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Marine Bioactive Compounds and Their Health Benefits: A Review

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Abstract: The significance of marine creatures as a source of unique bioactive compounds is expanding. Marine organisms constitue nearly half of the wordwide biodiversity; thus, oceans and sea present a vast resource for new substances and it is considered the largest remaining reservoir of beneficial natural molecules that maight be used as functional constituents in the food sector. This review is an update to the information about recent functional seafood compounds (proteins, peptides, amino acids, fatty acids, sterols, polysaccharides, oligosaccharides, phenolic compounds, photosynthetic pigments, vitamins, and minerals) focusing on their potential use and health benefits.

Keywords: bioactive compounds, functional foods, health benefits, nutraceuticals, seafood.

Introduction

The oceans are probably the Earth's most valuable natural resource providing food mainly as fish and shellfish. Because of its phenomenal biodiversity, the marine world is a rich natural resource for many biologically active compounds. Marine organisms live in complex habitats and are exposed to extreme conditions, thus producing a wide variety of specific and potent active substances that cannot be found elsewhere.

Regular seafood consumption is associated with beneficial health effects. The growing need for novel substances for the treatment of human diseases such as cancer, microbial infections, and inflammatory processes has increased the exploration for new bioactive compounds. Marine organisms are viewed as the best potential reservoir for such compounds. Many marine compounds have been detected as having various biological activities: peptides isolated from fish as well as algal polysaccharides have been reported to have anticancer, anticoagulant, and antihypercholesterolemic activities (Lordan and others 2011). Marine bacteria and fish oils contain great amount of omega-3 fatty acids, whereas seaweeds and shellfish such as crustaceans have potent antioxidants including carotenoids and phenolic compounds (Rasmussen and Morrissey 2007). Thus, this paper emphasizes the possible use of marine bioactive compounds for human health benefits and for the protection against chronic diseases.

Defining Functional Food

Around 2400 years ago, Hippocrates set out guidelines for his students. One of his principles was "let food be your medicine and medicine be your food." The principle stressed the obvious relationship between food and good health (Chadwick 2003). The term "functional food" was first used in Japan in the 1980s for food products fortified with special constituents that had advantageous physiological effects. It was mainly the improved understanding of the relationship between nutrition and health that led to the development of the concept of functional foods. Functional foods can improve the general conditions of the body (such as pre- and probiotics), decrease the risk of some diseases (cholesterol-lowering products), and can even be used for curing some illnesses (cardiovascular disease and osteoporosis) (Siró and others 2008).

Today, foods are not only intended to satisfy hunger and to provide necessary nutrients for humans but also to prevent nutrition-related diseases and improve the physical and mental welfare of consumers. Such foods are called "functional foods."

Importance of Seafood

Seafood is any form of sea life regarded as food by humans. Seafood includes fish and shellfish. The latter includes molluscs: bivalves (mussel, oyster, and scallop), univalves (abalone, snail, and conch), and cephalopods (squid, cuttlefish, and octopus); crustaceans (crayfish, crab, shrimp, and lobster), and echinoderms. Most people would also include seaweeds and microalgae.

Seafood is tasty, nutritious, and easily available worldwide. Marine products have been identified as being rich in proteins containing all the essential amino acids, polyunsaturated fatty acids (PUFAs), Ca, I, vitamins, and many other nutrients (Venugopal 2005).

Recently, natural bioactive compounds have received greater attention, including those obtained from marine organisms. Since oceans occupy more than 70% of the surface, their high level of biodiversity makes them a logical target for looking for natural products (Kim and Wijesekara 2013). Marine bioactive constituents can be obtained from various marine animals, plants, and lower organisms. Each is unique as a species, and because of their life under different conditions, such as salinity, pressure,

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temperature, and illumination (Lordan and others 2011; Kulawik and others 2013), they potentially contain different natural products.

Marine Bioactive Ingredients

Proteins, peptides, and amino acids

Proteins, peptides, and amino acids are among the bioactive compounds (Harned and FitzGerald 2011).

Proteins. Proteins are complex polymers made up of a combination of 20 different amino acids coded by the genetic (DNA) code along with a number of other amino acids. In addition to their being required nutritionally, proteins have several important roles in biological and food systems acting as hormones (insulin, growth factors, and more), transport proteins (transferrin, hemoglobin, and others), and antibodies (immunoglobulins) (Damodaran 1997; Goodband 2002). Seafood is an excellent source of proteins and contains all the essential amino acids in close to the right proportions for humans. Table 1 shows the amino acid composition of several seafoods. The essential amino acids for humans are His, Phe, Val, Thr, Trp, Leu, Ile, Met, and Lys (Driskell 1999). Fish proteins compare favorably with proteins such as those from milk and soy (Tahergorabi and others 2002).

In addition, protein–pigment complexes, such as phycobiliproteins, are a relevant group of algae proteins. These hydrophilic proteins generally exist in some cyanobacteria and red algae. The phycobilin pigments can be present as phycocyanobilin in cyanobacteria or phycoerythrobilin in red algae. They have been shown to have hepatoprotective anti-inflammatory activities (Ge and others 2006) and also antioxidant activities which could be beneficial in the prevention or treatment of several diseases (neurodegenerative diseases, gastric ulcers, and cancer) (Burtin 2003). Phycobiliproteins are spontaneously fluorescent molecules (Kronick 1986) which makes them useful for some immunological methods (fluorescent immunoassays, fluorescent immunohistochemistry) (Aneiros and Garateix 2004). They are also used in cosmetics and in the food industry (Elias and others 2008). Moreover, in some countries (such as Japan, Thailand, and China), phycobiliproteins are applied as natural food colorings in, for example, dairy products, ice sherbets, chewing gums, and jellies (Lordan and others 2011). Aneiros and Garateix (2004) indicated that bioactive peptides obtained from different marine organisms (sponges, Ascidians, Mollusks, sea anemones, and seaweeds) had many pharmacological proprieties.

The high protein content of various microalgal species and their amino acid patterns compare favorably with that of other food proteins, suggesting that they could become a potential protein source. *Spirulina*, for example, has high protein content (60% to 70%), with great balance of the essential amino acids and bioavailability. *Spirulina* appears to be one of the most important microalgae used by humans. It has been used as a food by many civilizations (including Aztecs and Mayas) and by African populations near the alkaline lakes in Chad and Niger. Among its bioactivities are reductions in potential brain damage and anti-inflammatory activity. A daily supplement of *Spirulina* is believed to reduce allergy symptoms (Rasmussen and Morrissey 2007).

The commercial scale production of the microalgae, *Dunaliella*, yields protein at about 100-fold more per area compared to terrestrial crops. Purified peptides from *Chlorella vulgaris* can prevent cellular destruction (Lordan and others 2011).

Peptides. The hydrolysis of proteins leading to bioactive peptides has been receiving intensive investigation including those peptides derived from marine proteins. These peptides have been isolated from marine sources, for example, algae, crustaceans, and fish species. Bioactive peptides often have 3 to 20 amino acid residues depending on amino acid composition and sequence (Ibañez and others 2011). They are indicated to have biological functions, for instance, antioxidant, antithrombotic, antihypertension, immunomodulation, anticancer, and antimicrobial effects.

A number of studies have also demonstrated that peptides derived from different marine protein hydrolysates can act as potential antioxidants and have been isolated from marine organisms such as jumbo squid, tuna, and scad (Kim and Wijesekara 2010). Furthermore, several studies have suggested that peptides derived from marine fish proteins can be more powerful antioxidants than α-tocopherol (vitamin E) in some oxidative systems (Jun and others 2004).

Amino acids. Among the water-soluble components, seafood muscles are rich in amino acids, mainly taurine, Gln, Pro, Gly, Ala, and Arg. Cooking or thermal processing causes the loss of water-soluble components and so their positive properties are likely to be greater when seafood is minimally processed (Luten 2009).

Lys, sulfur-containing amino acids, and Thr are often not present in sufficient quantities in children's diets, especially when they are based on cereals. Therefore, consumption of fish muscle proteins, which are generally rich in those amino acids, is recommended to enhance the nutritional value of foods and to improve their nutritional status for humans.

The protein contents differ significantly from phylum to phylum in macroalgae and have all the essential amino acids in reasonable proportions, although their contents vary considerably with species. Red alga *Palmaria palmata* are rich in Leu, Val, and Met (Bocanegra and others 2009), and their mean levels are similar to those mostly noticed for ovalbumin. However, Ile and Thr concentrations are similar to those found with legume proteins.

According to Taboada and others (2009), the green alga *Ulva rigida* contains Leu, Phe, and Val as major essential amino acids. His, which is an essential amino acid for infant, is at levels close to those in legumes and eggs.

Lipids and fatty acids

The fatty acid composition of seafood is generally characterized by a relatively low content of saturated fatty acids (SFA). A low intake of SFA is recommended since a link between SFA consumption and the development of cardiovascular disease (CVD) has generally been assumed. However, recent research is questioning this assumption as carbohydrates are being considered a likely culprit. Seafood also contains PUFAs and substantial amounts of monounsaturated fatty acids (Pigott and Tucker 1990; Larsen and others 2011) which are considered beneficial as long as they are not oxidized.

