CHAPTER ONE

Aquaculture and its by-products as a source of nutrients and bioactive compounds

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Abstract

Underutilized marine resources (e.g., algae, fish, and shellfish processing by-products), as sustainable alternatives to livestock protein and interesting sources of bioactive compounds, have attracted the attention of the researchers. Aquatic products processing industries are growing globally and producing huge amounts of by-products that often discarded as waste. However, recent studies pointed out that marine waste contains several valuable components including high-quality proteins, lipids, minerals, vitamins, enzymes, and bioactive compounds that can be used against cancer and some

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cardiovascular disorders. Besides, previously conducted studies on algae have shown the presence of some unique biologically active compounds and valuable proteins. Hence, this chapter points out recent advances in this area of research and discusses the importance of aquaculture and fish processing by-products as alternative sources of proteins and bioactive compounds.

1. Introduction

The current food supply system based on intensive agriculture has not only limited the number of plants and animal species in our diet but also contributed to the depletion of natural resources (Nadathur, Wanasundara, & Scanlin, 2016). About 37% of cultivated land worldwide is used for feed production to generate animal protein. Besides, the production of vegetable proteins requires less water, land, nitrogen, and fossil fuel than those of animal-derived protein. Therefore, sustainable strategies (e.g., obtaining of proteins from alternative sources and the creation of new high-value products from underutilized waste streams) have been proposed in order to reduce environmental footprint (Henchion, Hayes, Mullen, Fenelon, & Tiwari, 2017). There are several options of highly nutritious protein sources still not mass exploited (e.g., indigenous pulses and root crops, ancient grains, insects, lower organisms, marine algae or by-products from different industries) (Bleakley & Hayes, 2017; Hayes, 2018; Kim et al., 2019; Nadathur et al., 2016).

In addition to environmental concerns, consumers are increasingly interested in safe, nutritious, and healthy food products. Moreover, the excessive intake of proteins from terrestrial animals, linked to saturated fatty acids and cholesterol, is considered as a risk factor of certain chronic diseases development. On the one hand, the consumption of aquatic products is believed to have several healthy effects, and consequently, the production of different edible marine species through aquaculture techniques for human consumption has risen over the last years (FAO, 2018a), leading to high volumes generation of by-products from fish processing. On the other hand, healthy bioactive compounds from natural sources, including those of marine origin, have gained great importance in recent years. Marine environment is constituted by a great amount and biodiversity of plants, animals and microorganisms adapted to so varied environmental conditions that the substances they produce for survival exhibit a broad panel of interesting biological activities (de Vera et al., 2018; Herrero, Mendiola, Plaza, & Ibañez, 2012; Ibañez, Herrero, Mendiola, & Castro-Puyana, 2012). In this sense, several types of secondary metabolites and a large mixture of biogenesis metabolites have been isolated from marine organisms, as well as many biological activities (antimicrobial, antitumor, antidiabetic, anticoagulant, antioxidant, anti-inflammatory, antiviral, antimalarial, antitubercular, anti-aging antifouling, and antiprotozoal) with industrial and therapeutic potential have also been described (Alves et al., 2018).

It is estimated that by 2050 the world population will exceed 9 billion people (Tian, Bryksa, & Yada, 2016). This expected increase in the global population will be associated with a high demand for food products with high nutritional quality that can be produced in an environmentally friendly way. Therefore, achieving a healthy diet through sustainable foods will be one of the challenges for researchers and food producers in the next years. In this context, special attention is given to protein and bioactive compounds from both underutilized marine species and fish processing by-products. In this regard, this chapter describes the valuable compounds that might be obtained from algae and seafood processing by-products, highlighting their biological activities and to a lesser extent their potential applications.

2. Fish by-products

The amount of fish produced worldwide reaches around 171 million tons, of which 80 million tons are from aquaculture (Marc Antonyak, Lukey, & Cerione, 2018). In 2016, a great diversity of species was raised in aquaculture, among them, common carp (*Cyprinus carpio*) (8%), Nile tilapia (*Oreochromis niloticus*) (8%), bighead carp (*Hypophthalmichthys nobilis*) (7%), Catla (*Catla catla)* (6%), Atlantic salmon (*Salmo salar*) (4%), and rainbow trout (*Oncorhynchus mykiss*) (2%) were the major species produced (Marc Antonyak et al., 2018).

In 2015, fish accounted for about 17% of animal protein consumed by the global population (Marc Antonyak et al., 2018). Moreover, FAO reported that the fish consumption raised an average rate of about 1.5% per year, i.e., from 9.0kg in 1961 to 20.2kg in 2015 (in per capita terms) (Marc Antonyak et al., 2018). Moreover, seafood is a valuable source of bioactive compounds such as peptides, amino acids, omega-3 long-chain polyunsaturated fatty acids (PUFAs), vitamins (e.g., vitamins A and D) and minerals such as calcium, potassium, and zinc (Kundam, Acham, & Girgih, 2019; Marc Antonyak et al., 2018). The fish composition consists of 15–30% proteins, 0–25% fat, and 50–80% moisture depending on the species, age, gender, health, and harvesting season (Caldeira et al., 2018).

For example, white fish, such as cod and hake, contains around 20% protein, 80% water, 0.5–3% oil, minerals, vitamins, carbohydrates, and other compounds. On the other hand, oily fish, such as mackerel and salmon, contain 20% protein, 10–18% oil, and 62–70% water (Kundam et al., 2019). Among 20% and 80% of fish is considered as waste by the fish processing industry, depending on several parameters such as the fish type and the processing specifications (Caldeira et al., 2018).

This waste usually includes head, viscera, skin, bones, and scales with ranges of 9–12%, 12–18%, 1–3%, 9–15% and 5% of the whole fish weight, respectively (Villamil, Váquiro, & Solanilla, 2017). It should be noted that recent studies showed that such waste can be considered as a valuable by-product source of value-added compounds. Consequently, considerable attention has been paid in the nutrients and bioactive compounds present in fish by-products. These materials are considered as sustainable sources for pharmaceutical, nutraceutical and cosmeceutical industries (Kundam et al., 2019; Marc Antonyak et al., 2018).

2.1 Nutrients and bioactive compounds from fish by-products

Fish bioactive compounds are substances present in fish by-products with biological activity. These constituents are beneficial to human health (Kundam et al., 2019). These health benefits are accomplished through multiple biological activities, including antioxidant activity, hormones mediation, immune system enhancement and facilitation of substances transition through the digestive tract, butyric acid production in the colon (it favors acidification, which improves intestinal health), and absorption and/or dilution of substances in the gut (Kundam et al., 2019).

