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Marine bioactive compounds: Sustainable sources, green extraction, and healthcare applications

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ABSTRACT

Marine ecosystems represent one of the most valuable yet underexplored sources of diverse bioactive compounds with significant potential for economic, healthcare, and environmental applications. Marine-derived bioactive compounds have emerged as promising active ingredients, exhibiting antibacterial, antiviral, anticancer, anti-inflammatory, and antioxidant properties, among others, with growing use in cosmetics and food supplements. Ongoing research in this area is aligned with the United Nations Sustainable Development Goals, particularly Goal 12, which relates to responsible production and consumption. The environmentally friendly extraction of these bioactive compounds from marine sources offers a path toward greener industrial practices and a more sustainable global economy. This review provides a comprehensive overview of the current state of the art on the main classes of marine bioactive compounds, their natural sources, green extraction methods, and their applications in health-related fields, including cosmetics and food supplements. Despite their potential, the use of marine bioactive compounds remains limited. Current research is largely based on *in vitro* studies using compound mixtures, with limited data on regulatory frameworks and human safety. To unlock their full therapeutic potential, future research should focus on: the standardization of clinical trial protocols, the isolation and characterization of individual compounds, and the expansion of *in vivo* studies in both animals and humans.

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1. Introduction

Over the years, advances in healthcare have significantly increased the average life expectancy of the world's population. There is a growing interest in innovative products that promote health and well-being, particularly those containing active ingredients derived from natural sources. These products have been extensively researched for their bioactivity and their potential to promote a circular economy, particularly in the cosmetics and food industries. Attention is also being paid to the sustainability and environmental impact of these natural sources. Consumers are now seeking for products with a green life cycle, from sourcing to post-consumer use [1]. To meet these demands, researchers and companies are developing new bio-derived products obtained from a variety of natural sources. While traditional plant-derived active ingredients are still commonly used, limitations regarding available arable land and investment have reduced their use [2].

The oceans' biodiversity is a significant source of active ingredients, with over 250,000 new species discovered in recent decades, along with over 25,000 new biologically active substances [3]. Bioactive compounds derived from marine species, such as plankton, algae, fish, crustaceans, sponges, and sea anemones, have been shown to have antioxidant, anti-aging, anti-inflammatory, and nutritional properties that are beneficial to human health [4].

Marine world represents a natural renewable and widely available resource for several unique marine-derived bioactive substances, which can be organized according to their chemical structure including polysaccharides, proteins and peptides, fatty acids, polyphenolics and simple phenolic derivatives, carotenoids, and vitamins (Fig. S1 in Supporting information). These components

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can be isolated from marine vertebrates and invertebrates, plant (seaweeds, phytoplankton) and microbial (bacteria, fungi, yest) sources of Porifera, Mollusca, Chordata, Cnidaria, Echinodermata, Euryarchaeota, Ascomycota, Arthropoda, Rhodophyta and Chlorophyta phylum, among others [5].

Indeed, in recent years, marine bioactive compounds have emerged as a new source of active ingredients. This review begins with an overview of the most common marine bioactive compounds and their natural sources, followed by a briefly discussion about the most promising green extraction methodologies and finally, their applications in cosmetics, and food supplements.

2. Types of marine bioactive compounds

2.1. Polysaccharides

Polysaccharides are biologically essential macromolecules found in all almost living species, exhibiting various biological activities for good body function and balance [6–8]. These marine-derived biopolymers can be obtained from different sources like marine plants, animals and microorganisms, where algae are the main source. Thus, the marine polysaccharides can be classified into three major groups: marine animal polysaccharides (*i.e*., chitin, chitosan, hyaluronic acid and chondroitin sulfate) marine plant polysaccharides (*i.e*., fucoidan, carrageenan, alginate, agar and ulvan) and marine microbial polysaccharides (*i.e*., xanthan gum and glucan) [6,9,10].

Chitin is the second most available biopolymer on earth after cellulose, and is mainly extracted from crustacean shells, mollusks (squid and cuttlefish), and fungal and yeast cell walls [9,11]. Currently, commercial chitin is generally obtained from byproducts of the seafood processing industry (shells discards of crabs and shrimps) due to the high availability of this waste [11,12]. On the other hand, chitosan is the *N*-deacetylated derivative of chitin and is the only natural commercially available positively charged polysaccharide known in nature to date [10,11].

There are others important appealing polysaccharides, namely fucoidan and alginate. Fucoidan is a sulfated polysaccharide containing high levels of L-fucose and sulfate groups, found in a branched form in brown algae cell walls and in linear form in some marine invertebrates (*i.e*., sea cucumbers and sea urchins) [10,13,14]. Alginate is an abundantly available edible polysaccharide that can be also extracted from brown algae [9,10,15].

2.2. Proteins and peptides

Proteins and peptides play a vital role in the existence and functioning of all Earth's living species, including marine organisms. The most interesting and useful proteins isolated from these marine sources are collagen, gelatin**,** and phycobiliproteins (PBPs). Collagen is the main fibrous structural protein of connective tissue found in all vertebrates, being the most abundant protein in mammalian species, representing around 30 % of the body's total protein [13]. This polypeptide is typically obtained from bovine and porcine skin and has been extensively applied although, due to the risk of certain zoonotic disease transmission and ethical issues, the bovine and porcine collagen use is very limited [13,16]. Hence, the marine collagen becomes a favourable alternative. Marine collagen can be recovered from marine fishery discards, a sustainable and affordable source, for example, cod skin fish scales, tuna skin and scales, squid fins and arms, and salmon scales and skin, as well are present in red seaweeds and the tissues of both marine vertebrates and invertebrates (fish, sponges, sea urchins, octopi, squid, jellyfishes, cuttlefishes, starfishes, sea anemones, and prawns) [13,14]. Furthermore, collagen is mostly transformed into gelatin by partial hydrolysis followed by heat, a water-solute denatured protein. Gelatin is an essential commercial biopolymer containing hydrophobic amino acids (hydroxyproline, valine, glycine, proline, and alanine) with a certain range of peptides [14], and it is principally derived of marine fishery discards, especially shark cartilages, swim bladder of tuna, yellowfin tuna skin, and bone of red snapper and grouper [15]. In addition to these great molecules, PBPs are natural pigments discovered mostly in red seaweeds and brown seaweeds [14,17].

2.3. Fatty acids

Fatty acids are vital dietary supplements for human health-beneficial consumption. They can vary in length, levels of unsaturation, and the number of bonds they contain. Thus, they are categorized as monounsaturated fatty acids (MUFAs) when they possess a single double bond, and as polyunsaturated fatty acids (PUFAs) when there are two or more unsaturations [18,19]. In marine environments, most fatty acids are PUFAs, and are two main types, omega-6 fatty acids, such as linoleic acid (C18:2$\omega-6$), and omega-3 fatty acids, which include α-linolenic acid (C18:3$\omega-3$), eicosapentaenoic acid (EPA, C20:5$\omega-3$), and docosahexaenoic acid (DHA, C22:6$\omega-3$) [20,21].

Fatty acids are available in marine by-products, [14] algae (mainly red macroalgae), yeasts [22] bacteria and fungi species as alternative source for seafood, the predominant source for humans [23]. Jiménez-González *et al*. found palmitic acid (C16:0), linoleic acid, linolenic acid, arachidonic acid (C20:4$\omega-6$), and EPA in *P. palmata* and *Porphyra* species [17]. In another study, the squid loligo was considered a potential new source for omega-3 and omega-6 oils, with a high percentage of linoleic acid, EPA, and DHA [24].

