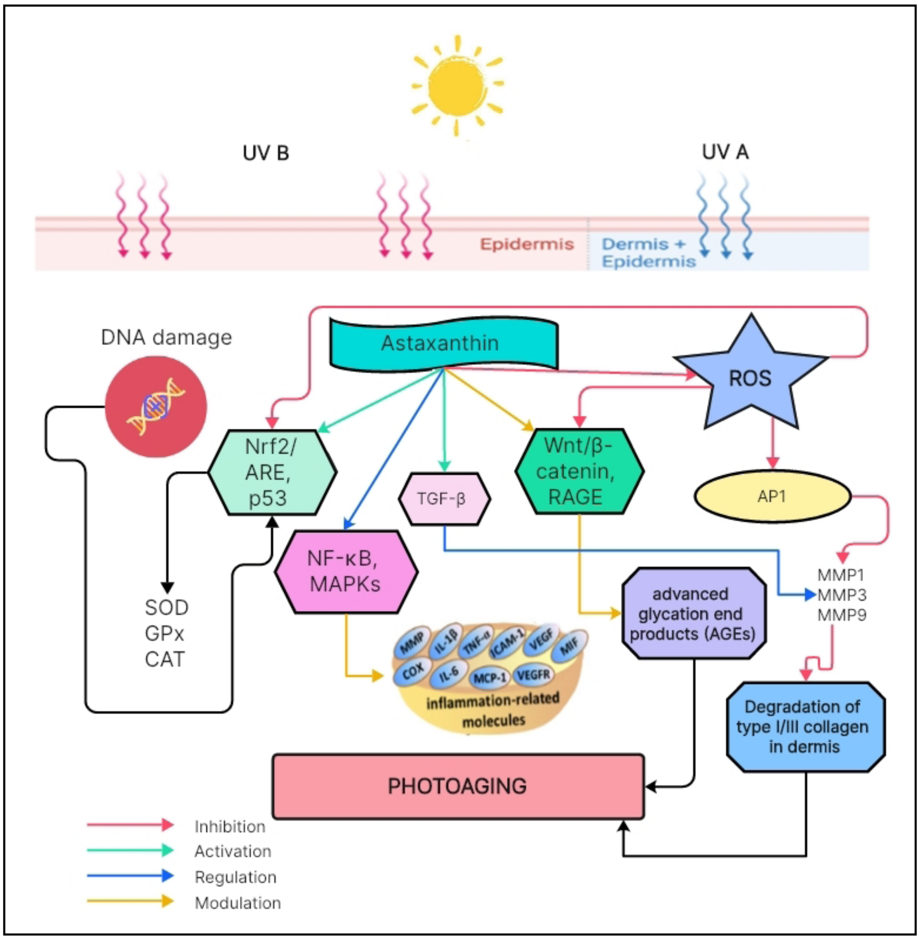

Figure 1. Effects of astaxanthin in many molecular pathways related with skin aging. Astaxanthin increases the activity of the Nrf2/ARE, TGF-β, and MAPKs pathway, reducing MMP activity, in addition to suppressing the activation of the NF-κB pathway, which can reduce inflammation and damage caused by excessive inflammatory responses in the skin.

ing cascade involved in the inflammatory response [23]. Chronic inflammation accelerates skin aging by degrading connective tissue and promoting the overproduction of pro-inflammatory cytokines. By inhibiting NF-κB activation, astaxanthin helps to reduce skin inflammation, thus preventing inflammation-induced tissue damage and preserving skin integrity [22].

The TGF-β pathway is another critical signaling mechanism affected by astaxanthin. This pathway regulates cell proliferation, differentiation, and the production of extracellular matrix components, particularly collagen [24]. By activating the TGF-β pathway, astaxanthin helps to maintain the structure and function of skin connective tissue. This activation leads to enhanced collagen production, which not only improves skin texture but also reduces wrinkles and other signs of aging. Increased collagen synthesis inhibits the activity of collagen-degrading enzymes, such as MMP-1, further supporting the skin's regenerative processes [71].

Additionally, astaxanthin has been shown to inhibit the expression of MMPs in various cell types, including macrophages and chondrocytes, and in human dermal fibroblasts, where it suppresses both MMP-1 and MMP-3 expression, leading to increased collagen content [72-74]. Furthermore, astaxanthin increases pathway activity MAPK (Mitogen-activated protein kinase). MAPKs are involved in various cellular processes, including responses to oxidative stress, inflammation, and cell proliferation [25]. Astaxanthin is becoming an attractive ingredient in anti-aging and photoprotection skincare products.

Understanding the natural sources of astaxanthin, its biological benefits, and its mechanisms of action allows for better application in anti-aging strategies. Astaxanthin's potential to protect, repair, and renew skin makes it a compelling ingredient in modern skincare formulations aimed at slowing the aging process (Figure 1).