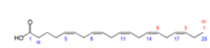
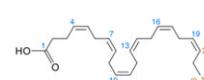
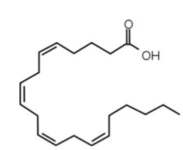
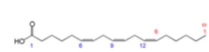
Polyunsaturated fatty acids. The lipid fraction of seafood consists primarily of PUFAs that have been well documented as essential for human health (Berquin and others 2007; Juturu 2008; Chan and Cho 2009; Zheng and others 2013). Humans are incapable of synthesizing PUFAs with more than 18 carbons; thus, they should get them from food. Seafoods are the major sources of long-chain PUFAs (Lordan and others 2011), although the synthesis actually occurs in the algae eaten by the fish. Table 2 shows the structures and the main sources of PUFAs found in marine organisms. The long-chain omega-3 fatty acids such as eicosapentaenoic acid (EPA, $C_{20:5}$) or docosahexaenoic acid (DHA, $C_{22:6}$) are beneficial in the protection against CVD (Kris-Etherton and others 2003). The composition and extraction of PUFAs from algae, fish, and other marine sources have been studied extensively (Fleurence

Table 1–Amino acid compositions of some seafood[a] (g/100 g).

Amino acid	Herring[b] *Clupea harengus*	Mackerel[b] *Scomber scombrus*	Crab[c] *Chionoecetes opilio*	Mussels[d] *Mytilus galloprovincialis*	Oyster[e] *Crassostrea madrasensis*	Shrimp[f] *Aristeus virilis*	Seaweed[g] *Porphyra tenra*	Microalgae[h] *Spirulina platensis*
Ala	5.97	5.87	1.46	0.704	5.3	2.12	7.4	9.5
Arg	5.93	6.33	2.35	0.869	6.4	1.45	16.4	7.3
Asp	9.92	10.39	1.23	1.36	11.8	2.15	7	11.8
Cys	1.73	0.81	-	0.261	0.9	0.35	-	0.9
Glu	13.5	13.8	1.97	1.78	0.73	-	7.2	10.3
Gly	4.48	4.73	1.3	0.801	2.3	0.67	7.2	5.7
His	2.71	4.82	1.45	0.426	7.7	0.53	1.4	2.2
Ile	4.29	4.57	0.96	0.592	4.5	0.84	4	6.7
Leu	8.03	8.03	1.58	0.954	2	1.96	8.7	9.8
Lys	8.98	9.28	2.07	1.05	14.3	2.03	4.5	4.8
Met	2.41	3.69	0.48	0.249	4.7	0.67	1.1	2.5
Phe	4.00	4.07	1.3	0.844	4.1	0.95	3.9	5.3
Pro	3.47	3.50	0.91	1.523	1.03	1.13	6.4	4.2
Ser	3.83	4.18	1.64	0.812	10.6	2.24	2.9	5.1
Thr	4.54	5.50	1.58	0.718	12.3	1.21	4	6.2
Trp	1.21	1.33	-	-	2.17	0.34	1.3	0.3
Tyr	3.57	3.69	0.98	0.683	5.9	0.94	2.4	5.3
Val	6.00	5.47	1.38	0.66	2.6	1.22	6.4	7.1
Total[a]	**94.6**	**100.**	**22.6**	**14.3**	**99.3**	**20.8**	**92.2**	**105**
Reference	Shahidi and Venugopal (1997)		Vilasoa-Martínez and others (2007)	Şengor and others (2008)	Asha and others (2014)	Karuppasamy and others (2013)	Fujiwara-Arasaki and others (1984)	Lum and others (2013)

[a]The sum of the amino acids in a protein should be about 115 to 118 g/100 g
These amino acid analyses are only an estimate of the actual composition of the proteins. Concerns include the accuracy of the protein determination, the protein purity, and how well the sample represents the species. If high in collagen, the standard Kjeldahl factor is inappropriate. There are also important concerns with the amino acid analysis. How were the peak areas obtained with respect to the baseline and multiple peaks separated? How was the area under the individual peaks calculated and calibrated? Is the data for amino acids (+H_2O) or amino acid residues (−H_2O)? A 22 to 24 h hydrolysis may include some unbroken peptide bonds, and some amino acids that are partially degrade along with all of the tryptophan. How are any unusual amino acids accounted for? Finally, how was the data manipulated to provide the data presented? In a well-done amino acid analysis (not amino acid residues), a theoretical protein of 100 g should yield about 115 to 118 g of amino acids.
[b]Amino acids composition of the herring and mackerel is based on their thermostable aqueous dispersions (g/100g protein).
[c]Amino acid contents (g/100 g dry weight) of crabs analyzed (shell and discard meat).
[d]Amino acid composition of steamed mussels (g/100 g dry weight).
[e]Amino acids profile (g/100 g crude protein) of oyster.
[f]Amino acid composition (g/100 g dry weight) in shrimps.
[g]Amino acid compositions of the alkali-soluble proteins in *Porphyra tenra* (g amino acid-N/100 g protein-N).
[h]Amino acid profile of *Spirulina platensis* (g/100 g protein).

Table 2–PUFAs found in some marine organisms.

Name	Main sources	Structure	Reference
Eicosapentaenoic acid (EPA)	Herring, mackerel, sardine, salmon		Sijtsma and de Swaaf (2004)
Docosahexaenoic acid (DHA)	Herring, mackerel, sardine, salmon, *Spirulina*		Sijtsma and de Swaaf (2004) Lordan et and others (2011)
Arachidonic acid (AA)	*Mortierella*		Yap and Chen (2001)
γ-Linolenic acid (GLA)	*Mortierella, Spirulina*		Yap and Chen (2001) Lordan and others (2011)
Hexadecatetraenoic acid	*Ulva pertusa*		Lordan and others (2011)

and others 1994; Schmidt and others 2001; Sánchez-Machado and others 2004). Table 3 presents the fatty acid profiles of various seafoods. One of the main commercial sources of omega-3 PUFAs, including DHA and EPA, is the fatty fish such as herring, mackerel, sardine, and salmon. The amount and composition of these oils depend on the species, season and location of catching sites. (Sijtsma and de Swaaf 2004). Fungi such as phycomycetes are another source of omega-3 fatty acids. Those marine organisms, especially from the *Mortierella* genus, are known to yield high levels of either γ-linolenic (GLA) acid, arachidonic acid (AA), or EPA (Yap and Chen 2001). Krill oil has also been shown to have a complex combination of multiple active ingredients. Its unique composition shows it to be rich in phospholipids, omega-3 fatty acids, and diverse antioxidants, suggesting that it can take part in the reduction of the risk of CVD (Bunea and others 2004). However, PUFAs are susceptible to lipid oxidation and this is one obstacle for their utilization in functional foods. Therefore, PUFAs are frequently utilized in combination with other antioxidants to extend their shelf-life.

PUFAs in macroalgae are represented by omega-3 and omega-6 fatty acids (EPA and AA). PUFAs have the following health benefits: they help regulate blood clotting and blood pressure, and

Table 3–Fatty acid profiles of some seafood (% of total fatty acids).

Fatty acids	Atlantic salmon *Salmo salar L.*	Rainbow trout *Oncorhynchus mykiss*	Krill *Thysanoessa raschii*	Seaweed *Laminaria* sp.	Microalgae *Chlorella vulgaris*
Lauric acid C12:0_{SFA}	–	–		0.06	–
Palmitic acid C16:0_{SFA}	15.6	17.4	30.2	36	25.1
Hexadecatetraenoic acid C16:$4_{\omega\text{-}3}$	–	–	–	–	4.06
Oleic acid C18:$1_{\omega\text{-}9}$	17.7	21.1	14.4	12.8	12.6
γ-Linolenic acid (GLA) C18:$3_{\omega\text{-}6}$	–	–	0.7	1.60	19.1
Octadecatetraenoic acid C18:$4_{\omega\text{-}3}$	1.1	–	2.9	1.24	–
Arachidonic acid (AA) C20:$4_{\omega\text{-}6}$	–	–	0.7	12.4	0.23
Eicosapentaenoic acid (EPA) C20:$5_{\omega\text{-}3}$	6.5	5.64	4.5	16.2	0.46
Docosahexaenoic acid (DHA) C22:$6_{\omega\text{-}3}$	12.5	17.28	1	–	–
Reference	Jensen and others (2012)	Chávez-Mendoza and others (2014)	Saether and others (1986)	Dawczynski and others (2007)	Lum and others (2013)

develop function of the brain and nervous systems. They also decrease the risk of many chronic diseases such as arthritis, diabetes, and obesity (Wall and others 2010). Moreover, PUFAs regulate inflammatory responses by producing inflammation mediators called eicosanoids (Lordan and others 2011). The rate of omega-3 to omega-6 of macroalgae is close to ideal, therefore they are used as dietary complement as part of a balanced diet. Red and brown algae have high level of omega-3 fatty acids (EPA and GLA) and the omega-6 fatty acids (AA and linoleic acid) (Fleurence and others 1994). In fact, Sánchez-Machado and others (2004) showed that the omega-3 fatty acid octadecatetraenoic acid is rich in 2 brown algae, *Laminaria ochroleuca* and *Undaria pinnatifida*. However, green seaweeds, for instance *Ulva pertusa*, are characterized by hexadecatetraenoic (omega-3), oleic (omega-9), and palmitic acids (SFA) (Floreto and others 1993).