2.4. Polyphenolics and phenolics-derivatives

Marine ecosystems are a valuable rich source of new and unique polyphenolics, some of which cannot be found in terrestrial environments [25]. In marine nature, there are two main subfamilies of polyphenols according to the number of phenol rings in chemical structure: the flavonoids and the nonflavonoids. The flavonoids which have a common C6-C3-C6 skeleton with two phenyl rings linked by a heterocyclic ring can be grouped into six subclasses: flavones (*i.e*., apigenin), flavonols (*i.e*., quercetin), flavanols (*i.e*., catechin), flavanones (*i.e*., naringenin), isoflavones (*i.e*., daidzein) and anthocyanins (*i.e*., cyanidin). While non-flavonoids can be divided into phenolic acids (*i.e*., gallic, caffein and ferulic acids), tannins (*i.e*., dieckol), stilbenes, and lignans [23,25]. These bioactive chemicals can be abundantly obtained from marine macroalgae and microalgae, specially phlorotannin, phloroglucinol and its polymers, but also from cyanobacteria, fungi, seagrasses, and sponges. The quantity and variability of phenolic compounds in these marine organisms depends on species, seasonality and environmental conditions. Among polyphenolic compounds, bromophenols, phenolic acids, and flavonoids are commonly in red and green algae, whereas phlorotannin are structural components of brown algae cell wall [23,25].

2.5. Carotenoids

Carotenoids are terpenoid pigments with essential functions in various physiological processes. Carotenoids are biosynthesized by all photosynthetic organisms and acquired through the diet by animals and humans, who lack the ability to synthesize them [26]. They can be divided in carotenes (hydrocarbon carotenoids), such as β-carotene and lycopene, and xanthophylls (oxygenated derivatives), which include lutein, astaxanthin, fucoxanthin and zeaxanthin [27]. These valuable carotenoids can be natural found

as principal pigments in marine vertebrates (*i.e*., whales, dolphins, reptiles and fishes), marine invertebrates (*i.e*., sea urchins, mollusks, and crustaceans), marine algae, marine bacteria, marine yeast (*i.e*., *Rhodosporidium paludigenum*) and marine fungi [22]. Likewise, they can be recovered from seafood by-products, which include astaxanthin, zeaxanthin and β-carotene [14].

One of the most prevalent carotenoids is β-carotene, a cyclic carotene known for its bright orange color and significant biological roles across many species. It can be found in different types of macro and microalgae and, to a lesser extent, in seafood. In Europe, β-carotene derived from the algae *Dunaliella salina* is approved for use as a food additive [28,29]. Lycopene is a red acyclic carotene, naturally found in certain algae and pink seafood like salmon and shrimps [30]. Astaxanthin is derived from β-carotene or zeaxanthin, and can be found in certain algae and animals, such as krill, shrimp, salmon, trout and crayfish [31]. Some brown seaweeds, including species like *Hijikia fusiformis*, *Undaria pinnatifida*, *Laminaria japonica*, and *Sargassum fulvellum*, contain fucoxanthin. This carotenoid is one of the most abundant, making up over 10 % of the total carotenoids produced in nature, especially in ocean environments [32]. Zeaxanthin is an isomer of lutein. It ranks among the most common carotenoid alcohols in nature and is found in various algae, including *Rhodophyta spp*. and *Spirulina spp*[32]. Additionally, zeaxanthin is one of the two critical components of the macular pigment in the retina [28].

2.6. Vitamins

Vitamins are also crucial molecules, due to being essential for the proper functioning of the metabolism and, consequently, for maintaining the body's general health. They can be classified according to their physicochemical characteristics, such as hydrophilicity (water soluble) or hydrophobicity (fat soluble). Vitamins A, D, E, and K, are fat soluble, and are transported and absorbed by lipid transport processes. On the other hand, water soluble vitamins are not stored in the body and include vitamin C and all the vitamins B [33,34].

The structure of the vitamin A molecule has undergone various modifications, leading to a category of compounds known as retinols (*e.g*., retinol and its derivatives, such as retinoic acid, retinyl esters, 13-*cis* retinoic acid (isotretinoin), all-*trans* retinoic acid (tretinoin), 9-*cis* retinoic acid, and 3,4-didehydroretinoic acid), with retinol being the most prevalent form in the skin [35]. A significant source of vitamin A can be found in the liver oil of various marine species, including cod and sturgeon [36]. The vitamin B complex consists of a variety of vitamins B, which include B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantothenic acid), B6 (pyridoxine), B7 (biotin), B9 (folic acid), and B12 (cobalamin), along with their derivatives. Various sources of vitamin B, such as clams, oysters, salmon, trout, tuna, and microalgae, can be found in the ocean [37]. Vitamin C, or L-ascorbic acid, is an essential micronutrient for human health. Since humans cannot synthesize this vitamin due to the absence of the necessary biosynthesis enzyme, it must be obtained through dietary sources. Microalgae are the highest source of this vitamin in the sea [38]. On the other hand, humans can synthesize vitamin D sufficiently when exposed to direct sunlight for 5–30 min daily. However most comes through dietary intake (notably from fatty fish like salmon and tuna) [39]. Vitamin D is crucial for maintaining calcium balance and metabolism, existing in two forms: vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) [40]. Vitamin E, which is solely produced by photosynthetic organisms such as microalgae, must be obtained by animals through their diet. While all forms are absorbed in the small intestine, only alpha-tocopherol is metabolized, making it the sole form utilized by the human body [41]. The designation "vitamin K" encompasses a group known as naphthoquinones, which includes two primary types: phytonadione (vitamin K1), the main dietary source of vitamin K for humans, and menaquinones (vitamin K2), produced by specific intestinal bacteria. Microalgae are a key source of vitamin K found in marine environments [42].

2.7. Additional classes

Other classes of marine bioactive compounds, such as terpenoids, steroid compounds, alkaloids, have also attracted growing interest from researchers due to their potential health benefits. Terpenoids, in particular, represent a major category of natural compounds. Marine organisms, including bacteria and fungi, synthesize a wide variety of structurally diverse terpenoids. The broad spectrum of bioactivities exhibited by these compounds highlights their potential for further investigation across multiple research areas [43].

Steroids constitute another significant class of marine bioactives. Marine invertebrates such as echinoderms, tunicates, and sponges have yielded numerous novel steroid compounds. These often feature unique structural characteristics, such as hydroxylated side chains and sulfate groups, contribute to their diverse biological activities [44]. Marine alkaloids are also of considerable importance. Characterized by nitrogen-containing structures, they represent a chemically diverse group of compounds. Although still a relatively young field of research, interest in marine alkaloids is rapidly expanding. Many studies focus on elucidating their chemical structures and exploring their biological potential. Recently discovered alkaloids have primarily been isolated from algae, microorganisms, sponges, and other marine invertebrates [45].

3. Sustainable green extraction technologies

Conventional extraction procedures typically involve high processing temperatures and extended processing times, making them energy-intensive and reliant on large volumes of solvents. This increases the risk of both workplace hazards and environmental pollution. Therefore, promoting the development and application of alternative extraction techniques is essential. The growing global emphasis on sustainability and environmental preservation has encouraged the scientific community to adopt green extraction technologies. These approaches align with the principles of green chemistry, aiming to minimize environmental impact while enhancing efficiency, selectivity, and purity compared to conventional methods. Green extraction includes a variety of innovative techniques that utilize alternative solvents, milder operating conditions, and advanced technologies to maximize the potential of bioactive compounds. These cutting-edge methods not only increase extraction yield but also reduce processing time and resource consumption. Given the diversity of marine organisms and the variability in biomolecular characteristics, both the choice of extraction procedure and the operating conditions play a critical role in achieving high yields and superior quality of target substances [46].

Various environmentally friendly techniques have been studied including the use of green solvents, such as ionic liquids, natural deep eutectic solvents, supercritical fluids, water or solvent-free methodologies, the use of biotechnological based technologies, such as microbial fermentation and enzymatic extraction; and the use of eco-friendly alternative methodologies such as microwave-assisted and ultrasound-assisted extraction (Fig. S2 in Supporting information) [47].

3.1. Microbial fermentation extraction

Microbial fermentation extraction is a sustainable technique that utilizes microorganisms, such as bacteria, fungi, yeasts, to

break down complex materials and release bioactive compounds. This process depends on the extracellular proteolytic enzymes produced by these microorganisms to extract various compounds, including, carotenoids, polysaccharides, proteins and lipids [48].

