

## Marine Nutraceuticals

Asha K.K. and Suseela Mathew

Biochemistry and Nutrition Division

ICAR-Central Institute of Fisheries Technology, Cochin

Email: asha.santhosh5@gmail.com

Increasing consumer awareness about the relation between diet, health, and disease prevention has triggered research and development of new functional foods over the last years. The ageing of population, decrease in quality of life due to stress, high incidence of lifestyle diseases (cardiovascular disease, obesity, cancer, diabetes, and allergies) represent the driving forces in the search for different foods and diets that promote healthy active ageing, improve well-being, and prevent the incidence of many diseases. Food is known to play an important role in prevention or onset and progression of chronic diseases such as atherosclerosis, obesity, diabetes, hypertension, osteoporosis, cancer, and cardiovascular disease. The marine environment is a huge source of healthy food, including seaweeds with several marine species containing a plethora of chemicals, many of them with biological properties referred to as bioactive compounds. These chemicals can be extracted and incorporated in several food matrices leading to development of new functional foods

According to Health Canada, a functional food is similar to a conventional food, which is consumed as part of an usual diet that either provides physiological benefits or reduces the risk of chronic disease beyond its basic nutritional functions. According to the Food Agriculture Organization (FAO), functional foods are those foods similar to conventional food in appearance, intended to be consumed as part of a normal diet containing biologically active compounds that offer potential for enhanced health or reduced risk of disease. Foods that besides their nutritional effects, have demonstrated that they improve the state of health or well-being, reduce the risk of disease, as well as benefit one or more functions of the human organism are considered as functional food. Functionality could be intrinsic to a feature introduced in the food matrix, improving health or reducing any adverse health effect, accomplished, for example, by

- i) Elimination or promotion of a chemical change of a harmful ingredient.
- ii) Addition of new health-promoting food ingredients or probiotic microorganisms in an effective concentration.
- iii) Addition of an existing health-promoting food ingredient, increasing its concentration.
- iv) Increasing the bioavailability or stability of the health-promoting food ingredient.

The characteristics of the marine environment such as temperature, salinity, light, pressure, and nutrients are of special importance, since due to their broad range of values marine organisms had to evolve some protective mechanisms and metabolites. Crustaceans, macro or microalgae, fish, and fish by-products, as well as bacteria and fungi are the most representative groups of organisms of potential interest as healthy food or as a source of functional ingredients, which include polysaccharides, chitin, proteins and peptides, lipids, pigments, vitamins, minerals, and phenolic compounds.

The term “nutraceutical” was first coined by Stephen DeFelice in 1989 which consists of two words nutrient (nurturing element) and pharmaceutical (medicinal component). It had gained importance in the recent years with increase in the field of health based research. The nutraceuticals are the substances which as a whole or as a part are delivered in the form of dietary supplements/ingredients that are clinically proven to hold health benefits (prevention and treatment of disease). Marine nutraceuticals refer to the compounds derived from sea. The potential of the marine nutraceuticals in human health had already been established

### **Types of marine nutraceuticals**

Marine nutraceuticals can be broadly classified as follows: Marine lipids (animal origin and microalgal origin), Polysaccharides derived from macro algae, Marine probiotics, Marine natural pigments, Chitin and other related products, Bioactive marine peptides/enzymes and Vitamins.

#### **I. Marine lipids:**

##### **a. Lipids of animal origin**

Marine lipids are originated either from fish, crustaceans or other aquatic organisms. Phospholipids, sterols, triacyl glycerols, wax esters and their metabolic products form the main composition of marine lipids. Minor amounts of used lipids like glycerol esters, glycolipids, sulpholipids and hydrocarbons are also present in marine lipids. Marine lipids derived mainly from fatty fish flesh, lean fish liver and blubber of marine mammals. Fish oils and oils from marine mammals are rich sources of Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA). EPA and DHA have anti-inflammatory properties. Shrimp contains 1.8-2.6% of lipids based on wet weight basis. Crustaceans contain much sphingomyeline which is having anti-bacterial and anti-tumour property. Lobsters and crabs contain 0.8-2.0% of lipid. The lipid content of bivalves is below 1.0% but which is rich in polyunsaturated fatty acids (PUFA) i.e.50-64%. Lipids contain interesting health promoting compounds like sterols and alpha-tocopherols. Highly unsaturated fatty acids (HUFA) are found to reduce the effect of environmental change on the nervous system thereby reducing the stress in fish.

##### **b. Lipids of microalgal origin**

Lipids derived from marine microalgae have a wide range of applications in larval nutrition of aquaculture especially for enrichment of live feeds. They also exhibit various properties like anti-inflammatory, anti-allergic, anti-viral and therapeutic. The wide spectrum of the properties is due to the presence of various components like PUFA, HUFA and other substances. Various microalgal originated lipid/fatty acids and their activities are given in Table 1

Table.1

Lipid/Fatty acid	Activity
Eicosapentaenoic acid (EPA)	Nutraceutical; antimicrobial and anti-inflammatory
alpha-Linolenic acid (GLA)	Integrity of tissue and delay of aging
Arachidonic acid (ARA)	Aggregative and vasoconstrictive of platelets
Docosahexaenoic acid (DHA)	Nutraceutical and brain development