The major elements of the lipid fractions of the microalgae *C. vulgaris* include oleic, palmitic, and linolenic acids (Mendes and others 1995). The green microalga *Haematococcus* contains short-chain fatty acids with antimicrobial activity (Rodríguez-Meizoso and others 2010). Long-chain PUFAs are industrially obtained by microalgal cultivation for integration in newborn milk formulations and are also used as nutritional supplements and food additives (Spolaore and others 2006). *Spirulina* is an interesting source of GLAs, a precursor of leukotrienes, prostaglandins, and thromboxans implicated in the regulation of inflammatory, immunological, and cardiovascular disorders. This cyanobacterium contains active fatty acids including palmitic, oleic acids, and lauric along with DHA (Lordan and others 2011).

Sterols. Another class of lipids from marine sources is the sterol compounds. Table 4 shows the structure and main sources of some sterols in seafood. They are membrane lipids produced by eukaryotes as well as by some bacteria (Lewis and others 2001). Research has focused on the composition of sterols extracted from macro- and microalgae, fish, and other marine invertebrates (Patterson 1971; King and others 1990; Kanazawa 2001; Copeman and Parrish 2004; Özyurt and others 2013). Table 5 gives the sterol contents of some seafood. Sterols and some of their derivatives have been noticed to be involved in reducing low-density lipoprotein (LDL) cholesterol levels *in vivo*. Another bioactivity related to sterols is anti-inflammatory effect. In addition, phytosterols (C_{28} and C_{29} sterols) are essential precursors of some vitamins. For instance, ergosterol is a precursor of vitamin D_2 and cortisone (Ibañez and others 2011). *Spirulina* has been reported to have sterols, including clionasterol associated in increasing the formation of plasminogen-activating factor in vascular endothelial cells (Lordan and others 2011). Fucosterol, chondrillasterol, and sargasterol are found in brown algae and cholesterol has been found in red algae (Kayama and others 1989).

Carbohydrates and dietary fiber

Polysaccharides. Algal polysaccharides are easily isolated and are valuable as potential bioactive ingredients in functional foods since they have numerous human health benefits. Different polysaccharides found in macro- and microalgae are shown in Table 6. Polysaccharides including agar, carrageenans, and alginates are isolated from macroalgae. They are used extensively in the food, pharmaceutical, cosmetics, paper, and textiles industries as stabilizers and as water-thickening, emulsifying, and gelling agents. The ability of those ingredients to bind water to form a gel, and to form and stabilize emulsions, has led to many industrial applications. Those polysaccharides are found in glazes, icings, salad dressings, sauces, bakery products, beverages (milk shakes, ice milk, water ices, and more), puddings, flans, and toppings (Glicksman 1987). The carbohydrate type varies widely among algae. The soluble fibers are alginates, fucans, and laminarans for brown seaweeds (Phaeophyta), whereas the soluble fibers are sulfated galactans (agars and carrageenans), xylans, and floridean starch for red seaweeds (Rhodophyta) (Kraan 2012). Green algae contain starch, xylans, mannans, and ionic polysaccharides which contain sulfate groups (Zaporozhets and others 2014). Uronic acids, rhamnose, xylose, galactose, and arabinose are also found in this type of algae (Bocanegra and others 2009). Cellulose, an insoluble fiber, is found in all algae (Mabeau and Fleurence 1993; Rupérez and Saura-Calixto 2001). Many of polysaccharides are indigestible in the human gastrointestinal tract because of the absence of the required degradation enzymes, and, thus, they can be regarded as dietary fiber. Dietary fiber can be classified into 2 groups, those that are soluble and those that are insoluble. Soluble fibers can form viscous gels in the intestinal tract, whereas insoluble fibers are characterized by their fecal-bulking capacity. The total dietary fiber content of seaweeds (25% to 75% of the dry weight of marine algae) is higher than the fiber content of most fruits and vegetables (Jimenez-Escrig and Sanchez-Muniz 2000). Human consumption of algal fiber has been proven to be health-related and beneficial (with antitumor, anticoagulant, antiviral, and antihypercholesterolemic activities) (Noda 1993; Brownlee and others 2005; Dawczynski and others 2007; Wijesekara and others 2011). Many viscous-soluble polysaccharides have been correlated with hypocholesterolemic and hypoglycemic effects, while water-insoluble polysaccharides (cellulose) are mainly associated with a decrease in digestive tract transit time (Mabeau and Fleurence 1993; Løvstad Holdt and Kraan 2011).

Fucoidans, sulfated polysaccharides, are involved extensively in the cell walls of brown macroalgae. Fucoidans show various physiological and biological features, such as antitumor, anticoagulant, antioxidant activities, antiviral, and antithrombotic, in addition to the impact on the inflammatory and immune systems

Table 4–Structure of some sterols found in seafood.

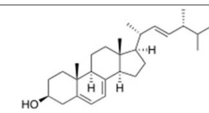
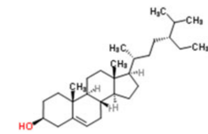
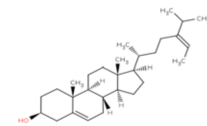
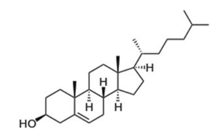
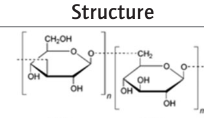
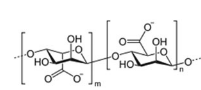
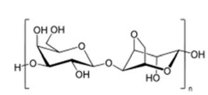
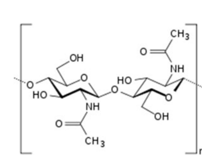
Name	Main sources	Structure	Reference
Ergostérol	*Chlamydomonas reinhardtii*		Brumfield and others (2010)
Clionasterol	*Spirulina*		Lordan and others (2011)
Fucosterol	Brown algae (*Pelvetia siliquosa, Cystoseira foeniculacea*)		Bouzidi and others (2014)
Cholesterol	Red algae (*Gracilaria salicornia* and *Hypnea flagelliformis*)		Nasir and others (2011)

Table 5–Sterol contents of some seafood.

Sterol (mg/100 g)	Blue crab *Callinectes sapidus*	Clams *Lamellibranchia* spp.	Sea urchin	Seabream *Sparus aurata*	Red mullet *Mullus barbatus*	Seaweed *Laminaria japonica*
Clionasterol	0.299	5.48	–	–	–	–
Fucosterol	–	–	89.4	–	–	206.4
Cholesterol	96.0	29.3	833	53.14	44.0	1.9
Reference	Phillips and others (2012)	López-Hernández and others (1999)	Özyurt and others (2013)	Honya and others (1994)		

Table 6–Some of the polysaccharides found in macro and microalgae.

Name	Main sources	Structure	Reference
Laminarin	Brown algae (*Eisenia bicyclis*)		Menshova and others (2014)
Alginate	Brown algae (*Laminaria digitat, Macrocystis pyrifera*)		Fertah and others (2014)
Agar	Red algae (*Gelidiella acerosa*)		Prasad and others (2006)
Chitin	Crabs, shrimps, lobsters, prawns, krill		Rinaudo (2006).

(Wijesekara and others 2011). Porphyran, another sulfated polysaccharide, is the major component of the red macroalga *Porphyra*. Fucoidan has been used as a gelling agent, a dietary complement as well as an antioxidant (O'Sullivan and others 2010). Furthermore, laminarin, the second main source of glucan in brown algae, has been detected as a regulator of intestinal metabolism through its impacts on mucus structure, intestinal pH, and short-chain fatty acid formation (Devillé and others 2007; Løvstad Holdt and Kraan 2011).

Carbohydrates such as starch, sugars glucose, and other polysaccharide exist in microalgae. There is no restriction for the use of dried total microalgae in foods or feeds, due to their high overall digestibility (Becker 2008). Besides, the biological functions of some microalgal species have been related to their polysaccharides. Complexes of polysaccharide from *Chlorella pyrenoidosa*, and *Chlorella ellipsoidea*, have glucose and a variety of combinations of mannose, galactose, rhamnose, *N*-acetylglucosamide, *N*-acetylgalactosamine, and arabinose. These complexes contain immune stimulatory effects (Pugh and others 2001; Bin and others 2013) and could have antiproliferative activity against *Listeria monocytogenes* and *Candida albicans* (Hasegawa and others 1995; Mata and others 2010).

β-1,3-Glucan is another polysaccharide from *Chlorella*; it is an active immunostimulator, a free radical collector, which thereby reduces blood lipids (Spolaore and others 2006). Furthermore, polysaccharides extracted from microalgae (*Porphyridium* and *Nostac flegelliforme*) were effective against Herpes simplex virus (HSV-1 and HSV-2) (Kanekiyo and others 2007; Vo and others 2011).

Chitin is another carbohydrate abundant in different marine sources. It is one of the most abundant biopolymers in nature (Xu and others 2013), and it exists in different marine sources including crustaceans where it is a part of the exoskeleton (Rinaudo 2006; Sharp 2013). Chitosan is formed by the alkaline deacetylation of chitin, and it is used in various applications (Giyose and others 2010; Kaur and Dhillon 2015). Some attractive impacts have also been related to this polymer, considered as a part of the nutritional fiber, decrease of lipid absorption, and hypocholesterolemic or antidiabetic impact, among others (Ibañez and others 2011).