The key benefits of this technique include sustainability which is transversal to other green extraction methodologies, and high yields and purity. However, it faces challenges such as complex optimization, time-consuming, a significant initial investment costs, and ongoing development for large-scale production [49].

3.2. Enzymatic extraction

Another environmentally friendly method currently being explored for extracting bioactive compounds is enzymatic extraction. This method employs enzymes that can be used at different stages of the extraction process, resulting in various products and by-products, as they are influenced by environmental factors. Enzymes provide a more selective and gentle technique for breaking down cell walls or membrane components to release desired intracellular substances. A major benefit of enzymatic methods is their sustainability, as they typically require lower energy consumption and minimize the use of harsh chemicals. Additionally, these methods effectively maintain the functionality and integrity of intracellular compounds. However, enzymatic extraction still faces some challenges, including slow reaction rates and higher operational costs. The effectiveness of these processes can vary depending on the cell type, and the need for precise control over conditions like temperature and pH adds complexity and expense. Furthermore, scaling up enzymatic extraction still presents some critical difficulties that limit its industrial application. The high costs and limited availability of certain enzymes, along with the challenges of reproducing the optimal conditions required for their activity, can restrict their application in large-scale production [49,50].

3.3. Microwave-assisted extraction

Microwave-assisted extraction is a technique that utilizes microwave energy to modify the cellular structures of a sample, enhancing the release and extraction of desired compounds. This method provides excellent recovery rates for compounds of interest and boasts several key advantages, including a streamlined one-step conversion process, reduced reaction times, and lower solvent usage. However, it does carry some risks, such as the potential for thermal degradation of the compounds, a limitation to polar solvents, and challenges in scalability for industrial use [51].

Over the past few decades, this technique has become increasingly acknowledged as an effective method for obtaining lipids, especially from microalgae [52].

3.4. Ultrasound-assisted extraction

Ultrasound-assisted extraction is a highly researched and efficient technology. This method utilizes ultrasonic waves with specific characteristics, to alter the physicochemical properties of the propagation medium. A key phenomenon in this technique is cavitation, which involves the formation, growth, and explosive collapse of microbubbles or cavities in a liquid when subjected to high-intensity ultrasonic waves. The localized shear forces created during cavitation effectively break down microbial cell walls while maintaining the integrity of sensitive intracellular compounds, such as proteins, lipids, and polysaccharides. This makes ultrasonication particularly valuable for high-value products like pharmaceuticals and nutraceuticals, where preserving bioactivity is essential. Its primary advantage lies in its tunability, allowing for adjustments in frequency, intensity, duration, and configuration to facilitate selective and controlled cell disruption, while also reducing extraction time and solvent use. However, scalability remains the biggest challenge for this method in both academic and industrial settings. Another limitation of ultrasonication is its reduced effectiveness when processing high-viscosity liquids. Increased viscosity hinders the uniform propagation of sound waves, which dampens cavitation bubble formation, crucial for efficient cell disruption, consequently, this results in less uniform cavitation, lower mechanical forces, and reduced effectiveness in breaking down cells. Intensification in the generation of bubbles during cavitation-based methods *via* innovative reactor design and uniform distribution of cavitation energy throughout the extraction solution should be explored [49,50].

3.5. Green solvents

Green solvents are chemicals designed to reduce the environmental impact associated with the use of conventional toxic organic chemicals in various chemical and extraction processes. They exhibit a variety of physical and chemical properties that make them ideal for different extraction techniques. These properties include being low or non-volatile, non-flammable, non-toxic, non-carcinogenic, easily recyclable, and biodegradable [52]. Ionic liquids are a class of organic salts that remain in a liquid state at relatively low temperatures (below 100 °C). These unique compounds made entirely of organic or inorganic cations and anions, offering favorable thermodynamic characteristics such as thermal stability, adjustable viscosity, and varying levels of miscibility and solubility. They are effective for extracting a wide range of compounds with different polarities [52]. Although often categorized as green solvents, their environmental sustainability is debatable due to the synthesis process, which frequently involves reagents derived from fossil sources, leading to overlooked environmental consequences and significant energy consumption. Additionally, the biodegradability of ionic liquids is crucial when evaluating their environmental impact, as numerous studies have reported varying findings on their biodegradability [53].

Supercritical solvents, which are easily attained at their critical points, include supercritical carbon dioxide, a commonly used option due to its safety and renewability. These solvents generally demonstrate high diffusivities similar to gases. However, to enhance the solubility of solid reactants and products, co-solvents like ethanol are often needed, as pure supercritical carbon dioxide has a low polarity [49]. The primary benefits of employing supercritical solvents are their enhanced selectivity for extracting neutral lipids, reduced extraction times, and the straightforward recovery of the solvent, which eliminates the reliance on halogenated organic solvents. On the downside, there are significant initial expenses involved in purchasing and installing the necessary equipment, as well as the need to train specialized personnel, along with the ongoing energy and capital costs related to regular maintenance [53].

Deep eutectic solvents have gained attention because they share similar thermodynamic properties with ionic liquids but are simpler to produce, and less harmful to the environment. They are biodegradable and made from natural, cost-effective, and recyclable components, making them suitable for applications in food, pharmaceuticals, and cosmetics [54]. However, cytotoxicity evaluations indicate that, at times, they exhibit a greater degree of toxicity than their separate components [55]. Water is regarded as the most natural solvent, and many researchers advocate for its status as the greenest solvent in chemistry from both experimental and industrial viewpoints [52].

Ultimately, the selection of the best extraction method depends on the application and the necessity to balance factors such as purity, cost, scalability, and environmental impact.

Future studies on extraction methods should focus on enhancing processes to attain greater yields, improved purity, and scalability, while also reducing energy usage and environmental impact. Additionally, investigating hybrid strategies that integrate existing technologies, combined with the economic recovery of these valuable components using industrially applicable technologies, would be a practical solution to maximize the use of these marine bioactive compounds.

Nevertheless, these green approach methods will help the sustainability requirement and are anticipated to become the standard in the future. The significance of green extraction extends beyond its technical aspects. It aligns seamlessly with the broader framework of green chemistry, striving for safer and more sustainable practices throughout the chemical lifecycle. This approach resonates with the increasing global emphasis on responsible production and consumption, as exemplified by the United Nations' Sustainable Development Goals [47].

4. Healthcare applications

The use of marine bioactive compounds to improve human health has gained prominence due to their significant nutritional and therapeutic benefits with minimal or no adverse effects. These compounds are widely applied in cosmetics and food supplements, driving industries to explore innovative approaches to connect them with health-promoting properties. Table S1 (Supporting information) shows examples of marine bioactive compounds with possible applications in cosmetics and food supplements, along with their biological activities.

4.1. Cosmetics

Over the years, as life expectancy has increased and lifestyles have improved, more attention has been paid to the appearance of the body, particularly the skin and hair. As a result, consumers have become more aware of the importance of using anti-aging cosmetics as part of their daily routine [56]. This demand for cosmetic products has driven significant growth in the global cosmetics market. According to Sharma *et al*. [57], the global cosmetic market is projected to reach a value of 463.5 billion dollars by 2027, reflecting the continued and increasing use of cosmetic products by both men and women worldwide. In particular, the demand for anti-aging products has improved due to demographic aging. People are seeking to prevent wrinkles, age spots, uneven skin tone, hyperpigmentation, and dry skin, leading to the development of innovative cosmetics and contributing to industry growth [58].

The following subsections present studies on bioactive compounds with biological activities of potential interest for cosmetic applications.

4.1.1. Antioxidant and anti-aging

Oxidation is a natural result of the body's metabolic processes, producing various free radicals and reactive oxygen species (ROS). Oxidative stress arises when the body is unable to effectively utilize its internal antioxidant enzyme systems and cellular antioxidants to remove excess free radicals and ROS, ultimately contributing to visible signs of skin aging (wrinkles, dryness, reduced elasticity) [59]. The studies outlined below emphasize the potential benefits of marine bioactive compounds for antioxidant and anti-aging applications.

