Marine-Derived Biomolecules with Antioxidant Properties

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Marine sources contain several bioactive compounds with high therapeutic potential, such as remarkable antioxidant activity that can reduce oxidative stress related to the pathogenesis of neurodegenerative diseases. Indeed, there has been a growing interest in these natural sources, especially those resulting from the processing of marine organisms (i.e., marine bio-waste), to obtain natural antioxidants as an alternative to synthetic antioxidants in a sustainable approach to promote circularity by recovering and creating value from these bio-wastes.

Keywords: antioxidants ; marine bio-waste ; bioactive compounds

1. Introduction

In recent years, the average consumption of fish, shellfish, and crustaceans has increased significantly, as they can contribute positively to human health and well-being, when combined with a healthy lifestyle [1][2]. However, this increase in the consumption of marine organisms has led to the annual production of tens of millions of tons of solid waste resulting from their processing. Currently, the Food and Agriculture Organization of the United Nations (FAO) recognizes the environmental, social, and economic problems resulting from the landfilling of this waste [1][3][4]. To overcome this challenge, an innovative solution has been proposed, consisting of the recovery and valorization of waste resulting from the processing of marine organisms, as this bio-waste is a rich reservoir of various bio-functional components [2][5]. There are already many investigations that demonstrate the potential of using these products to obtain bioactive compounds with different activities (e.g., anticancer, antimicrobial, antioxidant, and immunomodulatory) that can be used to develop value-added products in the pharmaceutical industry for the treatment of different diseases [2][3][4][6][7]. For example, bioactive compounds that can be isolated from shrimp waste include the chito-oligosaccharides present in chitin or chitosan, omega-3, and astaxanthin. Salmon nasal cartilage is a valuable source of proteoglycans with anti-angiogenic activity. Fish skin is an important source of collagen, which can be hydrolyzed to bioactive peptides. Algae contain high amounts of phytonutrients, particularly those belonging to the gender *Chlorophyta*, *Rhodophyta*, and *Phaeophyta*, which are rich in dietary fibers, omega-3, β-carotene, astaxanthin, vitamin C, and other compounds beneficial to human health [3][8].

2. Marine Derived Biomolecules with Antioxidant Properties

The origin of the inflammatory events that trigger several diseases, such as cancer, cardiovascular diseases, diabetes, and neurodegenerative diseases, is related to oxidative stress resulting from the high production of ROS and RNS, which are not counterbalanced by the body's antioxidant defenses [9][10][11]. Thus, the understanding of oxidative stress mechanisms, as well as the discovery of new compounds with antioxidant properties, have been the focus of various investigations that have already demonstrated the existence of a strong relationship between the use of antioxidant compounds and the reduction of the risk of developing these diseases [9][12].

In recent years, the biotechnological industry has been searching for antioxidant compounds from natural sources to replace artificial antioxidants, such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), whose safety profiles are increasingly controversial as they have been associated with liver damage and carcinogenesis. In this context, natural antioxidant molecules extracted from marine bio-waste, in particular carotenoids, bioactive peptides, and polysaccharides, constitute promising alternatives to the synthetic antioxidants [5][9][10]. **Table 1** presents examples of antioxidant biomolecules from marine organisms, and their properties and potential therapeutic applications.

Table 1. Examples of antioxidant biomolecules from marine organisms.

Biomolecule	Natural Source	Therapeutic Properties and Potential	References
Astaxanthin	**Shrimp/crab shells *Haematococcus pluvialis***	**Antioxidant and anti-inflammatory properties. Prevention and treatment of cardiovascular and neurodegenerative diseases.**	**[9][13][14][15][16][17]**
Fucoxanthin	**Brown algae *Laminaria japonica***	**Antioxidant and anti-inflammatory properties. Prevention and treatment of neurodegenerative diseases.**	**[7][13][18]**
β-carotene	**Turban shell Microalga *Dunaliella salina***	**Antioxidant properties. Prevention of liver fibrosis, acute and chronic coronary syndrome, and neurodegenerative diseases. Protection against UV radiation.**	**[9][19][20][21][22]**
Collagen	**Cod skin**	**Antioxidant properties. Anti-aging.**	**[2][23][24]**
Gelatin	**Tuna (*Thunnus* spp.) Flying squid (*Ommastrephes batramii*)**	**Antioxidant and anti-proliferative properties. Prevention of cancer.**	**[23]**
Chitin	**Crustaceans Cuttlefish Squid pen**	**Antioxidant, anticancer, antimicrobial, and anticoagulant properties. Immune system boosting. Wound healing.**	**[25][26][27][28]**