Oligosaccharides. Oligosaccharides are another group of carbohydrates. They are carbohydrate compounds with a small amount of polymerization. They generally contain 3 to 10 sugar units. Some authors, however, include disaccharides or carbohydrates with up to 20 residues in this group (Mussatto and Mancilha 2007; Patel and Goyal 2011). So far, various oligosaccharides with immunostimulation functions along with antioxidant and antitumor effects have been characterized. In addition, oligosaccharides have potential health benefits when they are incorporated into the diet to develop the growth of probiotic bacteria. For example, xylo-oligosaccharides and fructo-oligosaccharides are nondigestible oligomers that are not able to pass through the gastrointestinal tract so they can be used as prebiotics to encourage the growth of beneficial probiotic bacteria (Lordan and others 2011), for example, Bifidobacteria to the detriment of pathogenic organisms (Iji and Kadam 2013).

Functional oligosaccharides have also been used in food products as anticariogenic agents and low-sweetness humectants. The oligosaccharides are also commonly used in cosmetics as stabilizers and bulking agents.

Antioxidants

Marine algae like other photosynthesizing plants are exposed to both light and oxygen, which induce the formation of free radicals and other strong oxidizing agents. But the lack of oxidative damage in the structural components of seaweeds and their stability to oxidation during storage suggest that their cells have antioxidative defense systems (Jiménez-Escrig and others 2001). An antioxidant can be any substance that is able to inhibit oxidation when present at low concentrations, that is, more reactive than an oxidizable substrate (Jun and others 2004). The antioxidant ability of components has been associated with the protection against cancer, coronary heart disease (CHD), inflammatory troubles, neurological deterioration, and aging (Wollgast and Anklam 2000; Castro-Puyana and others 2013). Some of these antioxidants in algae are shown in Table 7.

Polyphenolic compounds. Polyphenolic components are among the antioxidant compounds that have been extracted from micro- and macroalgae. There are at least 8000 various bioactive polyphenols (Bravo 1998). Usually, phenolic constituent are separated into 10 categories according to their structure. These 10 classes include phenolic acids, hydroxycinnamic acids, simple phenols, coumarins, xanthones, naphthoquinones, flavonoids, stilbenes, anthraquinones, and lignins (Ibañez and others 2011). Phlorotannins, which belong to polyphenolic components, have been detected in various brown algal families and they have an efficient antioxidant activity (Lordan and others 2011). In addition, phlorotannins are known to have other activities including antibacterial, chemopreventive, UV-protective, and antiproliferative effects. They are also known to detoxify heavy metals and have other bioactivities that could possibly be utilized in functional foods (Ibañez and others 2011).

Photosynthetic pigments. The photosynthetic pigments are bioactive compounds that are able to capture solar energy. They are used by autotrophs for photosynthesis. For macroalgae, the major pigments are carotenoids and chlorophylls. More than 600 known carotenoid structures are characterized in the literature (Faulks and Southon 2005; Pizarro and Stange 2009; Klassen 2010), and these natural pigments generally color the numerous natural matrices.

Carotenoid pigments have antioxidant properties as well (Krinsky 1989). These pigments are formed by algae, plants, fungi, and other microorganisms; however, humans and animals require ingesting them in their diets. Dietary carotenoids have nutritional and therapeutic importance since they act as provitamin A, which is converted into vitamin A. Carotenoids are known to be active agents for the protection against cancer, CVD, and macular degeneration (Ibañez and others 2011). Microalgal formation of carotenoids, including β-carotene (Emeish 2012) and astaxanthin (Lorenz and Cysewski 2000), is an active area of research as they can be present at relatively high concentrations. β-Carotene is one of the major natural colorants and it has been employed to a vast spectrum of food and drinks in order to enhance their aspect. Moreover, β-carotene with intense antioxidant properties helps to reduce the harmful effects of free radicals, which have been related to various life-threatening conditions, such as different kinds of cancer, CHD (Stahl and Sies 2003), premature aging (Pandel and others 2013), and arthritis (Cerhan and others 2003; Cooper 2007). β-Carotene with its antioxidant properties could reduce the actions of UV rays on premature aging in the skin (Godic and others 2014). Microalgal-derived β-carotene compared to synthetically β-carotene has been shown to be more biologically active (Gómez and González 2005) and can be labeled as a natural food additive (Chacón-Lee and González-Mariño 2010).

In the food sector, chlorophylls have generally application as natural colorants in foods and drinks. In addition, chlorophylls and their derivatives have some biological activity such as anticancer properties (Hosikian and others 2010).

Vitamins

Vitamins are required for the human body for various chemical and physiological functions. Seaweeds are generally a good source of B group vitamins (B_1, B_2, and B_{12}) (Kim and Taylor 2011). The vitamin composition varies with many factors including species, geographic area, season, and environmental parameters (Norziah and Ching 2000). Table 8 shows the vitamin contents of some seaweeds and microalgae. Ortiz and others (2006) reported that 100 g seaweed provides more than the daily requirement of vitamins A, B_2, B_{12}, and two-thirds of the vitamin C requirement. Vitamin B_{12} exists in red macroalgae (such as *Palmaria longat* and *Porphyra tenera*) and in particular green seaweeds, whereas vitamins C and E are both found in *U. pinnatifida* and *Laminaria digitata*. Microalgae are crucial sources of almost all other essential vitamins such as A, B_1, B_2, B_6, B_{12}, C, E, and so on, and also are abundant in chlorophylls (Lordan and others 2011).

Table 7–Antioxidants and vitamins found in algae.

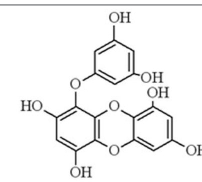
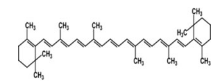
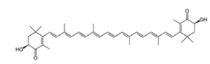
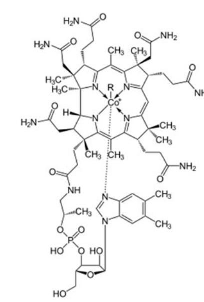
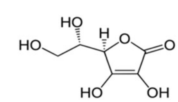
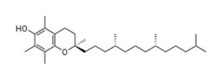
Name	Main Sources	Structure	Reference
Phlorotannin	Brow algae (Fucaceae, Sargassaceae, Cystoseiraceae, Laminariaceae)		Shibata and others (2004)
β-Carotene	*Dunaliella salina*		Guedes and others (2011)
Astaxanthin	*Haematococcus pluvialis*		Spiller and Dewell (2003)
Vitamin B_{12}	*Porphyra* sp, *Enteromorpha* sp, *Spirulina*		Kim and Taylor (2011)
Vitamin C	*Undaria pinnatifida*, *Porphyra umbilicalis*, *Ulva* spp.		MacArtain and others (2007)
Vitamin E (α-tocopherol)	*Nannochloropsis oculata*		Durmaz (2007)

Table 8–Vitamins in some seaweeds and microalgae.

	Seaweed (mg/g)			Microalga (mg/kg)		
Vitamin	*Laminaria digitata*	*Undaria pinnatifida*	*Porphyra umbilicalis*	*Spirulina platensis*	*Chlorella pyrenoidosa*	*Senedesmus quadricauda*
A	–	–	–	840	480	554
B_1	0.011	0.403	0.077	44	10	11.5
B_2	0.011	0.936	0.274	37	36	27
B_3	4.90	7.20	0.761	–	–	–
B_6	0.513	0.259	0.119	3	23	–
B_8	0.513	0.015	–	0.3	0.15	–
B_9	0	0.528	1.00	0.4	–	–
B_{12}	0.495	0.345	0.769	7	–	1.1
C	2.84	14.8	12.9	80	–	396
E	0.275	1.39	0.114	120	–	–
Reference		MacArtain and others (2007)			Becker (2008)	

- No data available

Fatty fish are one of very few dietary sources of vitamin D. Vitamin D deficiency causes many problems such as rickets in infants and children, and osteomalacia in adults (Luten 2009). Some of the vitamins that are found in algae are shown in Table 7.

Vitamin B_{12} (cobalamin) is widely found in algae in higher concentrations in green and red algae than in brown algae (Ragan 1981). Vitamin B_{12} is a cobalt-containing tetrapyrrole related to chlorophyll and heme. Cobalamin is a cofactor of enzymes. Cobalamin deficiency may cause serious health disorders such as megaloblastic anemia and neuropsychiatric disorders (Misurcova 2011). The highest content of vitamin B_{12} in seaweed measured to date is found in red *Porphyra* sp. (134 μg B_{12}/100 g dw). It has also been reported that a high content of this vitamin is found in green algae (*Enteromorpha* sp., dulse and *Spirulina*) (Kim and Taylor 2011). Vitamin B_{12} is recommended for treatment of the effects of aging, chronic fatigue syndrome, and anemia (Ravishankar and others 2005).

Vitamin C (ascorbic acid) is present in all red, brown, and green seaweeds. A red alga (*Porphyra*) was historically used to prevent scurvy caused by vitamin C deficiency (Karleskint and others 2012). In addition, this vitamin has other health benefits such as radical scavenging, strengthening of the immune system, and antiaging activity (Packer 1997; Witting and Stocker 2003; Haidara and others 2006).

Vitamin E is a mixture of tocopherols. α-Tocopherol is the only form known to occur in all species of red, green, and brown seaweeds. Phaeophyceae also contain β- and γ-tocophérols. This vitamin is recognized for its antioxidant activity (Ragan 1981; Misurcova 2011). α- and γ-Tocophérols have been shown to help prevent CVD (Ravishankar and others 2005). The amounts of this vitamin found in some algae are shown in Table 7.