For instance, Lee *et al*. investigated the effects of a topical hydrolyzed collagen tripeptide on the facial skin. In this study, it was conducted a clinical trial in 22 Asian women with noticeable periorbital and glabellar wrinkles, with an average age of 47.1 years, who applied a hydrolyzed collagen tripeptide ampoule twice a day. After 4 weeks, there was a significant reduction in mean periorbital skin roughness from 20.77 ± 3.51 μm to 19.24 ± 3.52 μm ($P < 0.001$), and the mean glabellar skin roughness also decreased significantly from 21.40 ± 3.09 μm to 20.21 ± 2.83 μm ($P < 0.001$). Additionally, the maximum periorbital skin roughness decreased from 191.11 ± 32.58 μm to 182.01 ± 33.63 μm ($P < 0.001$), and the maximum glabellar skin roughness decreased from 169.92 ± 21.57 μm to 159.76 ± 21.58 μm ($P < 0.001$). The mean initial depressed depth of periorbital wrinkles was 0.06 ± 0.01 mm, which improved significantly to 0.05 ± 0.01 mm ($P < 0.001$). Moreover, there was a significant increase in the skin density from 55.66 ± 7.61 to 59.67 ± 7.84 ($P < 0.001$), while the skin surface elasticity increased from 0.81 ± 0.03 to 0.83 ± 0.03 ($P < 0.001$). Furthermore, the maximum collagen strength significantly increased from 68.02 ± 5.48 to 70.24 ± 5.14 ($P < 0.001$). The researchers suggested that the topical hydrolyzed collagen tripeptide may improve clinical aging phenotypes by inhibiting glycation and oxidative stress, delaying cellular aging [60].

The antioxidant and moisturizing properties of astaxanthin were examined in three different skin lotions containing varying concentrations of the compound (1%, 3%, and 5%). The results indicated that all three formulations significantly increased skin moisture with 95% confidence after 4 weeks of testing. Additionally, the 2,2-diphenyl-1-pyridylohydrazinyl (DPPH) test demonstrated the strong antioxidant activity of astaxanthin, with half-maximal inhibitory concentration (IC_{50}) values of 98.961 ppm for the 1% formula, 88.921 ppm for the 3% formula, and 87.571 ppm for the 5% formula [61].

The potential use of fucoxanthin in cosmetic products was also demonstrated. In a study by Kang *et al*., a 0.03% fucoxanthin concentrate cream was applied twice daily on 21 women (aged from 35 to 50) for 8 weeks. The results showed a significant reduction in periorbital wrinkles after 8 weeks and improved skin moisture and elasticity after 4 weeks, while no adverse effects were observed. The researchers attributed these positive outcomes to the fucoxanthin cream's ability to enhance procollagen synthesis in fibroblasts and reduce the expression of certain enzymes responsible for degrading dermal fibers [62].

In a study by Kawada *et al*., 30 women applied a cosmetic containing 4% of niacinamide in their facial wrinkles for 8 weeks. The treatment resulted in marked and moderate improvement in 64% of the participants, with significant differences compared to the control ($P < 0.001$). Wrinkle grades in the treated area were significantly reduced compared to the pre-treatment area ($P < 0.001$) and the control ($P < 0.001$). Moreover, the Ra value in the treated was significantly reduced compared to the pre-treatment area ($P < 0.01$) and the control ($P < 0.05$). Only one participant discontinued the study due to minimal irritation [63].

In a study involving fifty female volunteers aged from 30 to 65, a 20% vitamin C serum was applied to one side of their face for 8 weeks. The volunteers also used their regular facial skin products during this period. Dermatological assessments were conducted on both the treated and untreated sides, after 4 and 8 weeks. The results indicated that the treated side showed significant improvements in melanin index and elasticity compared to the untreated side after 8 weeks ($P < 0.0001$). Skin radiance also improved significantly after 4 and 8 weeks ($P = 0.02$). However, there were no significant changes in skin moisture or transepidermal water loss (TEWL) between the treated and untreated sides. Skin texture assessments revealed significant improvements in smoothness, scaliness, and wrinkles after 4 and 8 weeks (all $P < 0.0001$), but increased roughness was observed on the treated side after 8 weeks. The serum was well tolerated, with no adverse reactions, such as redness, swelling, dryness, itching, or burning. Mild adverse reactions reported were tingling and tightness. It was concluded that

the vitamin C serum has anti-aging and brightening effects on the skin [64].

Another important vitamin for the skin is vitamin B5 (panthenol), which helps prevent dehydration and loss of moisture. A study conducted by Stettler *et al*. compared the skin moisturization and barrier restoration potential of a topical panthenol-containing emollient in healthy subjects. During the study, 23 volunteers were exposed to a 0.5 % sodium dodecyl sulfate solution in one area, while leaving another unchallenged, and then treated with panthenol for 3 weeks. Throughout the study, measurements were taken for TEWL, skin hydration, and intercellular lipid lamellae organization. The results indicated that the panthenol-containing emollient led to a more significant reduction in TEWL compared to the control (-168.36 *vs.* $-123.38\,g\,m^{-2}\,h^{-1}$, $P = 0.023$). Additionally, the emollient showed statistically significant improvements in stratum corneum hydration and an increase in intercellular lipid lamellae length from baseline (day 22: 120.61 *vs.* 35.85 nm/1000 nm^2, $P < 0.001$). Importantly, the treatment did not originate adverse effects on skin microflora [65].

4.1.2. Sun protection and light defense

Skin photoaging is the result of extended exposure to sunlight, leading to aging changes in the skin. Ultraviolet (UV) can penetrate the skin's epidermis, reaching the basement membrane and causing issues like sunburn and premature aging due to its short wavelength and high energy. Additionally, UV light can accelerate skin aging by activating matrix metalloproteinases (MMP), which are enzymes that break down important elements of the extracellular matrix, including elastin, collagen, and fibronectin [59]. Marine bioactive compounds are gaining attention for their potential in photoprotection, as highlighted in the studies below.

Recent research has shown that PBPs have photoprotective effects. For example, Jang *et al.* investigated the effects of spirulina-derived C-phycocyanin against UVB radiation on keratinocytes. The researchers first assessed the cytotoxicity of C-phycocyanin at different concentrations (5, 10, 20, 40 and 80 μg/mL) and found that the compound was not toxic. In addition, at concentrations of 40 and 80 μg/mL, the compound was found to stimulate cell growth by 11.4 % and 12.2 %, respectively (both $P < 0.001$). Subsequently, the protective effects of C-phycocyanin on cells exposed to damaging UVB radiation were tested. It was observed that untreated cells subjected to UVB irradiation experienced a decrease in viability to 50.8 %, compared to the negative control group. However, when the cells were pre-treated with 80 μg/mL of C-phycocyanin, their viability increased by 29.5 % ($P < 0.001$), suggesting that this PBP offers protection against UVB-induced cell damage. In addition, researchers studied the impact of C-phycocyanin on the release of matrix metalloproteinases (MMP-1 (collagensase-1) and MMP-9 (gelatinase-B)) induced by UVB, and observed a progressive inhibition of the MMP-1 and MMP-9 release with increasing concentrations of C-phycocyanin, compared to the UVB-exposed group. The concentration of MMP-1 was 10 times higher and that of MMP-9 was 18 times higher in the UVB-exposed group, compared to the negative controls. However, in the group treated with C-phycocyanin (80 μg/mL), the levels of MMP-1 and MMP-9 were significantly reduced by 73.8 % and 78.7 %, respectively (both $P < 0.001$) [66].

