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RESEARCH MINIREVIEW

Application of Marine Biomaterials for Nutraceuticals and Functional Foods

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Abstract Recently, a great deal of interest has been paid by the consumers towards natural bioactive compounds as functional ingredients in the diets due to their various health beneficial effects. Hence, it can be suggested that bio-processed marine products are alternative sources for synthetic ingredients that can contribute to consumer's well-being, as a part of nutraceuticals and functional foods. The ultra filtration membrane bioreactor is a novel technology to bio-process marine products. This review presents an overview of bio-processing and perspectives of bio-processed marine products for use as nutraceuticals and functional foods.

Keywords: bioactive peptide, chitooligosaccharide derivative, sulfated polysaccharides, phlorotannin, lectin

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Introduction

The world's oceans cover more than 70% of our planet's surface. Marine biomaterials are rich sources of structurally diverse compounds with various biological activities. The importance of marine biomaterials as a source of novel bioactive substances is growing rapidly. Right now, more than 20,000 new compounds have been isolated from marine biomaterials; numbers of these naturally occurring derivatives are developed as potential candidates for pharmaceutical applications (1,2). With marine species comprising approximately one half of the total global biodiversity, the sea offers an enormous resource for novel compounds (3-6). Moreover, very different kinds of substances have been procured from marine biomaterials because when compared with the terrestrial environment, the marine environment gives marine microorganisms, unique genetic structures, and life habitats (7).

With the recent advent of biotechnology for deriving products from oceans, there is a need to find different ways to develop more suitable and sustainable process relative to earlier. It is evident that marine bioprocess engineering will play an important role in this development. The bio-processing of marine food products to develop novel functional ingredients has been previously reviewed (8,9). Recent studies have identified a number of bioactive compounds from marine foods as well as marine food processing byproducts using various bio-processing techniques mainly ultrafiltration membrane bioreactor system (10). Marine food products can be consumed to play a vital role in growth and development the body's structural integrity and regulation as well as other functional properties. Apart from that, marine food proteins have been used as essential raw materials in most industries but most of marine food sources are underutilized. Recently, both marine-derived food proteins and biopeptides have

potential in novel commercial trends, as they are widely commercialized in the food, beverage, pharmaceutical, and cosmetic industries, in addition, to other fields such as photography, textiles, leather, electronic, medicine, biotechnology, *etc* (11,12). The industrialists are eager to embrace a novel product if it can deliver what consumers want and at the same time; industry needs to balance its involvement against the perceived market potential for a new trend (3).

Moreover, consumer's demand for food products with functional ingredients has increased recently and this situation has underlined the need to guarantee the safety, traceability, authenticity, and health benefits of such products. Therefore, commercially available marine food products have also prompted newer challenges. The bioactive marine-derived biopeptides, collagen, gelatine, chitooligosaccharides derivatives (COS), sulfated polysaccharides (SPs), phlorotannins, sterols, carotenoides, and lectins have been isolated by bio-processing of various marine sources including marine invertebrates, fishes, and algae byproducts (13,14). They are potential candidates as functional ingredients for new commercial trends by industries. In this sense, this review presents an overview of membrane bio-processing of marine food products and their current status with future perspectives in the functional food industry.

Bio-processing of Marine Products by Membrane Bioreactor

There is a great potential in marine bio-process industry to convert and utilize most of marine food products and marine food byproducts as valuable functional products. Apparently, there has been an increasing interest on utilization of marine products and novel bio-processing technologies are developing for isolation of some bioactive substances from marine food products. Development of these functional ingredients involves certain bio-transformation processes through enzyme-mediated hydrolysis in batch reactors. Membrane bioreactor technology equipped with ultrafiltration membranes is recently emerging for the bio-processing and development of functional ingredients and considered as a potential method to utilize marine food products efficiently (8,15,16).

This system has the main advantage that the molecular weight distribution of the desired functional ingredient can be controlled by adoption of an appropriate ultrafiltration membrane (17,18). Enzymatic hydrolysis of marine food products allows preparation of functional ingredients such as bioactive peptides and chitooligosaccharides. The physico-chemical conditions of the reaction media, such as temperature, and pH of the reactant solution, must be adjusted in order to optimize the activity of the enzyme used. Proteolytic enzymes from microbes, plants, and animals can be used for the hydrolysis process of marine food products to develop bioactive peptides and chitooligosaccharide derivatives. Moreover, one of the most important factors of bioactive functional ingredients with desired functional properties is the molecular weight of the bioactive compound (19-21). Therefore, for the efficient recovery and to obtain bioactive functional ingredients with both a desired molecular size and functional property, a suitable method is the use of an ultrafiltration membrane system. In order to obtain functional peptides, it is a suitable method to use a three enzymes system for sequential enzymatic digestion. Moreover, it is possible to obtain serial enzymatic digestions in a system using a multi-step recycling membrane reactor combined with ultrafiltration membrane system to bio-processing and development of marine food derived bioactive peptides and chitooligosaccharide derivatives (19,22,23). This membrane bioreactor technology equipped with ultrafiltration membranes is recently emerging for the development of bioactive compounds and considered as a potential method to utilize marine food products as value added nutraceuticals with beneficial health effects.