Minerals

Seaweeds are also very rich in essential minerals and trace elements. This is associated with their ability to maintain inorganic atoms from seawater. Most of these essential minerals are found in high level in seaweeds compared to terrestrial foods. All of the essential minerals and trace elements required for human diet exist in macroalgae (Ito and Hori 1989) and so this is considered as an important functional food for that reason alone. The mineral composition of seaweeds can vary according to the phylum, season, environment, geography, and physiology (Mabeau and Fleurence 1993). The mineral composition of some seafood is shown in Table 9. Some phaeophyceae (*U. pinnatifida* and *Sargassum*), and some rhodophyta (*Chondrus crispus* and *Gracilariopsis*) can be considered as dietary complement to encounter the daily intake of some major minerals (Na, K, Ca, and Mg) as well as trace minerals (Fe, Zn, Mn, and Cu) (Rupérez 2002). In addition, analysis of *Ulva rigida* showed a balanced content of Na and K from a nutritional point of view. High Na/K ratios have been related to incidences of hypertension (Taboada and others 2009). Moreover, seaweeds are one of the most important vegetable sources of Ca. Therefore; seaweed intake could be useful risk for Ca deficiency risk, especially pregnant women, adolescents, and the elderly (Iji and Kadam 2013). The most outstanding feature of marine plants is their high I content. I is an important nutrient in metabolic regulation and growth patterns. It is abundant in most seaweeds (MacArtain and others 2007).

Ca is one of the most important essential minerals for humans. Ca is needed to form bones and keep them strong during pregnancy and lactation, since there is a high Ca demand at these stages. Ca is vital for the proper development and maintenance of calcified dental tissues as well. If Ca needs are not met through dietary intake, the deficiency in this mineral will cause many diseases such as hypocalcia symptom and osteoporosis (Weaver and Heaney 2007; Venugopal 2008; Nguyen and others 2011).

Dietary I is essential for the production of the thyroid hormones thyroxine and triiodothyronine, which regulate many important physiological processes in humans. An I deficiency can cause several problems including an effect on growth and development due to insufficient formation of the thyroid hormones leading to spontaneous abortion, stillbirth, cretinism, goiter, and mental defects. I is ubiquitous in seawater. In fact, kelp, a type of macroalgae, is a rich source of I and is used as a functional food and nutritional supplement (Li and others 2009; Catarina Guedes and others 2013).

Seafood and Health Benefits

Seafood has an essential role in the human diet and is not only a reliable source of protein, but it also has a nutritional impact due to its lipids and vitamin and mineral constituents. Seafood proteins are highly digestible, and easily absorbed by the body. Lys and Met are 2 of the most important essential amino acids. These are generally found in high concentrations in fish proteins.

Health benefits of seafood as a source of antioxidants

Synthetic antioxidants such as butylated hydroxyanisole, butylated hydroxytoluene, *tertiary*-butylhydroquinone, and propyl gallate have been widely used to retard lipid oxidation. However, those synthetic compounds are under strict regulation in most countries owing to their potential health hazards (Park and others 2001).

Antioxidant activity has been reported for fish protein hydrolysates (FPH) prepared from a number of marine species such as tuna, mackerel, yellowfin sole, and Alaska pollock (Wu and others 2003; Jun and others 2004; Je and others 2005; Je and others 2007). Peptides isolated from fish can be derived from muscles, skin, scales, bones, and other tissues. Although all free amino acids can generally interact with free radicals, the most effective are those that can easily donate hydrogen atoms. These are the amino acids containing nucleophilic sulfur-containing side chains (Cys and Met) or aromatic side chains (Trp, Tyr, and Phe). The antioxidant nature of FPH is mainly dependent on peptide size and amino acid composition (Kim and Wijesekara 2013).

Microalgae and seaweeds have been shown to produce reactive oxygen species (ROS) due to the tough environmental conditions (such as temperature and high irradiation) that they are exposed to. Excessive ROS has been linked to many illnesses including cancer, diabetes mellitus, and neurodegenerative and inflammatory diseases (Zubia and others 2007; Cornish and Garbary 2010). This is due to ROS reacting with biomolecules such as DNA, membrane lipids, and proteins causing cell and tissue injuries. To deal with ROS, seaweeds (macroalgae) deactivate the ROS whith their high cellular contents of antioxidant compounds such as carotenoids, phycobilins, polyphenols, and vitamins. Romay and others (1995) tested phycocyanin, a pigment found in blue-green algae, for its antioxidant effects. Phycocyanin was evaluated *in vitro* by using luminol-enhanced chemiluminescence (LCL). Luminol reacts with 3 different free radical species ($O^-{}_2$, $OH^\bullet$, $RO^\bullet$) and emits a luminous signal that can be measured before and after adding the antioxidant. Antioxidant activity was also assayed *in vivo* using the glucose oxidase-induced inflammation in mouse paw. The diminution of the luminecence indicated that phycocyanin is able to scavenge $OH^\bullet$ and $RO^\bullet$. This was confirmed with the *in vivo* reduction of edema caused by inflammation.

Besides their use in the food and pharmaceutical industries, algal antioxidants are used in the cosmetic industry in anti-aging products (Cornish and Garbary 2010). Guerin and others (2003) identified a carotenoid pigment (astaxanthin) found in the microalga *Haematococcus pluvialis* which is able to act as a strong coloring agent and a potent antioxidant. It was proposed that this compound could provide protection against inflammation, cancer, and aging, and also improve immune responses.

Anticardiovascular effects

Fish consumption is known to have a beneficial effect on CDV and CHD mainly due the PUFAs in fatty fish. Many studies have been conducted to prove the relation between fish consumption and decreasing CDV and CHD. It has been shown that populations that consume the most marine products like Alaskans and the Japanese suffer less from heart diseases (Kinsella 1989).

Another study showed that Mediterranean people who consume high amounts of seafood (as part of a Mediterranean diet) showed

Table 9–Minerals in some seafood.

Mineral (mg/100 g)	*Labeo pangusia*	*Ompok bimaculatus*	Seaweed *Hypnea valentiae*	Microalga *Chlorella vulgaris*
Ca	9.70	24.3	–	106
Cu	0.500	–	–	4.88
Mg	56.6	107	38.7	282
Mn	0.500	0.132	3.7	–
K	234	121	746	986
Na	58.9	103	–	129
Fe	5.97	1.71	–	147
Zn	3.75	0.921	3.1	10.2
Reference	Hei and Sarojnalini (2012)		Rohani-Ghadikolaei and others (2012)	Yusof and others (2011)

reduced CHD mortality because omega-3 fatty acids decrease the risk factors associated with triglyceride concentrations, blood pressure, platelet aggregation, and heart arrhythmias (Juturu 2008; Chan and Cho 2009). In addition, fish intake in the Mediterranean has also been associated with less severe symptoms of depression in adults and less asthma and respiratory allergies in children (Lloret 2010). Omega-3 PUFAs also protect against the development of certain cancers such as mammary (Zheng and others 2013) and prostate cancers (Berquin and others 2007).

Several epidemiological studies have shown correlations between fish intake and mortality from heart diseases. The people who at least eat some fish weekly had a lower CHD mortality rate than those who ate none. After collecting the data, it was concluded that there was an inverse association between fish consumption and death from CHD (Daviglus and others 1997; Kris-Etherton and others 2003; Mozaffarian and others 2003; Holub and Holub 2004; Mozaffarian and Wu 2011). Zhang and others (1999) have reported that fish consumption was associated with a reduced risk of ischemic heart disease and stroke mortality. In addition, Mizushima and others (1997) reported a dose–response relationship between the frequency of weekly fish intake and reduced CVD risk factors (such as obesity, hypertension, glycohemoglobin, and ST-T segment changes on the ECG).

For centuries, many populations in Asia (China, Korea, and Japan) have consumed macroalgae that can be a reservoir for unique and interesting biologically active compounds. Hypertension is one of the major risk factors in CVD. Hypotensive peptides derived from marine and other sources (soy, meat, egg, and cereal) have already been incorporated into functional food such as beverages and soups (Fitzgerald and others 2011). Moreover, many enzymes such as the angiotensin-converting enzyme I (ACE-I) are known to increase blood pressure, a risk factor for the development of CVD. Chemically synthesized ACE-I inhibitors, including captopril (capoten), enalopril, alcacepril, and lisinopril, are often prescribed for the treatment of high blood pressure. However, natural ACE inhibitors are safer than the existing artificial inhibitors because they tend to have fewer side effects. For instance, peptides derived from macroalgae have been shown to have hypotensive effects in the human circulatory system, specifically as an ACE-I inhibitor (Kim and Wijesekara 2013). In the past, the primary source of bioactive peptides has been dairy products, but the variety of macroalgae represent a reservoir of potential peptides that may be able to combat illness such as CVD. Moreover, omega-3 PUFAs, such as EPA and DHA from microalgae, are used in the treatment of heart and inflammatory diseases.