In the research conducted by Su *et al*., it was investigated the potential of a fucoidan extract as a protective agent against UVB-induced skin damage and ROS excessive production and cellular damage. The study involved *in vitro* experiments using human keratinocytes and *in vivo* tests using a zebrafish model. Before evaluating the extract's protective effect on keratinocytes, toxicologic tests were conducted to evaluate its safety. The results indicated that the fucoidan extract exhibited no cytotoxic effects (the viability was above 90 %), while showed positive effects at a concentration of 50 μg/mL. Additionally, the extract demonstrated a protective effect against UVB-induced damage, as indicated by decreased intracellular ROS levels ($P < 0.01$) and increased cell viability ($P < 0.01$) in a dose-dependent manner. In the *in vivo* tests, zebrafish were pre-treated with different fucoidan extract concentrations and subsequently exposed to UVB radiation. The results showed that the zebrafish treated showed a dose-dependent reduction in the production of ROS before being exposed to UVB radiation. This result indicates that ROS levels decreased by 237.64 % in zebrafish treated with 100 μg/mL of fucoidan extract ($P < 0.01$). These findings suggest the potential of fucoidan for use in cosmetic products as a natural and effective anti-UVB agent [67].

Wang *et al*. investigated the impact of dieckol on UVB-induced skin wrinkling in human dermal fibroblasts. The study assessed the levels of collagen synthesis and the activity of the MMP-collagenase. The findings revealed that dieckol effectively inhibited collagenase in a dosage-dependent manner. At concentrations of 12.5, 25, and 50 μmol/L, the collagenase inhibitory rates were 53.94 %, 59.82 %, and 64.95 %, respectively. The study also demonstrated that the collagen synthesis level in UVB-irradiated cells was significantly reduced compared to non-irradiated cells. However, in cells treated with dieckol, collagen synthesis levels increased in a dosage-dependent manner. Additionally, dieckol-treated cells showed reduced intracellular ROS levels (268.56 %, 245.75 %, and 223.80.5 %), compared to UVB-irradiated cells (294.45 %). The viability of UVB-irradiated human dermal fibroblasts was notably restored in the presence of dieckol (54.64 % *vs*. 62.19 %, 71.96 %, and 78.74 %, all $P < 0.01$). These results suggest that dieckol exhibits *in vitro* photoprotective effects, presenting a promising potential for its use as an ingredient in the cosmetics industry [68].

Vitamin E is the skin's most predominant antioxidant and is found in higher concentrations in the epidermis than in the dermis, particularly in areas exposed to the sun, such as the cheeks and forehead [69]. Researches has shown a connection between vitamin E and exposure to UV radiation, being reported that applying vitamin E to the skin provides protection against skin carcinogenesis [70]. In a study involving UV-irradiated mice, it was demonstrated that skin cancer induced by UV radiation was reduced from 81 % to 42 % after the application of 25 mg of vitamin E three times per week for three weeks before UV irradiation [70]. Additionally, the treatment with vitamin E was shown to decrease erythema by 40 %–55 % and skin sensitivity ($P < 0.07$) caused by UV exposure in mice [71].

4.1.3. Whitening effects and spot fading

Melanin is the primary factor responsible for pigmentation in human skin. One of the key approaches to reducing melanin production is by inhibiting the activity of the enzyme tyrosinase. This enzyme plays a crucial role in the biosynthesis of melanin and serves as an important marker for the differentiation and maturation of melanocytes. Many skin whitening agents work by decreasing melanin production through their role as competitive inhibitors of tyrosinase. Common active ingredients found in these whitening products include hydroquinone, kojic acid, and mercury compounds. However, prolonged use of these substances can lead to various negative effects, including hypercortisolism, high blood pressure, skin thinning, and potentially cancer [59]. Therefore, it is essential to explore new alternatives, and bioactive compounds derived from marine sources may offer promising options.

In another study, Baarathi *et al.* demonstrated that astaxanthin (20 mg/mL) is a strong tyrosinase inhibitor, with IC_{50} values of 30.37 and 41.02 μg/mL at 60- and 120-min intervals, respectively. Comparatively, ascorbic acid (vitamin C), a known tyrosinase inhibitor, had IC_{50} values of 34.05 μg/mL at 60 min, showing promising results for using astaxanthin to reduce hyperpigmentation [72].

In a study on the treatment of melasma, 11 women with the condition used a 0.05 % lycopene cream twice a day for 12 weeks. The results showed a significant reduction in the size and severity of melasma from 6.59 ± 3.47 to 5.97 ± 3.83 ($P < 0.05$). The group using the lycopene cream showed a much greater improvement in the melasma area and severity index score, as well as the rate of skin discoloration (0.53 ± 0.47 and 3.73 ± 1.90, respectively), compared to the placebo group (0.14 ± 0.20 and 0.91 ± 0.07, respectively; $P < 0.05$) [73].

Niacinamide (vitamin B3) has been found to be effective in improving hyperpigmented spots on ageing skin. In a clinical trial, the effectiveness of niacinamide was investigated in 79 Japanese women with various types of brown hyperpigmentation. The trial involved a double-blinded, randomized, split-face design where group 1 applied a moisturizer containing 5 % of niacinamide and group 2 applied a moisturizer containing 2 % of niacinamide. Both groups also used a vehicle moisturizer. The application was done twice a day for 8 weeks. Results showed that after 4 ($P < 0.05$) or 8 ($P < 0.01$) weeks, the areas of the face treated with the 5 % niacinamide-containing moisturizer exhibited a greater reduction in hyperpigmented spots compared to the areas treated with the vehicle moisturizer. However, the 2 % niacinamide moisturizer did not show a significant effect in comparison to the vehicle moisturizer. Furthermore, over the regression period, the effectiveness of the 5 % niacinamide moisturizer gradually decreased and became statistically similar to the vehicle moisturizer after 42 weeks. This suggests that the skin depigmenting effects of topical niacinamide on humans are dose-dependent and reversible [74].

4.1.4. Wound healing and skin regeneration

The process of healing a skin wound demonstrates a remarkable cellular mechanism. It involves the collaboration of various cells, growth factors, and cytokines to effectively close the injury. The challenges associated with wounds often stem from the treatment and management approaches that hinder the repair process, rather than the restoration of tissue integrity itself. Consequently, numerous studies are focused on developing more effective wound therapies aimed at decreasing healthcare expenses, offering long-term relief, and promoting successful scar healing [75].

PUFAs have been found to be beneficial in treating cutaneous wounds, including second-degree burns, chronic wounds, and ulcers. Research suggests that PUFAs play a crucial role in cell membrane formation, anabolic processes during skin tissue regeneration, and can also modify or amplify local inflammatory responses at wound sites, thereby expediting the healing process [76]. For instance, researchers examined the effects of applying docosahexaenoic acid to wounds on rats over a 15-day period. The results showed that the group treated with docosahexaenoic acid experienced significantly faster wound healing, compared to the control group. By the 15^{th} day, the wounds in the docosahexaenoic acid group had completely closed, while the control group still had 30 % of the wound remaining unhealed (99.7 % *vs*. 71.2 % closure on day 15, $P < 0.01$). These findings suggest that docosahexaenoic acid may be involved in the activation of anti-inflammatory genes [77].

In another study, Wu *et al*. evaluated the benefits of using a topical treatment containing linolenic acid for improving wound healing and skin quality after fractionated ablative laser resurfacing of the face. The procedure was applied to 34 volunteers that were randomly assigned to either use the topical linolenic acid (24 participants) or a control regimen (10 participants) post-procedure. The outcomes revealed that the application of topical linolenic acid led to a notable reduction in edema, on day 3 ($P = 0.04$), and itching, on days 1 and 3 ($P = 0.03$ and 0.04). Furthermore, the linolenic acid regimen resulted in significant improvements in wrinkling and elastosis by day 14 [78].