Thus, fish by-products are an effective source of bioactive compounds that may be used as nutritional supplements and provide medical and health benefits. Fig. 1 shows the main by-products from fish processing and some compounds obtained from them. Many studies have been conducted to extract bioactive compounds from different by-products. Some of these studies are listed in Table 1.

2.1.1 Proteins

Fish proteins are rich sources of essential (e.g., leucine and lysine) and non-essential amino acids (e.g., aspartic and glutamic acids) (Shahidi & Ambigaipalan, 2018). Protein-rich by-products include backbone, skin, head, viscera, and blood that may be used to produce collagen/gelatin and proteoglycan, bioactive peptides, protein hydrolysates, among others.

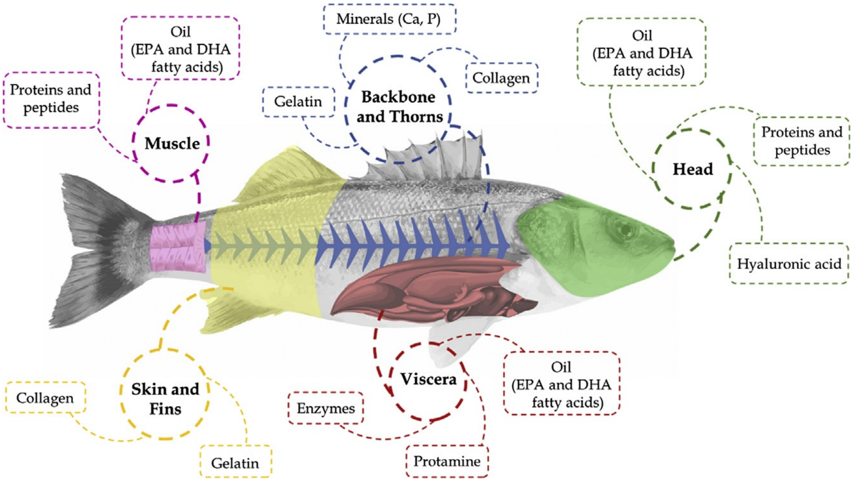

Fig. 1 Fish by-products and main compounds obtained from them. *Adapted from Marti-Quijal, F. J., Remize, F., Meca, G., Ferrer, E., Ruiz, M.-J., & Barba, F. J. (2020). Fermentation in fish and by-products processing: An overview of current research and future prospects.* Current Opinion in Food Science, 31, *9–16. https://doi.org/10.1016/j.cofs.2019.08.001*.

Up to 10–20% of total fish protein can be present in the fish by-products (Zamora-Sillero, Gharsallaoui, & Prentice, 2018). Both these essential amino acids and the bioactive peptides obtained from fish by-products have great potential as beneficial compounds for improving health (Hamed, Özogul, Özogul, & Regenstein, 2015).

2.1.1.1 Collagen and gelatin

Collagen is a fibrous and structural protein present in the extracellular space of fish and contributes to the physiological function of tissues in bones, tendons, skin, head, cartilage, and muscle (Raman & Gopakumar, 2018). It is the most abundant single protein present in fish, representing 25% of the total protein (Caldeira et al., 2018).

Collagen has a wide range of applications in the health-related sectors, specifically in cosmetics, pharmaceutical industry and medical care (including plastic surgery, orthopedics, ophthalmology, and dentistry) (Silva et al., 2014). In fact, there are many types of collagen however the most common form in fish by-products is Collagen type I and it is found in the connective tissues, skin, muscles, bone (Caldeira et al., 2018) and cornea (Raman & Gopakumar, 2018). Actually, collagen has been obtained from the skin of different fish types (Chi et al., 2014). Furthermore, fish collagen, following their extraction, may be further enzymatically hydrolyzed to release

Table 1 Examples of valuable compounds with biological activities that are extracted from the by-products of various marine species.

By-products	Source	Valuable compounds	Biological activities	References
Skin	Tilapia (*Oreochromis niloticus*)	Gelatin hydrolysate/ active peptides	ACE inhibitory simulated gastrointestinal digestion	Thuanthong, De Gobba, Sirinupong, Youravong, and Otte (2017)
	Chum salmon (*Oncorhynchus keta*)	Collagen peptide/ bioactive peptides	Antioxidant	Pei et al. (2010)
	Atlantic salmon (*Salmo salar* L.)	Collagen hydrolysates	Antihypertensive	Gu, Li, Liu, Yi, and Cai (2011)
	Salmon (*Oncorhynchus keta*)	Oligopeptides	Antidiabetic	Zhu, Peng, Liu, Zhang, and Li (2010)
	Seabass (*Lates calcarifer*)	Gelatin hydrolysate/ bioactive peptides	Antioxidant, immunomodulatory, antiproliferative	Sae-leaw, O'Callaghan, Benjakul, and O'Brien (2016)
		Gelatin hydrolysate/ bioactive peptides	Antioxidant	Mirzapour-Kouhdasht, Sabzipour, Taghizadeh, and Moosavi-Nasab (2019)
	Pacific cod (*Gadus macrocephalus*)	Gelatin hydrolysate/ bioactive peptides	ACE inhibitory	Ngo, Vo, Ryu, and Kim (2016)
	Bluefin leatherjacket (*Navodon septentrionalis*)	Bioactive peptides	Antioxidant	Chi, Wang, Hu, et al. (2015) and Chi, Wang, Wang, Zhang, and Deng (2015)
	Tilapia (*Oreochromis niloticus*)	Three bioactive peptides	Antidiabetic	Wang et al. (2015)
Scales	Tilapia (*Oreochromis niloticus*)	Gelatin hydrolysate/ bioactive peptide	ACE inhibitory	Zhang, Tu, Shen, and Dai (2019)