Potential Functional Ingredients from Marine Products

The bio-processing of marine food products to improve the functional characteristics of marine food ingredients could be the way to novel food products to be used as functional foods and nutraceuticals. Some potential functional products from bio-processing of marine food sources are discussed below.

Lectins Lectins are carbohydrate binding proteins or glycoproteins that are highly specific for their sugar moieties, lectins are finding valuable commercial trends in the food and bio-medical industries (24-28). They are found in a variety of different species, ranging from prokaryotes to corals, algae, fungi, marine invertebrates, and vertebrates (29,30). They play a role in biological recognition phenomena involving cells and proteins. Moreover, oligosaccharides are present in the form of lectins in all cell walls mediating a variety of events such as inflammation, cell-cell recognition, immunological response, metastasis, and fertilization (31,32). In the food industry, calcium binding marine food-derived lectins can be incorporated in nutraceutical or functional food to prevent calcium deficiency. Moreover, some marine algae lectins can be developed as antibiotics against marine vibrios (33). These include members of the amino glycoside

family, such as streptomycin, gentamycin, tobramycin, netilmycin, and abekacin which are effective against aerobic gram negative bacilli and also *Staphylococcos aureus* and *Enterococcus* species (34). Anticancer drugs are usually extremely toxic, and kill malignant, and normal cells. Liu *et al*. (35) have developed a more potent therapeutic regimen for carcinoma by combining immunotherapy with chemotherapy from cuttlefish, *Sepiella maindroni,* and rochebruns, which is a popular sea food. Cuttlefish ink, the byproduct of marine product processing, is mainly composed of melanin and proteoglycan. Due to its antitumor, immunomodulatory, and haemostasia effects, cuttlefish ink is widely used in traditional Chinese medicine. The sulfated polysaccharides/glycoproteins are found to act as antitumor agents (36). More than 200 polysaccharides/ glycoconjugates have been isolated from *Ganoderma lucidum*, which is a well-known traditional Chinese medicine (37,38).

Bioactive peptides Components of proteins in marine foods are containing sequences of bioactive peptides, which could exert a physiological effect in the body. These short chains of amino acids are inactive within the sequence of the parent protein, but can be released during gastrointestinal digestion, food processing, or fermentation. Marine-derived bioactive peptides have been obtained widely by enzymatic hydrolysis of marine proteins (39). In fermented marine food sauces such as, blue mussel sauce and oyster sauce, enzymatic hydrolysis has already been done by microorganisms, and bioactive peptides can be purified without further hydrolysis. In addition, several bioactive peptides have been isolated from marine processing byproducts or wastes (8). Marine-derived bioactive peptides have been shown to possess many physiological functions, including antihypertensive or ACE inhibition (40), anticoagulant (41), and antimicrobial activities. Moreover, some of these bioactive peptides have identified to possess nutraceutical potentials that are beneficial in human health promotion (42) and recently the possible roles of food-derived bioactive peptides in reducing the risk of cardiovascular diseases has been reported (43). The use of marine-derived antioxidative peptides (Table 1) as natural antioxidants in functional foods is promising.

Chitooligosaccharide derivatives (COS) Chitin is the second most abundant biopolymer on earth after cellulose and one of the most abundant polysaccharide. It is a glycan of β (1→4)-linked *N*-acetylglucosamine units and it is widely distributed in crustaceans and insects as the protective exo-skeleton and cell walls of most fungi. Chitin, a partially deacetylated polymer of *N*-acetylglucosamine, is usually prepared from the shells of crabs and shrimps. Chitosan is prepared by alkaline deacetylation of chitin (54). COS are chitosan derivatives (polycationic polymers comprised principally of glucosamine units), and can be generated via either chemical or enzymatic hydrolysis of chitosan (55,56). Recently, COS have been the subject of increased attention in terms of their pharmaceutical and medicinal applications (15), due to their missing toxicity and high solubility as well as their positive physiological effects such as ACE enzyme inhibition (57), antioxidant (58), antimicrobial (59), anticancer (60), antidiabetic (61), hypocholesterolemic (62), hypoglycemic (63), anti-Alzheimer's (64), anticoagulant (65), properties, and adipogenesis inhibition (66).

Phlorotannins Phlorotannins are phenolic compounds formed by the polymerization of phloroglucinol or defined as 1,3,5-trihydroxybenzene monomer units and biosynthesized through the acetate-malonate pathway. They are highly hydrophilic components with a wide range of molecular sizes ranging between 126-650,000 Da (67). Marine brown algae and red algae accumulate a variety of phloroglucinol-based polyphenols, as phlorotannins could be used as functional foods with potential health effects. Among marine algae, *Ecklonia cava*; an edible brown algae is a

Table 1. Some antioxidative bioactive peptides from bio-processing of marine products