4.1.5. Other relevant bioactivities

Chitin and its derivative chitosan have gained significant attention as biopolymers, particularly in industries where safety is a top priority, such as the cosmetic industry. For example, they have been found to have the capacity to stimulate hair growth. In a study conducted by Azuma *et al*., the effects of chitosan and surface-deacetylated chitin nanofibrils on hair growth were investigated. For the experiments, human follicle dermal papilla cells were cultured *in vitro* with 0.01 %, 0.1 %, or 1 % concentrations of chitosan or surface-deacetylated chitin nanofibrils, and the growth factors levels were measured. For the *in vivo* experiments, mice were shaved on their dorsal region and 150 µL of the substances were applied to the area, following hair length measurements and histological studies. The findings revealed that chitosan and surface-deacetylated chitin nanofibrils were able to enhance cell proliferation by day 3 of treatment initiation ($P < 0.01$ for the 0.01 % and 0.1 % chitosan groups and the 1 % surface-deacetylated chitin nanofibrils group; $P < 0.05$ for the 1 % chitosan and 0.1 % surface-deacetylated chitin nanofibrils groups). Additionally, the 1 % chitosan group exhibited a remarkable increase in the growth factor production compared to the control group ($P < 0.05$). Moreover, in the *in vivo* study the application of chitosan and surface-deacetylated chitin nanofibrils was linked with enhanced hair growth (both $P < 0.01$). Overall, the results of this study indicate that chitosan and surface-deacetylated chitin nanofibrils have the potential to promote hair growth and could be considered for counteracting the hair loss [79].

Although the applications of alginate are diverse, it is mainly used in cosmetics as a gelling agent and humectant. Recently, other applications of alginate have been discovered. Sayin *et al.* reported that alginate extracted from *Sargassum vulgare* can serve as a natural preservative in cosmetic products. The researchers compared the antimicrobial effect of natural alginate with a commercially used herbal 705 preservative containing glyceryl caprylate and glyceryl undecylenate and found that the alginate from *Sargassum vulgare* (2.55×10^{-7} CFU/g) demonstrated faster antimicrobial activity against *Staphylococcus aureus,* when compared to the herbal 705 preservative (3.5×10^{-8} CFU/g). Furthermore, after 7 and 28 days, it was observed significantly lower microbial counts for the alginate (3.00×10^{-3} and <10 CFU/g, respectively) compared to the herbal 705 preservative [80].

Cellulite, also known as orange-peel or dimpled skin, is a common condition affecting 80 %–90 % of women [41]. Studies have suggested that retinol can help improve this condition by increasing collagen synthesis. In a 6-month study involving 20 women with cellulite, where a 0.3 % retinol cream was applied twice daily to one side of their thighs, the results showed that 13 out of 19 participants rated the retinol-treated side as showing more improvement, with 7 reporting positive effects. The study also demonstrated enhanced skin condition and a decrease in the density of hypoechogenic areas from 53 % to 18 %. Additionally, measurements (from 1.44 mm to 1.60 mm) showed significant increases in blood flow and skin thickness on the retinol-treated sides [81].

4.2. Food supplements

The food industry faces the challenge of meeting consumer demand for products that are both delicious and convenient, as well as healthy and nutritious. As a result, this industry has been working on new approaches, such as developing food supplements with more nutraceutical value, *i.e*., products that can provide health benefits [28]. These products, also known as functional foods, are expected to push the global nutraceutical products market to reach $991.09 billion by 2030. Nutraceuticals encompass food supplements, natural products, and functional foods, which can be consumed in various forms, including capsules, gummies, tablets,

powders, or liquids [82]. Normally, they contain one or more ingredients that provide added nutritional value to the diet.

Bioactive marine compounds possess biological properties that are important for human health and nutrition, making them suitable for use in food supplements. The following subsections highlight studies on compounds with biological activities that may be of particular interest for such applications.

4.2.1. Weight management and fat reduction

Being overweight and/or obese is a lifestyle-related issue that can lead to various health problems and are linked to many chronic diseases, such as cancers, diabetes, and heart disease. The World Health Organization (WHO) has projected that by 2030, 30 % of global deaths will be related to lifestyle diseases, which can be prevented through the proper identification and management of relevant risk factors and proactive behavioral policies [83]. Therefore, it is crucial to explore new methods for preventing these conditions, and incorporating marine bioactive compounds may be one viable option.

For instance, Huang *et al*. aimed to investigate the therapeutic effects of chitin on obesity induced by a high-fat diet. For the study, 72 rats were divided into 5 groups: normal control, high-fat diet, high-fat diet with low-dose chitin ($0.25\,g\,kg^{-1}\,d^{-1}$), high-fat diet with medium-dose chitin ($0.5\,g\,kg^{-1}\,d^{-1}$), and high-fat diet with high-dose chitin ($1\,g\,kg^{-1}\,d^{-1}$). The results revealed that after 4 weeks of treatment, the body weight of the low-dose chitin (419.5 ± 15.0 g) and medium-dose chitin (426.8 ± 11.3 g) groups significantly decreased, compared to the high-fat group (458.5 ± 19.6 g, $P < 0.05$). In contrast, the high-dose chitin group showed similar results to the high-fat group. Additionally, the low-dose and medium-dose chitin groups exhibited significant reductions in perirenal adipose tissue, periepididymal adipose tissue, total adipose tissue, and the adipose tissue index (all $P < 0.01$), while no significant differences in body adipose tissue data were observed between the high-dose chitin and high-fat groups. Furthermore, the treatment significantly reduced serum lipid levels, including total cholesterol, total glyceride, and low-density lipoprotein cholesterol, in the low-dose and medium-dose chitin groups (all $P < 0.01$) [84].

In another study, Guo *et al*. found that the consumption of sodium alginate (0.7 %) had notable metabolic benefits. The researchers evaluated the effects of both short-term and long-term intake of sodium alginate on food consumption and metabolic regulation through *in vitro* and *in vivo* experiments. The results showed that sodium alginate formed a gel in stomach conditions, which reduced the digestibility of dextrin, the release of glucose, and the rate of whey protein isolate hydrolysis *in vitro* (all $P < 0.05$). In the *in vivo* short-term feeding experiments, rats showed reduced food intake due to the formation of a gel mass in the stomach, potentially affecting stomach distension and prolonging gastric emptying time. The *in vivo* long-term feeding experiments revealed that sodium alginate intake led to reduced food intake, body weight ($P < 0.05$), and apparent protein digestibility ($P < 0.05$). Blood glucose levels were significantly lower ($P < 0.05$) in the group consuming sodium alginate, indicating impaired nutrient digestibility and reduced maximal glucose entry rate. However, the length of the small intestine increased ($P < 0.05$) in order to compensate for impaired nutrient absorption. These findings suggest the potential of sodium alginate for the treatment of metabolic syndrome and obesity in humans [85].

Other studies have reported anti-obesity activity for fucoxanthin. For example, Jeon *et al*. investigated the efficacy of an ethanol extract of fucoxanthin-rich seaweed for reducing body fat and combating obesity in mice. For the experiments, mice were supplemented with 2 different concentrations of fucoxanthin (1.43 % or 5.72 %) for 6 weeks, and showed significant reductions in body and abdominal white adipose tissue weights ($P < 0.05$), as well as decreased plasma and hepatic triglycerides ($P < 0.05$) and cholesterol concentrations, compared to the high-fat control group ($P < 0.05$). From these results it was suggested that fucoxanthin affects fecal lipids, fatty acid synthesis, and lipid absorption [86].