Head	Bluefin leatherjacket (*Navodon septentrionalis*)	Protein hydrolysate/ bioactive peptides	Antioxidant	Chi, Wang, Wang, et al. (2015)
	Bluefin tuna (*Thunnus thynnus*)	Protein hydrolysate	Antioxidant	Bougatef et al. (2012)
	Tilapia (*Oreochromis niloticus*)	Bioactive peptides	Antimicrobial	Robert et al. (2015)
	Sardinella (*Sardinella aurita*)	Four bioactive peptides	Antioxidant	Bougatef et al. (2010)
	Salmon (*Oncorhynchus keta*)	ω-3 PUFAs, EPA, and DHA	Nitric oxide (NO) inhibitory, tumor necrosis factor alpha (TNFα) inhibitory, and anti-inflammatory	Ahmad, Rudd, Kotiw, Liu, and Benkendorff (2019)
Bone	Indian mackerel (*Rastrelliger kanagurta*)	Protein hydrolysate/ bioactive peptides	Antioxidant	Sheriff, Sundaram, Ramamoorthy, and Ponnusamy (2014)
	Alaska pollack (*Theragra chalcogramma*)	Bioactive peptides	Ca-binding	Jung et al. (2006)
	Tuna (*Thunnus alalonga*)	Bioactive peptides	Antioxidant	Je, Qian, Byun, and Kim (2007)
	Hoki (*Johnius belengerii*)	Calcium peptide	Ca-binding	Kiml and Jung (2007)
		Bioactive peptide	Antioxidant	Kim, Je, and Kim (2007)
Liver	Atlantic cod (*Gadus Morhua* L.)	ω-3 PUFAs, EPA, and DHA	Antibacterial	Ilievska, Loftsson, Hjalmarsdottir, and Asgrimsdottir (2016)

Continued

Table 1 Examples of valuable compounds with biological activities that are extracted from the by-products of various marine species.—Cont'd

By-products	Source	Valuable compounds	Biological activities	References
Viscera	Rain bow trout (*Oncorhynchus mykiss*)	Protein hydrolysate/ bioactive peptides	Antibacterial	Wald, Schwarz, Rehbein, Bußmann, and Beermann (2016)
	Black pomfret (*Parastromateus niger*)	Protein hydrolysate/ bioactive peptides	Antioxidant	Jai Ganesh, Nazeer, and Sampath Kumar (2011)
	Black scabbardfish (*Aphanopus carbo*)	Protein hydrolysates/ bioactive peptides	Antioxidant	Batista, Ramos, Coutinho, Bandarra, and Nunes (2010)
	Sardinella (*Sardinella aurita*)	Protein hydrolysate/ bioactive peptides	Antioxidant	Souissi, Bougatef, Triki-Ellouz, and Nasri (2007)
	Smooth hound (*Mustelus mustelus*)	Protein hydrolysate/ bioactive peptides	Antioxidant, anti-ACE and antibacterial activities	Abdelhedi et al. (2016)
	Sardine (*Sardinops sagax*)	Omega-3 PUFAs, EPA, and DHA	Nitric oxide (NO) inhibitory, tumor necrosis factor alpha (TNFα) inhibitory, and anti-inflammatory	Ahmad et al. (2019)
	Red snapper (*Lutjanus campechanus*)	Protolithic enzyme (protease)	Protolithic activity	Sabtecha, Jayapriya, and Tamilselvi (2014)
	Seer fish (*Scomberomorus commerson*)			
	Great barracuda (*Sphyraena barracuda*)			

ACE, angiotensin-converting enzyme; PUFA, polyunsaturated fatty acids; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

physiologically active peptides. Especially, some collagen-derived peptides could exhibit interesting antioxidant activity (Chi et al., 2014), antimicrobial activity against different strains of bacteria (Ennaas, Hammami, Beaulieu, & Fliss, 2015), potent antihypertensive activity through ACE inhibitory properties (Alemán, Gómez-Guillén, & Montero, 2013).

Gelatin is a proteinaceous macromolecule obtained by thermal denaturation of collagen with a kinetic irreversible process. It shares some of the collagen's properties because of their similar composition. Thus, it can be used to improve the consistency, elasticity, and stability of foods, as well as, to produce edible and biodegradable films that increase the shelf life of food products (Caldeira et al., 2018). Moreover, it was also reported that fish gelatin had higher antioxidant activity those of synthetic ones (Ishak & Sarbon, 2018). Several studies extracted gelatin from fish by-products whereas fish skin was the main source of gelatin (Irwandi et al., 2009). It was extracted from the skin of seabass (*Lates calcarifer*) (Sae-leaw et al., 2016) and pacific cod (*G. macrocephalus*) (Ngo et al., 2016). Also, gelatin was extracted from the bones (black tilapia) (Zakaria, Hidayah, & Bakar, 2015) and scales bighead carp (*Hypophthalmichthys nobilis*) (Huang et al., 2017) and the head of mackerel (*Scomber scombrus)* (Khiari, Rico, & Ana Belen Martin-Diana, 2011).

2.1.1.2 Bioactive peptides

Fish bioactive peptides mainly consist of 2–20 amino acids, which are available in all parts of fish or incorporated in fish protein. However, these peptides are inactive within the native proteins and are activated after being released by digestion in vivo (proteolysis) or by enzymatic hydrolysis in vitro which is the best method to obtain protein hydrolysate or bioactive properties (Zamora-Sillero et al., 2018).

Moreover, active peptides extracted from fish by-products display multiple biological activities based on amino acid composition and sequence. They also play a great role in pharmaceutical and medical applications which result in the promotion of human health and may be helpful in the prevention and treatment of several chronic diseases. Thus, the obtained peptides can act as antioxidants, antidiabetic, immunomodulatory, antiproliferation and antimicrobial agents among others (Kim & Wijesekara, 2010).

Different fish species by-products are rich in bioactive peptides. Several studies have shown that head, viscera, skin, and backbone are good sources of protein hydrolysates. Seven antioxidant peptides were purified from the combined head and viscera of sardinella (*Sardinella aurita*); these peptides demonstrated high antioxidant activity, measured with DPPH radical scavenging assay (Bougatef et al., 2010). Tilapia by-product (head, frames, and viscera) hydrolysate had a high peptide content and a well-balanced amino acid profile; Robert et al. (2015) characterized the peptide fraction that yielded 1374 unique peptides and highlighted the high peptide diversity of the hydrolysate. Also, bioactive peptides, isolated from the head (Bougatef et al., 2012) and bone (Je et al., 2007) of tuna, have shown good antioxidant activities.

In addition to the antioxidant peptides that can be naturally present, peptides from protein hydrolysates have been reported to have bioactivity. In this context, bioactive peptides isolated from Atlantic salmon (*Salmo salar*) skin, bone and muscle extraction of gelatin hydrolysate have several biological activities such as antioxidant, ACE inhibitory and antidiabetic activity through DPP-IV inhibition (Neves et al., 2017).