Amino acid sequence	Marine product
Arg-Pro-Asp-Phe-Pro-Leu-Glu-Pro-Pro-Tyr	Yellowfin sole (44)
Asn-His-Arg-Tyr-Asp-Arg	Horse mackerel (45)
Gly–Ala–Leu–Ala–Ala–His	Sardinelle (46)
Gly-Asn-Arg-Gly-Phe-Ala-Cys-Arg-His-Ala	Croaker (45)
Leu-Gly-Leu-Asn-Gly-Asp-Asp-Val-Asn	Conger eel (47)
Leu-Leu-Gly-Pro-Gly-Leu-Thr-Asn-His-Ala	Rotifer (48)
Leu-Lys-Glu-Glu-Leu-Glu-Asp-Leu-Leu-Glu-Lys-Glu-Glu	Oyster (49)
Phe-Asp-Ser-Gly-Pro-Ala-Gly-Val-Leu	Jumbo squid (50)
Phe-Gly-His-Pro-Tyr	Blue mussel (51)
Val-Glu-Cys-Tyr-Gly-Pro-Asn-Arg-Pro-Glu-Phe	Micro algae (52)
Val-Lys-Ala-Gly-Phe-Ala-Trp-Thr-Ala-Asn-Glu-Glu-Leu-Ser	Tuna (53)

Table 2. Phlorotannins and their potential health effects

Phlorotannin	Health effect
6,6'-Bieckol	Anti-HIV, anti-MMP (69, 77)
7-Phloroeckol	Skin protection (80)
Dieckol	Antidiabetic, anti-HIV, anti-MMP (73, 69, 78)
Dioxinodehydroeckol	Antiproliferative (74)
Eckol	Radioprotective (79)
Fucodiphloroethol G	Antiallergic (81)
Phlorofucofuroeckol A	Antiallergic (81)

rich source of phlorotannins than others (68). Phlorotannins have several health beneficial biological activities including, anti-HIV (69), anti-proliferative (70), anti-inflammatory (71), radioprotective (72), anti-diabetic (73), anti-Alzheimer's disease (acetyl- and butyryl- cholinesterase inhibitory) (74), antimicrobial (75), antihypertensive (76), and anti-matrix metalloproteinase activities (anti-MMP) (77,78). In addition, eckol, phlorofucofuroeckol A, dieckol, and 8,8'-bieckol have shown a potent inhibition of phospholipid peroxidation at 1 μM in a liposome system (79,80) and these phlorotannins have significant radical scavenging activities against superoxide and DPPH radicals effectively compare to ascorbic acid and α-tocopherol. Hence, phlorotannins can be used as potential antioxidants in the food industry (Table 2).

Sulfated polysaccharides (SPs) SPs are recognized to possess a number of biological activities including anti-coagulant, antiviral, and immuno-inflammatory activities that might find relevance in nutraceutical/functional food, cosmetic/cosmeceutical, and pharmaceutical applications (82). Many species of seaweed (marine macroalgae) have attracted special interest in traditional medicine because of their richness in SPs (83). Marine algae are the most important source of non-animal SPs and the chemical structure of these polymers varies according to the species of algae. The amount of SPs present is found to be differing according to the 3 major divisions of marine algae, green algae, red algae, and brown algae. The major SPs found in marine algae include fucoidan and laminarans of brown algae, carrageenan of red algae, and ulvan of green algae (84-86). In recent years, various SPs isolated from marine algae have attracted much attention in the fields of food, cosmetic, and pharmacology. Carrageenans, a family of SPs isolated from marine red algae, are widely used as food additives, such as emulsifiers, stabilizers, or thickeners (87). Ulvan displays several physiochemical and biological features of potential interest for food, pharmaceutical, agricultural, and chemical applications. Compared with other SPs, fucoidans are widely available commercially from various cheap sources; hence, more and more fucoidans have been investigated in recent years to develop drugs and functional foods. These chemically anionic SPs polymers are widespread not only in seaweeds but also occur in animals such as mammals and invertebrates. Bourgougnon and colleagues found that there was a significant annual variation in the composition and the *in vitro* anti-HIV-1 activity of a water-soluble sulfated glucuronogalactan from *Schizymenia dubyi* (88,89). For the therapeutic using of algal polysaccharides, it seems that high molecular weights often given their low bioavailability, It is may based on observations with heparin (90), that algal SPS will display some, albeit low, degree of oral bioavailability (91). It also emphasizes the importance of understanding the structural requirements for biological activity and whether low molecular weight derivatives, which are potentially more bioavailable, remain active.

Conclusion

Recent studies have provided evidence that marine derived functional ingredients play a vital role in human health and nutrition. The possibilities of designing new functional foods and nutraceuticals from marine products by ultrafiltration membrane bioreactor are promising. In addition, marine food processing byproducts like food proteins can be easily utilized for producing nutraceuticals and functional foods via membrane bio-processing. These evidences suggest that due to valuable biological functions with health beneficial effects, bio-processed marine-derived foods have potential as active ingredients for preparation of various functional foods and nutraceutical products. Furthermore, the wide range of biological activities associated with the natural compounds derived from marine food sources have potential to expand its health beneficial value not only in the food industry but also in the pharmaceutical and cosmeceutical industries.

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