Impact on prebiotics

Macroalgae contain various polysaccharides that could be used as prebiotic compounds for health applications. Different polysaccharides are found in all the species. Chlorophyta contains highly complex sulfated heteropolysaccharides. Alginates, fucans, and laminarin are found in brown algae. Agar and carrageenans are also extracted from red algae. The benefits of macroalgal polysaccharides have been shown *in vitro* and *in vivo*. The results were promising as laboratory animals have been shown to have increased numbers of *Bifidobacterium* and *Lactobacillus* (Kuda and others 2005; Hu and others 2006; Wang and others 2006). Other parameters indicating a prebiotic activity are the pH of the cecal content, organic acid concentrations, and fecal weight (Wang and others 2006; Ishihara and others 2010). To be considered prebiotic, a compound must possess 3 criteria: first, it must not be digested in the upper gastrointestinal tract (GIT); second, it must be a selective substrate for the growth of beneficial bacteria; and, third, it must have beneficial effect on the host's health. Pathogenic and beneficial bacteria coexist in the GIT, but research is focusing on changing this composition to a more beneficial equilibrium, by decreasing the potentially harmful bacteria while favoring the developement of other species that have advantageous results on the body (increase resistance to infection, reduce risk of colon cancer, and reduce risk of obesity) (O'Sullivan and others 2010). In addition, prebiotics have been shown to increase the absorption of Ca and Mg, influence blood glucose levels, and improve plasma lipids (Al-Sheraji and others 2013).

Influences on anti-inflammatory activity

The anti-inflammatory effects of seafood are due to the fact that the PUFAs, especially omega-3, are able to inhibit certain inflammation mediators (Calder 2009). Several studies indicate that by increasing the ratio of omega-3 to omega-6 fatty acids in the diet, inflammation is decreased. In fact, eicosanoids derived from omega-6 PUFAs (such as AA) have pro-inflammatory and immunoactive functions, while eicosanoids derived from omega-3 PUFAs (EPA and DHA) have anti-inflammatory properties. Unfortunately, the Western food has a much bigger ratio of omega-6 PUFAs compared with omega-3 PUFAs (Calder and Grimble 2002; Wall and others 2010).

Preclinical and clinical research has shown that consumption of fish oils, which contain EPA and DHA, have an effect on inflammation. The prostaglandins and leukotrienes which are formed from EPA by cyclooxygenases (COXs) and lipoxygenases (LOXs) are less pro-inflammatory than those derived from AA (omega-6) (Moreillon and others 2012). For that reason, the increase of the (DHA + EPA)/AA ratio deceases the inflammatory mediators. The omega-3 fatty acids are also known to inhibit the activity of the pro-inflammatory transcription factor nuclear factor κB (NF-κB), which induces the expression of many pro-inflammatory genes that encode adhesion molecules (for example, intercellular adhesion molecule 1), cytokines, chemokines, and other effectors of the innate immune response (Zwart and others 2010; Rahman and McFadden 2011). Moreover, fish oils have been tested as alternatives for nonsteroidal anti-inflammatory drugs (NSAID). Different research has been conducted on patients with rheumatoid arthritis (RA), which is an autoimmune diseases characterized by flare-ups of arthritis involving small and large joints. It is mediated by an exaggerated production of eicosanoids and cytokines (Adam and others 2003). Replacing the NSAID eliminates side effects such as gastric ulcers, bleeding, myocardial infarctions, and even death. In many studies, patients with RA were divided into 2 groups: one received an anti-inflammatory diet which included omega-3 and the other group received the placebo. They were also asked to reduce their NSAID dosage. After a few months, the results showed that fish oil was anti-inflammatory for the patients with RA. Omega-3 fish oil appears to be a safer alternative to NSAID for reducing arthritic pain (Lau and others 1992; Kremer and others 1995; Maroon and Bost 2006; Mehra and others 2006; Galarraga and others 2007).

The anti-inflammatory property is found in algae as well. Photosynthetic pigments are known to have anti-inflammatory activities. For example, fucoxanthin (Fx) isolated from brown algae reduces the prostaglandin E_2 (PGE_2) production and inhibits cyclooxygenase 2 (COX-2) protein expressions (Heo and others 2010). Pheophytin isolated from *Enteromorpha prolifera* has been reported to suppress the 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced superoxide radical ($O_2^{\cdot-}$) and the inflammatory responses in mouse macrophages (Pangestuti and Kim 2011b). The polysaccharide of the brown alga *Turbinaria ornate* is another functional ingredient that is considered as an anti-inflammatory agent. In fact, Ananthi and others (2010) studied this effect *in vivo* using a carrageenan-induced paw edema in rats and a vascular permeability test in mice. In both cases, the polysaccharide was administered orally and the results were encouraging. For the first group, the paw edema was reduced and the vascular permeability reduced. The sulfoglycolipidic fraction (SF) was isolated from the red alga *Porphyridium cruentum*. It has been shown to have an anti-inflammatory effect. A fatty acid analysis showed that SF contained large amounts of palmitic acid (26.1%), AA (6.8%), and EPA (16.6%), and noticeable amounts of the 16:1 omega-9 fatty acid (10.5%) (Bergé and others 2002).

Health benefits related to preventing obesity

Obesity is a chronic metabolic disorder caused by an imbalance between energy intake and expenditure. Excessive fat accumulation leads to many health problems such as high blood pressure, type 2 diabetes mellitus, high blood cholesterol levels, CHD, and sleep apnea (Dietz 1998; Must and others 1999). Obesity also has a negative social effect. Obese individuals may be stigmatized and face multiple forms of prejudice and discrimination because of their weight (Puhl and Heuer 2009). The increasing incidence of obesity has become a medical problem around the world. It has been shown that fish oil can assist in weight loss. Even if the human studies are relatively few and have generally been conducted over short time periods (Buckley and Howe 2009), the results obtained can be used to conclude that fish consumption can help with obesity.

Gunnarsdottir and others (2008) conducted a study on 324 men and women, aged between 20 and 40 years, who came from different countries (Spain, Iceland, and Ireland). They were given a diet with sunflower oil or with fish oil. Various measurements were made: total cholesterol (TC), high-density lipoprotein (HDL), LDL, cholesterol, triacylglycerol (TG), and anthropometric measurements. The weight-loss diet with fish oil resulted in the greater TG and TC reduction. HDL remained steady.

Another interesting study compared the body mass index (BMI) between people who received different diets (fish-eaters compared with meat-eaters). The participants were men and women aged 20 to 97 years. The people who ate fish had the lower BMI (Spencer and others 2003).

DHA and EPA prevent obesity by, for example, inhibiting key enzymes responsible for lipid synthesis, such as fatty acid synthase and stearoyl-CoA desaturase-1. These enzymes enhance lipid oxidation and thermogenesis, and they prevent free fatty acids from entering adipocytes for lipogenesis. PUFAs also exert suppressive effects on several key factors involved in adipocyte differentiation and fat storage, as well as improving insulin sensitivity (Li and others 2008). Animal studies suggest that increased consumption of EPA and DHA can protect against obesity in animals exposed to an obesogenic diet and reduce body fat when they are already obese. A study on mice by Arai and others (2009) tested various groups of mice by feeding them lard/safflower oil or fish oil. In this research, the level of plasma lipids, hepatic triglycerides, and cholesterol, as well as the hepatic mRNA expression of lipogenic and lipidolytic genes, was measured. The results were positive for the fish-oil-fed group which had the lower body weight. In addition, the hepatocytes of the lard/safflower-fed mice were filled with numerous fat droplets while fat accumulation was inhibited with the fish oil fed mice.

Algae are also considered to have anti-obesity activity, especially the brown algae *U. pinnatifida, Hijikia fusiformis*, and *Sargassum fulvellum,* which are part of the Asian diet but are also consumed in many other places. Fucoxanthin (Fx) has been reported to have an antidiabetic effect (Maeda and others 2009), which has an unique structure containing an allenic bond and a 5,6-monoepoxide (Løvstad Holdt and Kraan 2011), whose structure has been linked to the anti-obesity effect (Miyashita 2009). The molecular mechanism of Fx action has been identified after several *in vivo* studies. A nutrigenomic research showed that Fx induces uncoupling protein 1 (UCP1) expression in white adipose tissue (WAT) mitochondria leading to oxidation of fatty acids and heat production in the WAT (Løvstad Holdt and Kraan 2011). UCP1 is considered to be a key anti-obesity enzyme since its expression contributes to the total organism's energy expenditure, and its dysfunction leads to obesity (Maeda and others 2007). Fx induced a clear UCP1 signal and its mRNA was detected using Western and Northern blot analyses of abdominal WAT (Maeda and others 2008). Further experiments with obese rats and mice showed that the Fx-fed groups always had improved insulin resistance and decreased blood glucose (Miyashita 2009; Woo and others 2009). In another study, purified Fx and macroalgae lipids containing Fx were compared, in which the latter induced a higher expression of UCP1 when Fx was present with the other components, especially lipids (Maeda and others 2007, 2009). Furthermore, Miyashita (2009) noticed a synergistic action of omega-3 fatty acids on the anti-obesity effect of Fx.

Fucoidan, as seen earlier, is able to reduce lipid accumulation by stimulating lipolysis which decreases weight gain. Park and others (2011) have studied the lipolitic activity of fucoidan by examining the protein level of the hormone-sensitive lipase (HSL) and the phosphorylated HSL (p-HSL) using Western blots. The HSL is one of the most important targets of lipolytic regulation. The subsequent phosphorylation and activation of HSL resulted in an increase in the hydrolysis of stored triacylglycerols into monoacylglycerols and free fatty acids. The level of HSL and p-HST had increased compared to the controls after fucoidan treatment of differentiated 3T3-L1 adipocytes.