Moreover, peptides hydrolysates were extracted by other authors from skin gelatin of seabass (*Lates calcarifer*) (Sae-leaw et al., 2016) and unicorn leatherjacket (Karnjanapratum, O'Callaghan, Benjakul, & O'Brien, 2016) having both immunomodulatory and antiproliferative activities. Moreover, Gu et al. (2011) isolated 11 peptides from salmon skin collagen after enzymatic hydrolysis, which showed an important ACE inhibitory activity and might be functional as useful foods and antihypertensive agents. In another study, Alaska Pollock collagen skin was used to generate iron-chelating peptides after being treated by commercial enzymes and one tripeptide contained amino acid sequence with high iron-chelating activity was detected (Guo et al., 2013).

2.1.2 Lipids

Fish oils containing omega-3 PUFAs and providing a myriad of health benefits have been produced from fish by-products (Soldo et al., 2019). They diminish the likelihood of vascular disease, cancer, diabetes and depression (Ivanovs & Blumberga, 2017). They also affect the immune system and ensure a proper neural development (Ivanovs & Blumberga, 2017). One of the main sources of omega-3 PUFAs (DHA and EPA) is fatty fish such as herring, sardine, salmon, and mackerel (Hamed et al., 2015; Kundam et al., 2019). The quantity and composition of these oils are highly dependent on the species, season and location of catching sites (Hamed et al., 2015).

In the whole, fish fatty acids (FA) are found in the subcutaneous tissue, viscera, muscle tissue, liver, mesenteric tissue, and head. Considering fish by-products, FA can be obtained mainly in the fish, skin, gut, head and bone from different fish species. For example, extraction of PUFAs was obtained from the bones of cod, blue whiting, salmon, trout, herring, mackerel and horse mackerel (Toppe, Albrektsen, Hope, & Aksnes, 2007) and from the viscera of tilapia *(Oreochromis niloticus*) (Shirahigue et al., 2016) and common carp (*Cyprinus carpio* L.) (Lisichkov, Kuvendziev, Zeković, & Marinkovski, 2014). Also, PUFA (omega-3) was extracted from mackerel skin (Sahena et al., 2010).

In one study, lipids from Australian sardine (*Sardinops sagax*) viscera and salmon (*Salmo salar*) head were extracted and large amounts of omega-3 PUFAs, EPA, and DHA were found (Ahmad et al., 2019).

In addition, it is well known that fish oils are a rich source of vitamins (A and D). Vitamin A is concentrated mostly in fish liver oils. Halibut, sardine, and cod contain vitamin A and D in their liver (Kundam et al., 2019), while herring, mackerel, trout and salmon have vitamin D in their tissues, also yellow tuna contain vitamin D in its bone (Talib & Zailani, 2017). These vitamins are commonly included in dietary supplements for several applications, such as bone health or antioxidant formulations (Harris, Morrow, Titgemeier, & Goldberg, 2017).

2.1.3 Minerals

Fishbones generate a huge amount of minerals. Inorganic minerals constitute approximately 60% of fish bones. Thus, fish bones are an important source of hydroxyapatite, calcium, phosphate, zinc, selenium, and iron (Bruno, Ekorong, Karkal, Cathrine, & Kudre, 2019). Minerals were isolated from various fish species. Seabass (*Lates calcarifer*) bone was a source of calcium and phosphor (Pal et al., 2017). Also, calcium, phosphor, magnesium, and strontium were isolated from the scale of *Catla catla* fish (Paul, Pal, Roy, & Bodhak, 2017). These minerals are important compounds in nutraceutical formulations destinated to improve health, mainly bone health but also cardiovascular or immunological diseases (Webb, 2015).

3. Shellfish by-products

After industrial processing, 75% of shellfish weight ends up as by-products (Hamed, Özogul, & Regenstein, 2016). These by-products are currently disposed of by incineration or returning them to the environment, which might lead to health and environmental concerns. So, it is a real challenge both industrially and ecologically the processing of this waste

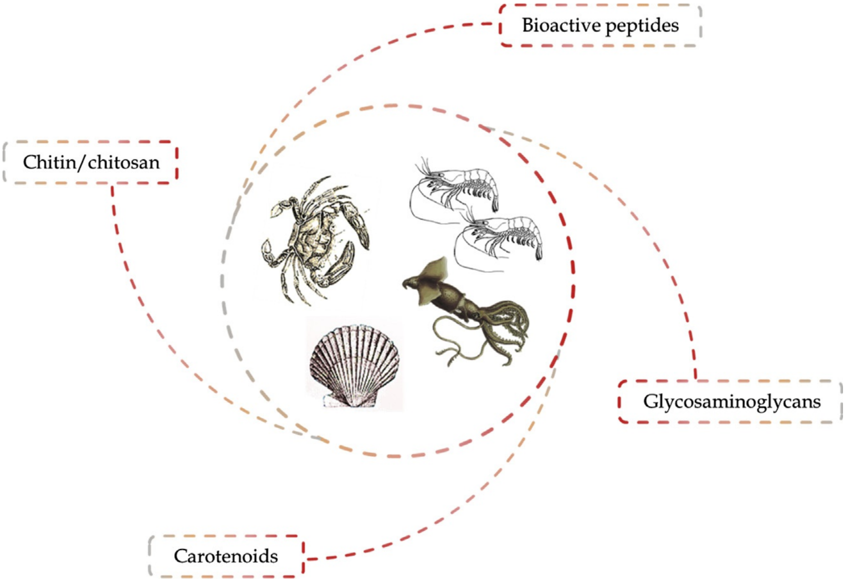

Fig. 2 Shellfish and main bioactive compounds obtained from them.

(Yadav et al., 2019). From these by-products, compounds with different biological properties of great interest can be obtained; as chitin/chitosan and its derivatives, carotenoids, glycosaminoglycans (GAG) or bioactive peptides, among others (Fig. 2). Therefore, a good approach for the utilization of this waste would reduce its environmental impact while revaluing.

3.1 Chitin/chitosan

Chitin is a biopolymer that can be obtained from shellfish waste, mainly from the exoskeletons of crustaceans. The shell of crustaceans is composed of 13–42% chitin, in addition to having a content of 30–50% mineral salts and 30–40% protein (Vo & Kim, 2014). It is the second most abundant polysaccharide in the world, after cellulose (Hamed et al., 2016). Both chitin and derivatives have great importance in biomedicine as they are biocompatible and non-potential toxic compounds. They are also renewable and biodegradable so their environmental impact is low.