4.2.2. Anti-oxidant and anti-aging

Recently, there has been an increase in the availability of food supplements containing collagen, aiming to improve skin appearance and slow down the aging process. Bolke *et al*. conducted a study to investigate the impact of consuming ELASTEN® on aging and skin health. The drinkable ampoules contained a combination of 2.5 g of collagen peptides, 666 mg of acerola fruit extract, 80 mg of vitamin C, 3 mg of zinc, 2.3 mg of vitamin E, and 50 µg of biotin. The study involved 72 healthy women aged 35 and over, with half of the participants receiving the supplement and the other half receiving a placebo for a period of 12 weeks. The group that received the supplement was monitored for more 4 weeks without taking the product to assess the duration of the changes induced by the supplement. In parallel, the researchers evaluated the skin parameters of hydration, elasticity, roughness, and density. After 12 weeks, it was observed a significant increase in the mean skin hydration (by 28.0 %) in the group that received the supplement, compared to the placebo group (44.5 ± 4.4 *vs.* 36.6 ± 5.7, $P < 0.0001$). Furthermore, the group that received the supplement showed an increase in skin elasticity compared to the placebo group (0.81 ± 0.04 *vs.* 0.75 ± 0.06, $P < 0.0001$). Although there was a slight reduction (0.76 ± 0.07) after 16 weeks, the value did not drop to the initial level (0.69 ± 0.05). Additionally, the depth of wrinkles also decreased in the tested group (from 161.6 ± 11.4 µm to 118 ± 16.4 µm) compared to the placebo group (from 161.7 ± 13.0 µm to 151.4 ± 15.9 µm), making the relative difference 4 times higher in the tested group ($-26.8\,\% \pm 8.1\,\%$ *vs.* $-6.4\,\% \pm 5.8\,\%$, $P < 0.0001$). Although at the end of the trial the depth of wrinkles increased to 131.6 ± 21.9 µm, it still represents a significant difference ($-18.9\,\% \pm 9.9\,\%$) compared to the initial state ($P < 0.0001$). Additionally, the measurements indicated a highly significant increase in the thickness of the epidermis and the corresponding skin density in the tested group by $24.8\,\% \pm 16.8\,\%$ (from 35.7 ± 7.2 µm to 44.0 ± 7.6 µm, $P < 0.0001$). However, after discontinuing the use of the product the mean skin density decreased to 36.7 ± 6.9 µm, but remained significantly higher compared to the initial value ($P = 0.0008$). From the results of this study, the researchers suggested that the high similarity between the collagen peptides in ELASTEN® and human collagen may be a determining factor to the significant improvement in skin parameters [87].

Another study suggested that gelatin may offer health benefits, including antioxidant activity. Chen *et al*. investigated the effects of oral administration of gelatin peptides derived from Pacific cod on UV-induced skin damage in mice. The study involved 65 female mice divided into 5 groups: normal group, model group, positive control group (administered vitamin C), and 2 gelatin peptide groups (administered 100 and 500 mg/kg per day). All groups, except the normal group, were exposed to UV irradiation 3 times a week. The results revealed that UV irradiation caused changes in the skin structure of the mice in all groups except the normal group. However, the mice treated with gelatin peptides demonstrated a reduction in skin damage compared to the model group, with the skin tissue of the gelatin peptide-500 mg/kg group showing similar patterns to that of the normal group. Moreover, the study found that UV irradiation led to decreased activity of endogenous antioxidant enzymes, such as total superoxide dismutase, catalase, and glutathione peroxidase in the model group compared to the normal group ($P < 0.05$, $P < 0.01$, $P < 0.01$). Conversely, the gelatin peptide-500 mg/kg group exhibited significantly increased

enzyme activity, comparable to that of the model group ($P < 0.05$, $P < 0.05$, $P < 0.01$), and the values were similar to those of the normal group. From these results, it was concluded that gelatin peptides may mitigate UV-induced oxidative stress by preserving antioxidant defense capabilities *in vivo* [88].

PUFAs, especially omega-3, are also connected to positive effects on skin. Barcelos *et al*. conducted a study to investigate the effects of dietary fatty acids, specifically omega-3, on skin health. Male rats were divided in 2 groups: 1 group receiving no supplementation (control) and 1 group receiving fish oil supplementation ($3\,g\ kg^{-1}\ day^{-1}$) for 90 days. Parameters affected by atopic dermatitis, such as scratching, TEWL, skin hydration, and local blood flow were monitored at 30-day intervals. The results showed that the rats supplemented with omega-3-rich fish oil experienced a decrease in TEWL, improved skin hydration, and reduced itchiness (all $P < 0.05$). From these findings, the researchers proposed that consuming or supplementing with omega-3 PUFAs may support the skin barrier protection [89].

In another study, Ozuguz *et al*. investigated the link between vitamin E deficiency and acne, where the researchers assessed the plasma levels of vitamin E in 94 patients. For the experiments, the patients were divided into 2 groups: group 1 included those with mild to moderate disease, and group 2 consisted of patients with severe to very severe acne. The results showed that vitamin E levels were significantly lower ($P < 0.001$) in both groups, compared to the control group. Group 2 exhibited lower levels than group 1, indicating a negative association between acne severity and vitamin E levels [90].

Studies involving animal models and *in vitro* experiments have revealed that vitamin C plays a crucial role in brain function by protecting neurons from oxidative stress, thus potentially impacting mental health. Sim *et al*. conducted a study to explore the connection between vitamin C levels and vitality as well as psychological functions. Initially, they carried out a cross-sectional study among 214 healthy young adults (aged from 20 to 39) to analyze the link between serum vitamin C concentrations and vitality (including fatigue and attention) as well as mood status (stress, depression, positive and negative affect). Subsequently, they conducted a double-blind randomized controlled trial involving individuals with inadequate serum vitamin C concentrations (<50 μmol/L). The trial participants were randomly assigned to receive either 500 mg of vitamin C twice a day for 4 weeks ($n = 24$) or a placebo ($n = 22$), and the same parameters were assessed. The cross-sectional data indicated a positive association between the serum vitamin C concentration and the attention level ($P = 0.02$), while no significant associations were found with fatigue and mood variables. In the trial, vitamin C supplementation significantly increased attention ($P = 0.03$) and work absorption ($P = 0.03$), with an evident improvement in fatigue ($P = 0.06$) and comprehensive work engagement ($P = 0.07$), compared to the placebo. Although mood and serum concentrations of brain-derived neurotrophic factor were not impacted by vitamin C supplementation, individuals who received vitamin C performed better in attention capacity and processing speed tests, compared to the placebo group ($P = 0.04$). In conclusion, the researchers hypothesized that inadequate vitamin C levels may be linked to lower mental vitality, and supplementation with vitamin C can improve work motivation, attentional focus, and cognitive performance in tasks requiring sustained attention [91].

4.2.3. Cardiovascular protection

Cardiovascular diseases pose a significant global health challenge, accounting for nearly half of all fatalities worldwide [92]. Consequently, there is growing research into marine bioactive compounds and their potential benefits for cardiovascular protection.

For example, Yang *et al*. investigated the relation between the levels of omega-6 PUFAs and the development of cardiovascular disease. In this study, the researchers first assessed the fatty acid levels in the blood of 1835 individuals without cardiovascular disease (with an average age of 60.6 ± 10.5 years). During the 2-year study period, 424 participants developed cardiovascular diseases. The results showed a negative association between the total omega-6 PUFAs levels and the risk of developing cardiovascular disease, with a 48% reduction ($P < 0.001$). Moreover, they estimated that about 20.7% of cardiovascular disease cases could have been prevented if the plasma omega-6 PUFAs levels had been higher [93].

Another study reported that the results from a randomized clinical trial involving 388 patients revealed that 200 participants who received 500 μg of vitamin K daily over a period of 3 years experienced significantly less ($P = 0.03$) progression of coronary artery calcification. Additionally, individuals with coronary artery calcification at baseline showed a 6% reduction ($P = 0.04$) [94].

In the study performed by Blas-Valdivia *et al*. examined the cardioprotective effects of oral C-phycocyanin in animal models with acute myocardial infarction. This condition leads to myocardial cell death due to an imbalance between oxygen supply and demand. The study involved 30 male rats divided into 4 groups: (1) sham + vehicle (0.9% saline solution), (2) sham + C-phycocyanin ($50\,mg\ kg^{-1}\ day^{-1}$), (3) acute myocardial infarction + vehicle, and (4) acute myocardial infarction + C-phycocyanin. Acute myocardial infarction was induced using isoproterenol, and serum cardiac enzymes were measured. After 5 days, the animals were euthanized and their hearts were examined to assess oxidative stress, redox environment, and inflammation. The results revealed that C-phycocyanin treatment led to a 53% reduction in creatine kinase and a 60% reduction in the isoform (both $P < 0.05$). However, C-phycocyanin did not affect the elevation of serum aspartate aminotransferase but did lead to an 18%–25% reduction in alanine aminotransferase serum levels during the evaluation period ($P < 0.05$). Additionally, treatment with C-phycocyanin prevented a 57% elevation in lipid peroxidation, a 50% increase in reactive oxygen species, a 46% rise in nitrites, and a 41% increase in oxidized glutathione (all $P < 0.05$). Finally, C-phycocyanin also mitigated aberrant histological changes associated with myonecrosis, interstitial oedema, and inflammatory infiltration in the heart muscle induced by acute myocardial infarction [95].