2.1. Carotenoids

Carotenoids share a C40 isoprene structure, called a terpenoid, and are divided into carotenes, which consist only of hydrocarbons, and xanthophylls, which are oxygenated products of carotenes [4][7][9]. These lipophilic compounds of different colors (e.g., yellow, orange, and red) have been widely used in the pharmaceutical and biotech industries, mainly due to their antioxidant properties [7][13]. For instance, astaxanthin is a red xanthophyll predominantly isolated from the microalga *Haematococcus pluvialis*, which accumulates very high levels of this compound under stress conditions, such as high salinity, high temperature, and nitrogen deficiency. However, astaxanthin can also be extracted from marine bio-waste, including shrimps and crab shells, where it is responsible for their orange pigmentation [29][30]. Chemically, astaxanthin is a high lipophilic molecule with the IUPAC name 3,3′-dihydroxy-β-β-carotene-4,4′-dione, whose structure contains two rings with a hydroxyl group and a carbonyl group separated by an unsaturated chain of carbon–carbon double bonds. This specific configuration, namely polyene chain, confers to astaxanthin a powerful antioxidant activity in scavenging free radicals, being 40 and 100 times more effective as antioxidant than β-carotene and vitamin E, respectively [29][31][32][33][34]. For this reason, the use of astaxanthin has been highlighted in several investigations due to its valuable impact on human health, namely in the prevention of cancer and in reducing the risk of developing cardiovascular and neurodegenerative diseases [9][33][35].

β-carotene is the main carotenoid produced by the halotolerant microalgae *Dunaliella salina*, although it can also be found in turban shells [9][22]. This compound is recognized for its antioxidant activity, in particular, its great ability to eliminate ROS due to its structure with conjugated double bonds that allow accepting electrons of reactive species, transforming them into neutral species [9][36]. Several investigations have shown that, in addition to its antioxidant properties and potential in the prevention of neurodegenerative diseases, β-carotene has other benefits for human health, such as the prevention of liver fibrosis, acute and chronic coronary syndrome, and the protection of the skin against UV radiation [9][19][36].

2.2. Bioactive Peptides

Bioactive peptides are small proteins with various physiological functions, in particular antioxidant activity. Generally, these peptides contain 2 to 20 amino acid residues and have the ability to scavenge ROS, chelate metal ions, and inhibit lipid peroxidation [2][5][23].

In recent years, there has been much research focused on the use of bioactive peptides, obtained from the enzymatic hydrolysis of marine bio-waste, in the promotion of human health as well as the prevention of chronic diseases. In particular, collagen, a protein found in the structure of fish skin, bones, and scales, and its partially hydrolyzed form, gelatin, are rich in hydrophobic amino acids, which appear to have a high free radical scavenging capacity. Peptides derived from the gelatin of the skin of marine animals, such as flying squid (*Ommastrephes batramii*) and tuna (*Thunnus* spp.), have demonstrated high antioxidant activity, similar to that of the potent natural antioxidant α-tocopherol [2][23].

Collagen has gained great interest in the cosmetic industry, in anti-ageing creams, and in nutritional supplements for bone and cartilage regeneration, vascular and cardiac reconstruction, and skin substitutes [24].

2.3. Polysaccharides

Several studies have reported that polysaccharides derived from marine organism's exhibit antioxidant activity, suggesting that these compounds could be used to mitigate diseases mediated by oxidative stress, such as liver damage, diabetes, obesity, colitis, some types of cancer, and neurodegenerative diseases [10].

Among the different polysaccharides that can be extracted from marine organisms, chitin is the most exploited as it can be easily obtained from the exoskeletons of marine arthropods, such as crustaceans, cuttlefish, and squid. Through chemical or enzymatic processes of chitin, it is possible to obtain its derivative chitosan, which is of interest to the pharmaceutical industry due to its anticancer, antimicrobial, anticoagulant, immunological, and antioxidant properties that enable it to act in the prevention of various diseases, including neurodegenerative ones [25][37].

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