Since chitin is a water-insoluble compound, its transformation into chitosan is often chosen. To obtain chitosan, a chemical or enzymatic process of deacetylation is followed. Chitosan is the name given to chitin when an acetyl group is removed, and different degrees of deacetylation can be achieved (Menon & Lele, 2015). When 50% of the acetylated form is exceeded with respect to the non-deacetylated form the compound becomes soluble in an acid solution (Shavandi, Hou, Carne, McConnell, & Bekhit, 2019). To be suitable for use, at least 70% deacetylation of chitosan is required (Menon & Lele, 2015).

Both chitin and chitosan have applications in the biomedical field. Among other uses, they are intended for the production of drugs, as it can be used to control their bioavailability (Nivethaa, Martin, Frank-Kamenetskaya, & Kalkura, 2020). It also has great applications in tissue engineering and wound healing (as a biomaterial) (De Masi et al., 2019; Jangid, Hada, & Rathore, 2019).

However, it is not only used as a carrier or excipient, but also for its own bioactivity. Among the most outstanding biological activities of chitin and its derivatives, it also has antitumor, antimicrobial, antioxidant, anticoagulant and even antifungal activity. The antitumor activity of these compounds has been demonstrated both in vivo and in vitro, mainly as consequence of a direct action of chitosan on tumor cells (Simonaitiene, Brink, Sipailiene, & Leskauskaite, 2015), by increasing the production of natural killer (Chatterjee, Chatterjee, & Guha, 2014; Lopez-Moya et al., 2015), or by inhibiting the angiogenesis of tumor cells and suppressing the tumor (Li et al., 2019). Its antimicrobial activity has also been demonstrated, and the mechanism of action depends entirely on the molecular weight of the polysaccharide. If the polysaccharide has a high molecular weight, it can bind to the bacterial cell wall and interfere with the ion exchange of the cell (Rahaiee, Shojaosadati, Hashemi, Moini, & Razavi, 2015; Salis et al., 2015). In contrast, polysaccharides with a small molecular weight penetrate the bacteria and interfere with the processes of DNA transcription and mRNA synthesis (Lindborg et al., 2015). It has been proven that the antimicrobial activity of chitosan is more intense in Gram-negative bacteria (Zeng et al., 2014).

Another remarkable biological activity of chitosan is its anticoagulant capacity. It has been reported that it has a slightly lower anticoagulant capacity than heparin, suggesting an alternative use (Arasukumar, Prabakaran, Gunalan, & Moovendhan, 2019; Yang et al., 2013).

On the other hand, chitosan displayed antioxidant properties. The antioxidant capacity depends on both its molecular weight and the degree of acetylation, since they also depend on the molecular weight, being more active a lower molecular weight and a higher degree of deacetylation (Anraku et al., 2018). The mechanism by which this is explained could be related to the chemical structure of the chitosan molecule, more specifically to the amino group present in C2 and the hydroxyl group present in C6 (Park, Koppula, & Kim, 2010). Due to its antioxidant capacity, chitosan has been proven effective in diseases in which oxidative stress has a great implication, such as metabolic syndrome or chronic renal failure (Anraku et al., 2018).

Finally, it has also been shown that chitin/chitosan has an antifungal activity that varies according to the fungus and plants that it contaminates depending on molecular weight and degree of acetylation (Verlee, Mincke, & Stevens, 2017). This could have great potential in the field of agriculture.

3.2 Carotenoids

Carotenoids are lipophilic compounds responsible for yellow and red colors in nature, both in plants and animals (Wade, Gabaudan, & Glencross, 2017). They can be divided into two groups: in the first one, the compounds are only composed of C and H atoms (e.g., carotene and xanthophylls), while in the second group the compounds have at least one functional group with O atoms (e.g., astaxanthin and lutein) (Shavandi et al., 2019). Specifically, the carotenoid responsible for the pink pigmentation of crustaceans is astaxanthin, so this carotenoid can be recovered from its by-products (Zhao et al., 2019).

For its extraction, the process consists a deproteinization and demineralization of the sample followed by carotenoid extraction through the application of organic solvents (Shavandi et al., 2019).

As for the biological activity of astaxanthin, its high antioxidant potential can be highlighted which is 500 times higher than that of vitamin E (Mao, Guo, Sun, & Xue, 2017), which makes it the largest natural antioxidant in the world. This high antioxidant power is due to the high presence of double bonds in its structure (Zhao et al., 2019). Thanks to its high antioxidant capacity, astaxanthin has different biological activities, such as antitumor activity, anti-inflammatory activity, prevention of cardiovascular diseases and atherosclerosis, liver protection and protection of the nervous system against diseases with a high component of oxidative stress (Amengual, 2019; Atalay, Kuku, & Tuna, 2019; Dutta, Mahalanobish, Saha, Ghosh, & Sil, 2019; Fakhri, Abbaszadeh, Dargahi, & Jorjani, 2018; Ni et al., 2015; Prameela et al., 2017).

3.3 Glycosaminoglycans (GAGs)

The GAGs are polysaccharides composed of repetitions of disaccharides linked by an oxygen atom. These disaccharides are generally formed by a unit of uronic acid and a unit of an amino sugar (Valcarcel, Novoa-Carballal, Pérez-Martín, Reis, & Vázquez, 2017). Within the GAG we find chondroitin sulfate, dermatan sulfate or heparin sulfate among others. These GAGs are part of the connective tissue, forming the extracellular matrix together with collagen and other structural molecules (Menon & Lele, 2015).

These molecules have various biological activities. One of the most important and also best known is anticoagulant activity. In this sense, several studies have obtained heparin from shellfish by-products, specifically from shrimp heads. However, its effectiveness as an anticoagulant is less than heparin from mammals (Brito et al., 2014; Chavante et al., 2014).

On the other hand, its anti-inflammatory activity is also remarkable. This property is also related to heparins. In fact, it has been seen that heparin obtained from shrimp has anti-inflammatory activity, reducing the activity of metalloproteinase 9, an enzyme involved in the inflammatory response (Brito et al., 2008).

Another widespread use of GAGs is their use in the field of regenerative medicine. The GAGs can bind to proteins and form proteoglycans. These proteoglycans can capture growth factors, which have great relevance in the process of differentiation and cellular function (Place, Evans, & Stevens, 2009). Therefore, this makes GAGs especially suitable for tissue regeneration. It was reported that hyaluronic acid and chondroitin sulfate are among the most important GAGs used in regenerative medicine (Salbach et al., 2012).

In addition to these very relevant applications, their use in other diseases, such as cancer, has been explored. In this sense, some studies have shown in vitro how sulfated GAGs, mainly dermatan sulfate and heparan sulfate, obtained from Norway lobster, have antiproliferative activity in human colon tumor cells (Sayari et al., 2016). This capacity can be explained by the high presence of sulfur in its composition.