4.2.4. Immune management

Yamada *et al*. investigated the effects of an oral quercetin supplement on allergic diseases. The study involved a randomized, placebo-controlled, double-blind parallel-group trial with 66 individuals (aged from 22 to 78) who had allergic symptoms related to pollinosis. The individuals were given either the test product (200 mg quercetin) or a control product (vehicle) daily for 4 weeks. The results revealed that the group taking the quercetin-containing supplement showed significant improvements in allergic symptoms, such as eye itching ($P = 0.02$), sneezing ($P = 0.04$), and sleeP disorders ($P = 0.01$) compared to the placebo group. In terms of safety, the test group had significantly lower scores (still in criterion range) for systolic blood pressure ($P = 0.003$), diastolic blood pressure ($P = 0.015$), and glucose levels ($P = 0.021$) compared to the placebo group. Additionally, the quality of life of these individuals significantly improved based on original questionnaires and visual analog scales. These findings suggest that oral intake of quercetin supplements may effectively reduce allergy symptoms associated with pollinosis [96].

Another study reported that taking astaxanthin resulted in significant improvements in asthma disease. Hwang *et al*. carried out a study to assess the inhibitory effect of astaxanthin on the airway inflammation in a mouse model of induced asthma. For the exper-

iments, mice were given with doses of 5, 10, and 50 mg/mL twice a day from day 23 to 27. The results showed that astaxanthin effectively reduced the respiratory system resistance ($P < 0.05$), elastance ($P < 0.05$), tissue damping ($P < 0.05$), and tissue elastance ($P < 0.01$). Furthermore, the astaxanthin treatment resulted in a reduction in the infiltration of inflammatory cells in the lungs ($P < 0.001$), decreased mucus production ($P < 0.01$), and mitigated lung fibrosis ($P < 0.05$) in the asthmatic mice. These findings indicate that astaxanthin could be used to support asthma treatment [97].

A recent study suggested that vitamin D supplementation may help prevent severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) infection among those at high risk of exposure. The study involved frontline healthcare workers from 4 hospitals who had tested negative for SARS-CoV-2. They were randomly given either 4000 IU of vitamin D (94 participants) or a placebo (98 participants) every day for 30 days. The results showed that the vitamin D group had a lower SARS-CoV-2 infection rate compared to the placebo group (6.4% *vs*. 24.5%, $P < 0.001$). Furthermore, the risk of acquiring SARS-CoV-2 infection was also lower in the vitamin D group [98].

4.2.5. Management of eye diseases

In a study carried out by Hui *et al*., the impact of vitamin B3 on the inner retinal function in individuals with glaucoma was investigated. Glaucoma is recognized as the primary cause of irreversible blindness globally and patients often exhibit low serum levels of vitamin B3. For the crossover, double-masked, randomized clinical trial, 57 participants diagnosed with and under treatment for glaucoma were selected from two tertiary care centers. The participants were assigned to receive either oral placebo or vitamin B3. The trial involved a sequence of 6 weeks of 1.5 g/day dosage, followed by 6 weeks of 3.0 g/day dosage, with a subsequent crossover without a washout period. Assessment of visual function was carried out using electroretinography and perimetry. The results showed that the amplitude of the photopic negative response improved by 14.8% ($P = 0.02$) in the vitamin B3-treated group, compared with 5.2% ($P = 0.27$) in the placebo group. Furthermore, the photopic negative response b-wave amplitude exhibited a 12.6% improvement ($P = 0.002$) with vitamin B3, whereas with placebo was 3.6% ($P = 0.30$). There was also a trend towards improvement in mean visual field deviation, with 27% of participants showing improvement with vitamin B3 and fewer (4%) showing deterioration compared to the placebo group ($P = 0.02$). From these results, it was concluded that vitamin B3 supplementation has the potential to improve inner retinal function in individuals with glaucoma, although further research is required to understand the implications of long-term vitamin B3 supplementation [99].

In another study, it was demonstrated that high plasma zeaxanthin concentrations are related to a reduced prevalence of age-related macular degeneration and to a potential reduction in the development of senile cataracts. These effects were attributed to the zeaxanthin's antioxidant properties, which protect retinal tissue, and block UV radiation. A study involving 4203 participants, aged from 50 to 85, who were at risk of developing late age-related macular degeneration, demonstrated that the administration of 2 mg of zeaxanthin over two years resulted in a hazard ratio of 0.90 ($P = 0.04$) for the onset of late age-related macular degeneration [100].

4.2.6. Other relevant bioactivities

In a recent study conducted by McBean *et al*., it was investigated whether oral fucoidan can improve adaptation to moderate exercise by improving muscle function and could be used as a supplement to improve athletic performance. For the experiments, mice were split into four groups: one receiving no treatment and no exercise ($n = 8$), one receiving fucoidan without exercise ($n = 10$), one receiving no treatment with exercise ($n = 10$), and one receiving fucoidan with exercise ($n = 10$). The mice were orally given fucoidan at a dose of 400 mg kg^{-1} day^{-1} for 4 weeks. The results demonstrated a significant increase in the size of muscle fibers in the extensor digitorum longus and soleus muscles in mice treated with fucoidan, accompanied by a notable increase in tibialis anterior muscle strength (all $P < 0.05$). However, there were no significant changes in grip strength or time to fatigue on the treadmill, and fucoidan or exercise did not impact the mass of the tibialis anterior, extensor digitorum longus, or soleus muscles. Overall, the study indicates that fucoidan increased muscle size and strength, regardless of whether the mice exercised, suggesting its positive impact on skeletal muscle physiology and its potential use in sports supplementation [101].

5. Conclusion

The growing concern for improving well-being and overall health, combined with environmental sustainability issues, has driven the discovery of new sources of natural compounds that are safe for human health. In this context, using marine bioactive compounds extracted directly from their natural sources appears to be a promising approach. In fact, by employing eco-friendly extraction techniques, it is possible to reduce environmental pressures and help industries transition toward a greener economy and a globally sustainable future. Although they are an improvement over traditional extraction methods, these techniques come with challenges such as high maintenance costs, scalability issues, thermal degradation, and inconsistencies in the extraction process.

Marine bioactive compounds are gaining increasing attention due to their beneficial properties, such as antioxidant, anti-inflammatory, sun protection, whitening, and weight management effects. These characteristics suggest promising applications in the cosmetics and food supplement industries. However, most published studies are based on *in vitro* experiments using mixtures of bioactive compounds, underscoring a lack of data on their safety for human use. In addition, regulatory frameworks lack standardized definitions. For example, the term "bioactive" is not officially defined by any recognized scientific authority. Regulatory requirements also vary significantly depending on the intended use of these compounds and differ across countries.

Therefore, future studies should focus on standardizing clinical study protocols and isolating individual bioactive compounds to better understand their specific functions and conduct further *in vivo* studies in both animals and humans. Thus, achieving global harmonization on safety and efficacy is essential for establishing regulatory standards.

Finally, it is important to note that, although marine organisms represent a promising source of bioactive compounds, some of these compounds have limited use due to challenges related to supply, availability, quality assurance, and regulation. Exploring innovative applications for these compounds, particularly through nanotechnology, holds promise for enhancing the stability of bioactive compounds, addressing their limitations, and expanding their industrial use.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Rita Favas: Writing – original draft, Investigation, Formal analysis, Conceptualization. **Marta Monteiro:** Writing – original draft. **Hugo Almeida:** Supervision. **Domingos Ferreira:** Supervision. **Andreia Filipa Peixoto:** Writing – review & editing, Supervision. **Ana Catarina Silva:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2025.111482.

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