Neuroprotective effects of seafood

Neurodegenerative diseases are considered to be one of the most common causes of death among the elderly (Bjarkam and others 2001). For this reason, scientists have been looking for novel neuroprotective agents to prevent apoptosis, neuronal cells damage, dysfunction, and deterioration of the central nervous system (CNS) (Zarros 2009). Although synthetic compounds have been used to act as neuroprotectives, there are side effects including anxiety, nervousness, drowsiness, mouth dryness, or tiredness (Pangestuti and Kim 2011a). There is a low incidence of neurodegenerative diseases in East Asia, which has been linked to their high fish and marine algae consumption. Most of the studies involve *in vitro* or animal models. However, there are not enough data currently from clinical trials (Cole and others 2009). Calon and Cole (2007) reported the association between DHA consumption or high DHA blood levels and a lower risk of developing Alzheimer's disease (AD) in the later stage of life. The work showed that animal models of AD are more vulnerable to DHA depletion than controls and that DHA exerts a beneficial effect against pathological signs of AD, including amyloid β (Aβ) peptide accumulation, cognitive impairment, synaptic marker loss, and hyperphosphorylation of tau. Another study conducted by Cole and others (2009) confirmed the results. A reduced intake of omega-3 fatty acids or fish consumption was correlated with an increased risk for age-related cognitive decline or dementia diseases like AD. DHA can be protective against AD using different mechanisms such as the limitation of the production and accumulation of the Aβ peptide toxin that is widely believed to drive the disease. Omega-3 fatty acids have shown to be effective with rats that have epilepsy by preventing hippocampal damage (Ferrari and others 2008). To demonstrate the neuroprotective activity, an animal immunocytochemical study using parvalbumin (PV) and calretinin (CR) distribution as markers was performed. The results were positive for the group that received omega-3 PUFAs as a larger number of PV-positive neurons and CR-positive neurons were observed (Ferrari and others 2008).

Marine algae represent another potential candidate for neuroprotective agents. Jin and others (2006) showed neuroprotective activity with *Ulva conglobata*. They tested methanol extracts of this alga and the effect on glutamate-induced neurotoxicity in murine hippocampal HT22 cells. The neurotoxicity was attenuated. The inhibitory effects of methanol extracts of *Hypnea valentiae* and *Ulva reticulata* seaweeds were studied *in vitro* by incubating various concentrations of the extracts with acetylcholinesterase (AChE) or butyrylcholinesterase (BuChE) and evaluating their activities using Ellman's colorimetric method. Kinetic parameters such as IC_{50}, K_i, and V_{max} were also obtained. The purpose of this study was to find a natural alternative to treat AD. The goal with most drugs used against AD is to enhance acetylcholine levels in the brain by inhibiting AChE. The inhibitory activities of the extracts were comparable to the standard drug Donepezil. An anticholinesterase activity was noticed in all of the extracts (Suganthy and others 2010). Fucoidan can inhibit the neuronal death induced by Aβ_{1-42}. Fucoidan acted by blocking the activation of caspase-3, -8, and -9, which are part of one of the enzyme systems responsible for apoptosis (Pangestuti and Kim 2011a). In addition, Lee and others (2007) reported that a growth in cell proliferation of human neuroblastoma (SH-SY5Y) cells was incited by Aβ following a fucoidan treatment.

Health benefits for preventing cancer

Cancers can be defined as diseases where cells stop responding normally to chemical signals from other cells. Instead of stopping, they continue to grow and divide. Those abnormal cells may kill by invading and subverting normal tissues (Silverstein and others 2006). It becomes important to look for molecules that are capable of triggering apoptosis (programmed cells death). Cell deregulation, either the loss of pro-apoptotic signals or the increase in anti-apoptotic signals (or both), can lead to a variety of pathological conditions such as cancer. Therefore, encouraging apoptosis is a major target for anticancer therapy (Kim and Taylor 2011; Kim and others 2013). Several studies have been conducted to prove the relation between cancer prevention and fish consumption. Picot and others (2006) have studied the antiproliferative activity of FPH *in vitro* on 2 lines of human breast cancer cells. Inhibition of the proliferation has been observed and an analysis of the hydrolysates' composition showed that they contained a complex mixture of free amino acids and peptides of various molecular weights ranging up to 7 kDa along with smaller amounts of lipids and NaCl.

The antitumoral and antimetastasis activities of omega-3 fatty acids found in fish oil were tested on mice bearing the Lewis lung carcinoma 3LL. The mice were fed a diet rich in omega-3 fatty acids and few parameters such as tumor growth, body weight, and lung metastasis were followed. The control diets contained soybean oil. These diets were tested in combination with the conventional cytotoxic agent cisplatin. Fish oil suppressed tumor growth and reduced the metastatic load. In the same study, it was noticed that the effects of omega-3 PUFA may be increased by adding vitamins E and C (Yam and others 2001). The same positive results of diets containing fish oil have been reported by others using other markers, such as the decreased growth of DU-145 human prostatic tumor cells in nude mice (Karmali and others 1987). Fish oil has been shown to increase the effectiveness of cancer chemotherapeutic drugs in MDA-MB231 breast cancer xenografts in mice (Hardman and others 2001).

Health benefits from unusual marine organisms

Another source of bioactive compounds is ascidian organisms, which are known to have anticancer activity. One of these components, trabectidin, extracted from a Caribbean ascidian, has been approved as an anticancer agent for soft tissue sarcomas and ovarian cancer (Carter and Keam 2007; Gennigens and Jerusalem 2011). Another chemical compound, aplidine, derived from the Mediterranean ascidian *Aplidium albicans*, shows strong anticancer properties with potential use in treatment of prostate, gastric, breast, and colon cancers. This molecule has been used in clinical trials (Brandon and others 2007). A research conducted by Broggini and others (2003) tested the effect of aplidine on the human leukemia cell line MOLT-4 and showed that aplidine inhibited the growth and induced apoptosis. The aplidine inhibited some factors necessary for the growth of these cells such as vascular endothelial growth factor (VEGF) secretion, which blocks the receptors VEGF/VEGFR-1

In addition to their antitumor action, some ascidians have other activities like antimicrobial activity (Liu and others 2005; Sivaperumal and others 2010). Moreover, many species of sponges from around the world have numerous compounds with various activities including antiviral, antimalarial, and antifungal.

Table 10–Summary of the health benefits of seafood.

Category	Functional ingredients	Source	Health benefits	References
Proteins	Chrysophsins	*Chrysophrys* (*pagrus*) *major*	Antimicrobial	Iijima and others (2003) Fulmer and others (2010)
	Parasin I, Pelteobagrin	Catfish (*Parasilurus asotus, Pelteobagrus fulvidraco*)	Antihypertensive ACE inhibitor Antimicrobial	Theodore and Kristinsson (2007) Ma and others (2008) Ryan and others (2011) Park and others (1998)
	Peptides	Bonito	ACE inhibitor	Ryan and others (2011) Yoshikawa and others (2000) Yokoyama and others (1992) Curtis and others (2002)
	FPH	Tuna	ACE inhibitor Antioxidant	Ryan and others 2011) Kohama and others (1988) Lee and others (2010b) Hsu (2010) Chalamaiah and others (2012)
	Peptides	Sardine	ACE inhibitor Antioxidant	Ryan and others (2011) Otani and others (2009) Najafian and Babji (2012)
	Peptides	Cuttelfish	Antihypertensive Antioxidant	Amado and others (2013)
	FPH	Salmon	ACE inhibitor Antioxidant Anticancer	Ryan and others (2011) Ono and others (2003) Ngo and others 2012) Chalamaiah and others (2012) Picot and others (2006)
	Peptides	Shrimp	ACE inhibitor Calcium-binding	Ngo and others (2012) Huang and others (2011)
	FPH	Shark meat	ACE inhibitor	Ngo and others (2012)
	Misgurin	Loach (*Misgurnus anguillicaudatus*)	Antimicrobial	Park and others (1997)
	FPH	Pacific hake (*Merluccius productus*)	Antioxidant	Samaranayaka and Li-Chan (2008)
	Protein hydrolysates	*Porphyra tenera*	ACE inhibitor Antioxidant Antitumor	Lee and others (2005) Harnedy and FitzGerald (2011)
	Protein hydrolysates	*Sargassum horneri*	Antioxidant Anticoagulant	Harnedy and FitzGerald (2011) Athukorala and others (2007)
	Protein hydrolysates	Prawn	Antioxidant	Suetsuna (2000)
Lipids	Omega-3 PUFA (DHA and EPA)	Herring	Anticardiovascular Anti-obesity Antitumor	Yam and others (2001) Rasmussen and Morrissey (2007) Li and others (2008)
	Omega-3 PUFA (DHA and EPA)	Salmon	Anticardiovascular Anti-obesity	Rasmussen and Morrissey (2007) Li and others (2008)
	Omega-3 PUFA (DHA and EPA)	Sardine	Anticardiovascular Anti-obesity	Rasmussen and Morrissey (2007) Li and others (2008)
	Omega-3 PUFA (DHA and EPA)	Tuna	Anticardiovascular Antitumor	Yam and others (2001) Rasmussen and Morrissey (2007)
	Omega-3 PUFA (DHA and EPA)	Mackerel	Anticardiovascular Antidementia Anti-obesity	Rasmussen and Morrissey (2007) Li and others (2008) Cole and others (2009)

(*Continued*)

Table 10–Continued.