Finally, they also have antiviral properties. Glycosaminoglycans obtained from squid have demonstrated their antiviral activity against viruses such as herpes simplex virus, T-cell leukemia virus or dengue (Valcarcel et al., 2017). It has also been seen that heparin sulfate groups can inhibit the human immunodeficiency virus (HIV) by electrostatic interaction with basic amino acids (Chen & Huang, 2018).

3.4 Bioactive peptides

Several articles have described different biological activities of peptides obtained from the by-products of shellfish. Bioactive peptides are amino acid sequences that are inactive when they are included in a protein but active when are released. They contain between 2 and 20 amino acids, and their bioactivity is based on the amino acid sequence and its length (Lorenzo et al., 2018). Specifically, peptides with antihypertensives (inhibiting angiotensin-converting enzyme), antioxidants, and antimicrobials have been obtained from shellfish by-products (Menon & Lele, 2015).

The antioxidant activity has been related to the presence of amino acids such as histidine, tyrosine, methionine, and cysteine in the peptide sequence. It is also related to other hydrophobic amino acids such as hydroxyproline, leucine, alanine, proline, glycine, valine and repetitive glycine-proline sequences (Neves, Harnedy, & FitzGerald, 2016). Suárez-Jiménez et al. (2019) have obtained peptides with antioxidant activity from hydrolysates of squid by-products. In this study, we observe that the peptides with the highest activity are those with a smaller size. In addition, these authors obtained peptides with antiproliferative activity and related the mechanism of action with the ability of these peptides to act directly on tumor cells and their cytotoxic effect.

On the other hand, antihypertensive activity is related to very short peptide sequences (less than nine amino acids), in whose sequence are the amino acids glycine, tyrosine, valine, phenylalanine, isoleucine, arginine or asparagine (Amado, González, Murado, & Vázquez, 2016; Neves et al., 2016). In this sense, Apostolidis, Karayannakidis, and Lee (2016) obtained peptides with antihypertensive activity from hydrolysates of squid by-products. This observation indicates that the most active peptides are those with a lower molecular weight.

The ability of some peptides to suppress appetite has also been described, and this is due to the structural similarity of these molecules with gastrin or cholecystokinin (Neves et al., 2016). Cudennec, Ravallec-Plé, Courois, and Fouchereau-Peron (2008) obtained peptides that stimulate cholecystokinin release in vitro from brown shrimp protein hydrolysates.

Peptides with antimicrobial activity are related to the presence of positively charged residues (Menon & Lele, 2015). Antimicrobial peptides obtained from shrimps and prawns have in their structure a high presence of proline, arginine and glycine residues (Hayes & Flower, 2013). Jiang et al. (2018) and Jiang, Liu, Yang, and Hu (2018) obtained antibacterial peptides from crab shells and squid by-products. In addition, several authors have obtained antimicrobial peptides from shrimp, scallop, abalone, and oyster (Harnedy & Fitzgerald, 2013; Hayes & Flower, 2013).

4. Marine algae (macro and micro)

Marine algae are a diverse group of photosynthetic organisms from aquatic environments. They are usually classified as macro- and microalgae. Macroalgae or seaweeds are multicellular organisms that can be divided into brown algae (Phaeophyta), red algae (Rhodophyta) and green algae (Chlorophyta), while microalgae are unicellular organisms constituted by prokaryotic green-blue algae (cyanobacteria) and eukaryotic microalgae (microalgae) (Martínez-Francés & Escudero-Oñate, 2018). The chemical composition of marine algae depends on the species, habitat, and environmental conditions. Fig. 3 shows some compounds obtained from macro- and microalgae with nutritional value. From a nutritional point of view, edible seaweeds are rich in minerals and vitamins, being recognized as an ideal food source of iodine as well as one of the few vegetable sources of vitamin B_{12} (Chandini, Ponesakki, Suresh, & Bhaskar, 2008). For centuries, different species of seaweeds such as *Ulva* (Chlorophyta), *Porphyra* (Rhodophyta), *Undaria*, *Laminaria*, *Himanthalia* and *Saccharina* (Phaeophyceae) have been harvested for human consumption, especially in coastal areas of the Asiatic continent. In the same way, the microalgae known as *Spirulina* have been consumed in Central America and Africa regions (Pereira & Carvalho, 2014). Later, the interest was in applying edible algae as food ingredients to improve the quality of different food products.

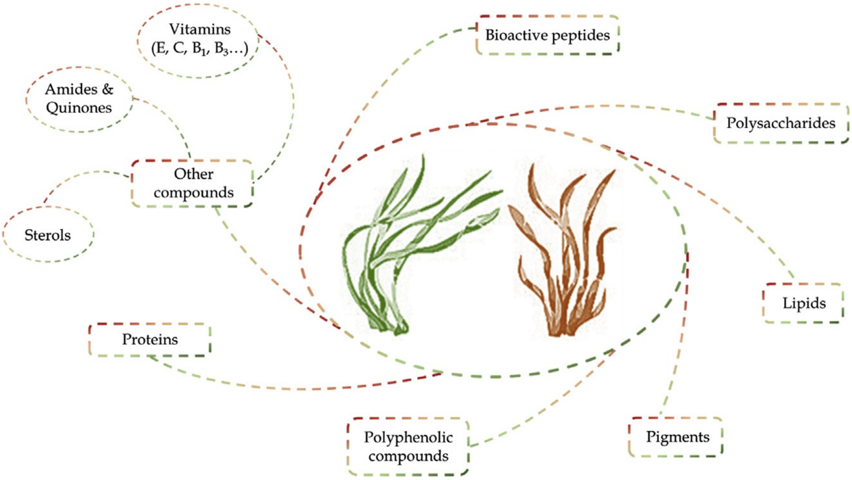

Fig. 3 Main proteins and bioactive compounds obtained from macro- and microalgae.

For example, sea spaghetti (*Himanthalia elongata*), nori (*Porphyra umbilicalis*) and wakame (*Undaria pinnatifida*) increased the content of sulfur amino acids and minerals in meat products, while *Ulva lactuca* and *Laminaria algae* were added to bread processing (Ścieszka & Klewicka, 2018). In contrast, European countries focused the interest on the gelling properties of algal polysaccharides and therefore, carrageenan, agar and alginates have been used as additive agents in the food industry (Pereira & Carvalho, 2014). In addition to the nutritional and industrial characteristics, the most recent scientific knowledge about their composition and biological activities have placed marine algae as a promising source of proteins and bioactive compounds. As a result, the high demand for both macro- and microalgae worldwide, sustainably led their production through aquaculture techniques.