In vitro, in vivo, in silico, and clinical studies have provided strong evidence of the benefits of astaxanthin in preventing and treating skin aging, slowing wrinkles, increasing skin elasticity, reducing IL-1α, TNF-α, IL-6, IL-8, MMP-1, ROS activity, brightening skin, increasing collagen production, and maintaining overall skin health and beauty (Table 1).

The main mechanism actions of astaxanthin include: 1) antioxidant activity, 2) scavenging free radicals, 3) protection against DNA damage, 4) anti-inflammation, 5) stimulation of collagen production, 6) repair of skin damage, and 7) skin penetration. The mechanism of astaxanthin as an antioxidant able to fight damage caused by free radicals produced by exposure to UV rays and pollution [78]. Free radicals can damage skin cells, cause skin aging, and increase the risk of skin cancer. Astaxanthin neutralizes free radicals produced by UV rays by capturing them before they damage the skin structure [6]. Astaxanthin works as an antioxidant by neutralizing ROS in the body. ROS are highly reactive oxygen molecules and can cause cellular damage if produced too much or are out of balance with the body's antioxidant system. ROS include free radicals such as superoxide anion, hydrogen peroxide, and hydroxyl radicals. Astaxanthin acts as a free radical scavenger, meaning it can bind ROS and prevent them from damaging other biological molecules, including DNA, proteins,

Table 1. Effect of astaxanthin on the skin.

Intervention	Model	Duration	Results	Reference
Astaxanthin supplementation	65 healthy female participants	16 weeks	IL-1α ↓ TNF-α ↓ IL-6 ↓ IL-8 ↓ MMP-1 ↓ Wrinkle ↓ Elasticity ↑	[75]
Astaxanthin supplementation	23 healthy volunteers	10 weeks	Rough skin ↓ Skin texture ↓	[76]
Astaxanthin oral treatments	Hairless mice	8 weeks	Wrinkle ↓ Epidermal thickness ↓ Density of collagen fibers ↑ Density of capillary vessels ↑ ROS activity ↓	[6]
Astaxanthin topical and oral treatments	60 women	84 days	Wrinkles ↓ Roughness↓ Spots (brown and visible) ↓ Elasticity ↑ Hydration ↑ Firmness ↑ Luminosity ↑	[72]
Astaxanthin administration	Protein data bank	Null	MMP-1 ↓ MMP-3 ↓	[71]
Astaxanthin administration	Normal human epidermal keratinocytes (NHEKs)	2 hours	ROS production ↓ Apoptotic ↑	[18]
Astaxanthin nano emulsion administration	Human skin	0-120 minutes	Wrinkle ↓ Skin-brightening ↑	[77]

and lipids in the body's cells. In this way, astaxanthin helps protect the body's cells from oxidative damage that can lead to various disease conditions and aging [71]. Exposure to UV rays cause damage to skin cell DNA. Astaxanthin has shown the ability to protect skin DNA from damage which may help prevent cell mutations and skin cancer [71, 79, 80]. Astaxanthin has anti-inflammatory properties that can help reduce skin inflammation due to exposure to UV rays [18, 81-83]. This can help prevent redness, swelling, and skin irritation. In addition, astaxanthin has been known to stimulate collagen production by skin cells, which can help maintain skin elasticity and suppleness [6]. Collagen is the main structural protein in the skin that provides strength and elasticity [72, 75]. Astaxanthin is also proven for its ability to repair existing skin damage, including wrinkles, fine lines, and age spots [72], by penetrating the layers of the skin, providing protection from the inside and outside. This makes it an effective supplement for skin health, whether used topically or through supplement consumption [84]. The use of astaxanthin in skin care can help reduce skin damage due to exposure to UV rays, increase skin elasticity, and reduce signs of skin aging [85].

Conclusions

Compounds derived from natural sources are gaining attention in the cosmetic industry and may be able to actively treat a variety of skin problems. This review attempts to shed light on the potential of the natural compound astaxanthin for slowing skin aging. Astaxanthin is an antioxidant that can prevent skin aging by increasing the activity of the Nrf2/ARE pathway and TGF-β, thereby reducing MMP1 activity, and suppressing the activation of the NF-κB pathway, which can reduce inflammation and damage caused by excessive inflammatory responses in the skin. It also increases the activity of the MAPK pathway, which is involved in several cellular processes, including the response to oxidative stress, inflammation and cell proliferation. Many studies provide strong evidence of the benefits of astaxanthin in preventing and treating skin aging, slowing wrinkles, increasing skin elasticity, reducing IL-1α, TNF-α, IL-6, IL-8, MMP1, ROS activity, brightening skin, increasing collagen production, and maintaining overall skin health and beauty. Finally, the use of astaxanthin in skincare products has become a potential product in the beauty industry. However, further studies are needed to fully understand the biological activity and precise mechanism of action of astaxanthin in slowing skin aging.

Declarations

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