Category	Functional ingredients	Source	Health benefits	References
	Omega-3 PUFA (DHA and EPA)	Bonito	Anticardiovascular Antidementia	Mozaffarian and Wu (2011) Rasmussen and Morrissey (2007) Cole and others (2009)
	Omega-3 PUFA (DHA and EPA)	Cod	Anticardiovascular Anti-inflammatory	Rasmussen and Morrissey (2007) Galarraga and others (2007)
	Omega-3 PUFA (DHA and EPA)	Krill (*Euphausia superba*)	Anticardiovascular Cholesterol reducing	Rasmussen and Morrissey (2007) Bunea and others (2004)
	Omega-3 PUFA (DHA and EPA)	*Undaria pinnatifida*	Antiallergic	Vo and others (2012) Li and others (2008) Kumari and others (2010)
	Omega-3 PUFA (DHA and EPA)	*Ulva pertusa*	Antiallergic	Vo and others (2012) Li and others (2008) Kumari, and others (2010)
	Omega-3 PUFA (DHA and EPA)	Ascidian	Anticancer	Mayer and Gustafson (2006)
Polysaccharides	Polysaccharide	Cuttlefish (*Sepiella maindroni, Euprymna berryi*)	Antimutagenic Antimicrobial	Liu and others (2008) Shanmugam and others (2008)
	Chitin and chitosan	Crustaceans (shrimp, crab, crayfish)	Antimicrobial Anticaner Anti-inflammatory Hypocholesterolemic	Tsai and others (2008) Xia, and others (2011) Mayakrishnan and others (2013) Shahidi and Abuzaytoun (2005)
	Polysaccharide	Squid (*Ommastrephes bartrami*)	Antitumor	Chen and others (2010)
	Porphyran	Nori (*Porphyra tenera*)	Antioxidant	Lordan and others (2011)
	Spirulan	*Arthrospira platensis*	Antiviral Anticoagulant	Hayashi and others (1996) Rechter and others (2006) Majdoub and others 2009)
	Fucoidan	*Laminaria japonica*	Anticoagulant Antioxidant	Wijesekara and others (2011) Wang and others (2010)
	Galactan	*Codium fragile*	Antiviral Immunostimulating	Wijesekara and others2011) Lee and others (2010a)
	Mannans	*Nemalion helminthoides*	Antiviral Immunomodulatory	Wijesekara and others (2011) Pérez-Recalde and others (2014)
Minerals	Ca	*Ulva pertusa, Scytosiphon lomentaria, Chaetomorpha crassa,* Fish bones	Strengthening of teeth and bone Anti-osteoporosis	Venugopal (2008) Nguyen and others (2011) Ito and Hori, (1989)
	I	*Ascophyllum nodosum, Laminaria digitata, Porphyra umbilicalis, Palmaria palmata*	Antigoiter Reduce risk of abortion, stillbirth	Li and others (2009) Catarina Guedes and others (2013) MacArtain and others (2007)
	Mg	*Ascophyllum nodosum* *Laminaria digitata* *Himanthalia elongata*	Neuroprotective Antidepressant Antiasmatic	Eby and Eby (2006) Szewczyk and others (2008) Watson and others (2012)
	Zn	*Eisenia bicyclis* *Hizikia fusiforme* *Sargassum ringgoldianum* *Enteromorpha compressa*	Antidepressant Reproductive health (Decrease risks of abortion, malformations and retarded growth)	Szewczyk and others (2008) Favier (1992) Rupérez (2002)
Vitamins	Vitamin B_{12}	*Porphyra tenera* *Sargassum fulvellum*	Anti-aging Antianemia Promotion of neurite outgrowth	Ravishankar and others (2005) Lordan and others (2011) Pangestuti and Kim (2011a, 2011b)

(*Continued*)

Table 10–Continued

Category	Functional ingredients	Source	Health benefits	References
	Vitamin C	*Gelidiella acerosa* *Padina pavonica* *Ulva reticulata,* *Laminaria digitata* *Porphyra umbilicalis* *Palmaria palmata*	Antioxidant Strengthening of the immune system	Packer (1997) Witting and Stocker (2003) Haidara and others (2006) Anantharaman and others (2011)
	Vitamin E	*Ascophyllum nodosum* *Porphyra umbilicalis* *Laminaria digitata* *Undaria pinnatifida* *Palmaria palmata*	Antioxidant Prevention of CVD	Ravishankar and others (2005) MacArtain and others (2007)
	Vitamin D	Fish oil	Antirickets Anti-osteomalacia	Luten (2009)
Photosynthetic pigments	Carotenoids: β-carotene, astaxanthin, zeaxanthin and lutein	Dunaliella salina Haematococcus pluvialis Nannochloropsis oculata Chlorella sorokiniana	Skin health benefits Antioxidant Protect against eye diseases (cataracts and macular degeneration) Anticancer	Roberts (2013) Mares-Perlman and others (2002) Jacob and Burri (1996) Jamieson (2013)
	Chlorophylls	All classes of algae and cyanobacteria	Anticancer	Marquez and Sinnecker (2007)
	Phycobilins: phycoerythrin and phycocyanin	Cyanobacteria (Spirulina, Nostoc, Anabaena) Red Algae (Porphyridium cruentum)	Antioxidant Anticancer	Shanab and others (2012) Hirata and others (2000)

Avilés and Rodriguez (2010) studied extracts from different sponges that showed both antiplasmodial and antituberculosis activities. It was observed that the extracts inhibited the *Plasmodium falciparum* W2 strain by more than 50% at both 250 and 50 μg/mL concentrations and showed >90% growth inhibition of *Mycobacterium tuberculosis* H37Rv at 128, 64, and 32 μg/mL. In Italy, the Mediterranean sponge *Rhaphisia lacazei* showed antiproliferative activity against human broncopulmonary cancer cells (Casapullo and others 2000).

A number of chemicals derived from opisthobranch organisms showed bactericidal, antifouling, or antitumor activities along with several other marine species (gorgonians, Bryozoans). For instance, the antifungal activity of the Mediterranean sea cucumber, *Holothuria polii,* has recently been shown (Lloret 2010). After using the well diffusion test with casitone agar medium, the aqueous and methanolic extracts from *Holothuria polii* showed an effect against several fungi such as *Aspergillus fumigates* (Ismail and others 2008).

Recently, Vo and others (2012) showed that marine algae-derived fucoidan is effective as an anticoagulant agent similar to that of heparin, which has been used as an anticoagulant drug for many years. However, due to heparin's side effects such as excessive bleeding, thrombocytopenia, mild transaminase elevation, and hyperkalemia, there is a need for alternatives. All of the health benefits from seafood mentioned in this paper are summarized in Table 10.

Conclusion

Marine resources offer important bioactive molecules that have advantages on the human body. They can be applied in many fields such as the drug, cosmetic, and food industries. Functional foods can easily be developed from marine products since they are widely available and they have the ability to prevent certain diseases and cure some illnesses. Various kinds of seafood are consumed as nutritionally beneficial food. The sea offers an enormous resource for finding novel compounds, and it is considered as the largest remaining reservoir of natural molecules that may be used as functional ingredients in the food industry. Consequently, efforts should be made to develop marine functional foods responsibly, since their consumption could result in the decrease of the occurrence and gravity of chronic diseases.

Abbreviations

AA: Arachidonic acid
Aβ: Amyloid beta
ACE-I: Angiotensin-converting enzyme I
AChE: Acetylcholinesterase
AD: Alzheimer's disease
Ala: Alanine
Arg: Arginine
Asp: Aspartic acid
BMI: Body mass index
BuChE: Butyrylcholinesterase
Ca: Calcium
CHD: Coronary heart disease
CR: Calretinin
Cu: Cuivre
CVD: Cardiovascular disease
Cys: Cysteine
DHA: Docosahexaenoic acid
ECG: Electrocardiogram
EPA: Eicosapentaenoic acid
Fe: Iron
FPH: Fish protein hydrolysate
Fx: Fucoxanthin
GIT: Gastrointestinal tract
GLA: γ-Linolenic acid
Glu: Glutamic acid

Gly: Glycine
HDL: High-density lipoprotein
His: Histidine
HSL: Hormone-sensitive lipase
I: Iodine
Ile: Isoleucine
K: Potassium
LDL: Low-density lipoprotein
Leu; leucine
Lys: lysine
Met: Methionine
Mg: Magnesium
Mn: Manganese
Na: Sodium
NSAID: Nonsteroidal anti-inflammatory drug
Phe: Phenylalanine
p-HSL: Phosphorylated hormone-sensitive lipase
Pro: Proline
PUFA: Polyunsaturated fatty acid
PV: Parvalbumin
RA: Rheumatoid arthritis
ROS: Reactive oxygen species
Ser: Serine
SF: Sulfoglycolipidic fraction
SFA: Saturated fatty acid
TC: Total cholesterol
TG: Triacylglycerol
Thr: Threonine
Trp: Tryptophan
Tyr: Tyrosine
UCP-1: Uncoupling protein 1
Val: Valine
VEGF: Vascular endothelial growth factor.
WAT: White adipose tissue
Zn: Zinc

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