Current aquaculture is the main source of edible aquatic plants, accounting for 96% of production in 2016. The volume of global farmed algae has increased by about 55% in the last two decades. Of the total million tons of algae from aquaculture in 2016, seaweeds represented 30 million tons while only 89,000 tons were recorded for microalgae (although this last value is understated because of unavailable data from important producers and farmed algae for scientific purposes are not included) (FAO, 2018a). There are more than 200 commercialized macroalgae, but only 10 species are intensively cultivated: *Saccharina japonica*, *Undaria pinnatifida* and *Sargassum fusiforme* for brown seaweed; *Porphyra* spp., *Eucheuma* spp., *Kappaphycus alvarezii* and *Gracilaria* spp. for red seaweed; and *Enteromorpha clathrata*, *Monostroma nitidum*, and *Caulerpa* spp. for green seaweed (FAO, 2018b). Regarding farmed microalgae, the main cultivated species are *Spirulina* spp., *Chlorella* spp., *Haematococcus pluvialis*, and *Nannochloropsis* spp. (FAO, 2018a).

4.1 Nutritional value

4.1.1 Proteins

From the nutritional point of view, algae are an interesting alternative source of proteins. Protein content in algae varies depending on the species, habitat and seasonal period. Microalgae present higher protein concentration than macroalgae. In general, protein fraction (dry weight) of green and red seaweed ranged from 10% to 47% while the protein percentage of brown seaweed is less than 15% (except for wakame (*Undaria pinnatifida*) whose protein level is 11–24%) (Fleurence, 1999; Herrero et al., 2012). Microalgae can contain more than 60% protein. The cyanobacteria *Spirulina platensis* present a protein composition of 43–63% so it is considered a food supplement

(Villarruel-López, Ascencio, & Nunõ, 2017). In addition, the essential amino acid profile of algae meets the requirements of the Food and Agriculture Organization of the United Nations (FAO). In this sense, the essential amino acid content of the most common microalgae and cyanobacteria has been reviewed by Barba, Grimi, and Vorobiev (2014). However, in vitro bioaccessibility studies suggest that unprocessed seaweed proteins have reduced digestibility compared to that of other protein sources (Villarruel-López et al., 2017).

On the other hand, other non-nutritional protein compounds such as enzymes produced by algae and peptides derived from their proteins have also been considered as bioactive compounds. For example, researchers revealed that various types of enzymes, such as mannuronan C5 epimerase, can be produced by algae (Parte, Sirisha, & D'Souza, 2017). Many of the algal producing enzymes are known to be important for the food and pharmaceutical industries (Inoue et al., 2016; Levy-Ontman, Fisher, Shotland, Tekoah, & Malis Arad, 2015). For instance, enzymes of *Closterium*, *Cylindrotheca*, and *Chaetoceros muelleri* are reported to be effective in diethyl phthalate degradation (Gao & Chi, 2015). Besides, glutathione peroxidase, ascorbate peroxidase, and catalase can be produced by algal (Babu et al., 2014; Moenne, González, & Sáez, 2016). Also, alginate can be produced from the brown algae wherein a symbiotic association between bacteria and seaweeds results in the production of alginate lyases (Ertesvåg, 2015). Moreover, a variety of bioactive peptides have been produced by enzymatic hydrolysis of the proteins of algal (Beaulieu, 2019). In this context, an investigation showed that the health state of bread can be enhanced by the incorporation of an algae renin inhibitory dulse protein hydrolysates (Fitzgerald et al., 2014). Such studies indicate that bioactive peptides obtained from algae can be considered valuable ingredients that can be used for food production.

4.1.2 Polysaccharides

Marine algae contain mucopolysaccharides, and storage and cell wall-structured polysaccharides. Some seaweed species contain polysaccharides in a range from 4% to 76% (dry weight), with the highest levels found in species such as *Ascophyllum*, *Palmaria*, *Porphyra* and *Ulva* (Usman, Khalid, Usman, Hussain, & Wang, 2017). Both, the cell wall structure and storage polysaccharides, are species-specific. Green algae contain sulfuric acid polysaccharides, sulfated galactans, and xylans. Also, the brown algae presents alginic acid, fucoidan, laminarin, and sargassan. Besides, the red algae contain agars, carrageenans, xylans, floridean starch, water-soluble sulfated galactan, as well as the mucopolysaccharide porphyrin (Chandini et al., 2008; Kraan, 2012). As polysaccharides do not participate in the nutritional value of algae, they are considered as a source of dietary fiber resistant to enzymatic hydrolysis of the intestinal microflora of the human digestive tract.

The dietary fibers included in marine algae are divided into insoluble (cellulose, mannans and xylene) and water-soluble (agars, alginic acid, furonan, laminaran, and porphyrin) dietary fibers (Kraan, 2012). The diverse chemical composition of dietary fiber polysaccharides has been considered responsible for their possible biological activities. In this sense, sulfated polysaccharides have shown many health benefits as anticoagulant, antioxidant, antiproliferative, antitumoral, anti-inflammatory, antiviral, and cholesterol-lowering agents (Mišurcová, Orsavová, & Ambrožová, 2015).

Fucoidan, in particular, has been shown to exhibit antiviral and anti-inflammatory properties as well as anti-metastatic effects in metastasized invasive human lung cancer cells (Khalid, Abbas, Saeed, Bader-Ul-Ain, & Ansar Rasul Suleria, 2018). In addition, a recent review concluded that fucoidan, laminarin sulfate, and carrageenan directly slowed the progression of the atherosclerotic lesion while alginate, ulvan (sea lettuce), and agar reducing the accompanying risk factors (Patil et al., 2018).

4.1.3 Lipids

The lipid content from marine algae differs between macro- and microalgae. While seaweeds usually present a low percentage of lipids (1–3% of the dry weight), many microalgae contain 20–50% of lipids (dry biomass) and even values ranging from 1% to 70% have also been reported (Barkia, Saari, & Manning, 2019). However, the lipid profile of both types of algae has raised considerable interest in recent years due to the high content of PUFAs. Typical PUFAs from seaweeds are α-linolenic (18:3n-3), octadecatetraenoic (18:4n-3), arachidonic (20:4n-6), and eicosapentaenoic (20:5n-3) acids (Kendel et al., 2015). On the other hand, the complete lipid profile (saturated, monounsaturated and PUFAs) from the most common used microalgae and cyanobacteria have been shown by researchers (Barba et al., 2014). In addition to playing an important role in the prevention of cardiovascular diseases, osteoarthritis, and diabetes, these PUFAs possess antimicrobial, antiviral, anti-inflammatory and antitumoral properties (Kendel et al., 2015). PUFAs and glycolipids obtained from *U. armoricana* and *S. chordalis* have been shown to have promising antitumor activities

(Kendel et al., 2015). As current unbalanced diets do not provide sufficient amounts of omega-3 PUFAs to satisfy human physiological requirements, marine algae are one the new alternative sources for helping to support healthy diets for people (Tocher, Betancor, Sprague, Olsen, & Napier, 2019).

4.1.4 Vitamins

In general, marine algae contain both water- and fat-soluble vitamins. Apart from the considerable vitamin functions for the body, vitamin E (α-tocopherol), vitamin C (ascorbic acid), and partially vitamin B1 and niacin have been considered responsible for the algal antioxidant activity (Škrovánková, 2011).

4.2 Bioactive and antioxidant compounds

Seaweed pigments are chlorophylls and carotenoids such as carotenes (β-carotene) and xanthophylls (fucoxanthin, violaxanthin, antheraxanthin, zeaxanthin, lutein, neoxanthin, among others) (Aryee, Agyei, & Akanbi, 2018). The most studied algae for natural carotenoids include brown seaweed (*Laminaria* spp. and *Undaria pinnatifida*), red seaweed (*Corallina elungata* and *Jania rubens*), and green microalgae (*Dunaliella salina*, *Chlorella* spp., *Haematococcus pluvialis*, and *Spirulina* spp.) (Christaki, Bonos, Giannenasa, & Florou-Paneria, 2013). Main algal carotenoids are astaxanthin, fucoxanthin, β-carotene, lutein and zeaxanthin. The antioxidant capacity of astaxanthin, the major carotenoid found in the unicellular green algae *Haematococcus pluvialis*, has been reported to be about 10 times greater than β-carotene, lutein, zeaxanthin, canthaxanthin and over 500 greater than that of α-tocopherol. In addition, the in vitro and in vivo studies have shown the effectiveness of astaxanthin against coronary, chronic inflammatory, diabetes, gastrointestinal, liver and neurodegenerative diseases as well as against atherosclerosis, ischaemic brain development and metabolic syndrome (Christaki et al., 2013).

Moreover, the β-carotene produced from the halophilic microalgae *Dunaliella salina* inhibited neoplastic cells and reduced fibrosarcoma in Wistar rats (Villarruel-López et al., 2017). Pigments from macroalgae have also shown health benefits. Fucoxanthin, the most important bioactive carotenoid in the chloroplasts of brown seaweeds such as *Ascophyllum nodosum* and *Laminaria* spp. has been reported for showing antiproliferative effects on prostate and human colon cancer cells, efficacy in the treatment of obesity and type 2 diabetes as well as anti-inflammatory and antioxidant properties (Christaki et al., 2013; Herrero et al., 2012). In addition, complex compounds constituted by protein-bound pigments that exhibit bioactivity have also been found. For example, phycobiliproteins, only present in red algae (phycoerythrin) and blue-green algae (phycocyanin), are characterized by containing the phycobilin pigment in their structure and this pigment has been related to hepatoprotective, anti-inflammatory and antioxidant properties of phycobiliproteins (Herrero et al., 2012).

Polyphenols are plant secondary metabolites whose structures vary from simple molecules to highly polymerized compounds. As aquatic plants, macro- and microalgae are the main marine sources of polyphenolic compounds. Green and red algae contain bromophenols, phenolic acids, and flavonoids while only in brown algae have been found phlorotannins (Gómez-Guzmán, Rodríguez-Nogales, Algieri, & Gálvez, 2018).

In general, these phytochemicals have been considered bioactive compounds with potential health benefits in numerous human diseases due to their antioxidant activity as well as enzyme inhibitory effect and antimicrobial, antiviral, anticancer, antidiabetic, antiallergic and anti-inflammatory activities (Gómez-Guzmán et al., 2018).

Phlorotanin, in particular, has been associated with anti-HIV, anticancer, bactericidal, radio-protective, antiallergic, and other health-beneficial biological activities shown by *Ecklonia cava*, *Ecklonia stolonifera*, *Ecklonia kurome*, *Eisenia bicyclis*, *Ishige okamurae*, *Sargassum thunbergii*, *Hizikia fusiformis*, *Undaria pinnatifida*, and *Laminaria japonica* (Freile-Pelegrín & Robledo, 2013; Khalid et al., 2018). Regarding microalgae, there is limited information about specific phenolic compounds in microalgae and the activity they provide. Jerez-Martel et al. (2017) identified and quantified the six widely distributed phenols in nature (gallic acid, (+) catechin, (−) epicatechin, syringic acid, protocatechuic acid, and chlorogenic acid) in crude extracts from several cyanobacteria and microalgae. They determined their antioxidant activity and observed a direct relation between the phenolic compounds and the activity tested for some strains (particularly, *Euglena cantabrica*).

Sterols are another interesting group of compounds extracted from marine algae. Not only sterols but also some of their derivatives have shown anticholesterol, anti-inflammatory and anticancer properties (Ibañez et al., 2012; Michalak & Chojnacka, 2015). On the other hand, as in bacteria and plants, glycolipids such as mono- and digalactosyldiacylglycerol as well as sulfoquinovosylacylglycerol are present in marine algae and they could have an important role in inflammatory diseases (Talero et al., 2015). Finally, several secondary metabolites (quinone-based natural products, small amides, and hierridin B) produced by different cyanobacteria have exhibited cytotoxicity toward HT-29 colon cancer cells (Olsen, Toppe, & Karunasagar, 2014; Talero et al., 2015).

5. Conclusions

Aquaculture provides a new source of high-quality food for the growing population. Besides, marine by-products offer many beneficial capabilities that make them valuable materials for the food and pharmaceutical industry. The nutritional value and bioactivity of these compounds and their derivates enlarge the scope of their applications. Researchers pointed out the potential value-added products that can be produced from aquatic waste. These include nutrients (e.g., high-quality oils, proteins, and polysaccharides) and bioactive compounds such as bioactive peptides and polyphenols. These findings might be later appreciated by the industry, resulting in developing commercial valorization techniques for processing the aquatic processing waste.

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