Brassicasterol and stigmasterol	Hypercholesterolemic
alpha-amino-butyric acid(GABA)	Neurotransmitter , antioxidant and anti-inflammatory
Okadaic acid	Antifungic, secretion of nerve growth factor (NGF)
Microcolin-A	Immunosuppressive

## II. Polysaccharides derived from macro algae

Seaweeds contain higher amounts of the polysaccharides like agar, alginates and carrageenans. These act as food fiber and are collectively called phycocolloids or hydrocolloids. Being rich in fiber, seaweeds exhibit health benefits like reducing the absorption of toxins, anti-carcinogenic and antioxidant properties. In addition to the phycocollids, seaweeds are sources of biologically active phytochemicals like carotenoids, phycobilins, fatty acids, vitamins, sterols, tocopherol, phycocyanins and others. Some of the polysaccharides of the seaweeds and their properties are as follows:

Polysaccharide	Property
Fucoidan	Antioxidant, antiangiogenic and antitumor activities, anticoagulant, immunomodulating and Hypolipidemic, anti-inflammatory
Sphinganine amide and caulerpicin (green algae)	Antiviral activity
Carrageenan	Antibacterial, anti- tumour, antiviral and anti-inflammatory activities
Alginic acid and xylofucans	Antiviral activity
Hyperoxaluria	Potential blood anticoagulant agent
Sulfated polysaccharides	Antioxidant, antithrombin activity, antitumor, cell recognition and cell adhesion or regulation of receptor functions.
Alginate	Stimulates immune system, Reduces intestinal absorption, Modulates colonic microflora and elevates colonal barrier function

## III. Marine probiotics

Microbial diversity of marine environments is very rich and can be helpful to develop safe and effective probiotics. Novel marine probiotics can be an effective alternative for fighting the antibiotic resistance. Lactobacillus and Bifidobacterium are found to possess anti- mutagenic and immunomodulatory activity in host animal. Different

strains of marine probiotic bacteria are Lactobacillus (*L. casei*, *L. acidophilus*, *L. rhamnosus* GG (ATCC53013), *L. johnsonii* La-1), Bifidobacterium (*B. bifidum*, *B. longum*, *B. infantis*, *B. breve*, *B. adolescentis*), Leuconostoc spp. (*Ln. lactis*, *Ln. mesenteroides* subsp. *Cremoris*, *Ln. mesenteroides* subsp. *dextranicum*) and Streptococcus spp. (*S. salivarius* subsp. *thermophiles*). The problem posed during the development of new marine probiotics is the isolation and identification of potential strain. Application of biotechnological and molecular biological tactics is necessary for the development of marine probiotic strains for use of aquatic industry.

#### IV. Marine natural pigments

Marine macro and micro algae provide various types of the bioactive compounds. The most important and the striking feature of the marine algae is their natural pigments. The natural pigments of the marine algae provide food by photosynthesis and also provide the pigmentation. In addition to these, the natural pigments are also found to exhibit health benefits which make them one of the important marine nutraceuticals. The marine natural pigments and their health benefits are given in Table 3.

Natural pigments	Health benefits
Chlorophyll a	Antioxidant and antimutagenic
Pheophytin a	Neuroprotective, Antimutagenic and anti-
Pheophorbide a	Antioxidant
Pyropheophytin a	Antioxidant
Phycoerythrobilin	Antioxidant
Lutein, zeaxanthin and canthaxanthin	Antimutagenic and antioxidant
alpha-Carotene	Antimutagenic and food additive
Fucoxanthin	Antioxidant, anticancer, anti-inflammatory, anti-obesity, anti-angiogenic and Neuroprotective
Siphonaxanthin	Anticancer and anti-angiogenic
Phycocyanin	Anti-inflammatory and antioxidant
Astaxanthin	Strong antioxidant, anti-inflammatory and dietary supplement

#### V. Chitosan and its derivatives

Chitosan is a natural polymer derived from chitin and it is the second most abundant polysaccharide after cellulose. Chitosan possesses special properties for use in pharmaceutical, biomedical, food industry, health, and agriculture due to its biocompatibility, biodegradability and nontoxic nature. Through encapsulation, it is being used as a vehicle for nutraceutical compounds and pharmacological compounds.

### *Antibacterial activity*

Chitosan disrupts the barrier properties of the outer membrane of gram-negative bacteria due to ionic interaction between the cationic groups of the chitosan molecules and the anionic groups of the microbial cell membrane, which can rupture the cell membrane. Sulfuryl chitin, phosphoryl chitin and some chitin derivatives prepared by nitrous acid deamination of DAC, inhibited bacterial growth and increased cytotoxicity of a macrophage cell line. NTM-DAC had higher bacterial inhibition activity than carboxymethyl chitosan.

### *Antifungal activity*

Chitosan can also function as an antifungal agent by forming gas-permeable coats, interference with fungal growth and stimulation of various defense processes like, buildup of chitinases, production of proteinase inhibitors and stimulators of callous synthesis.

### *Antioxidant activity*

This property could be attributed to the ability of chitosan to chelate metals and combine with lipids. Derivatives of chitosan, namely, N,O-carboxymethyl chitosan, N,O-carboxymethyl chitosan lactate, N,O-carboxymethyl chitosan acetate and N,O-carboxymethyl chitosan pyrrolidine carboxylate had also exhibited the antioxidant activity.

## **VI. Bioactive marine peptides/enzymes**

Peptides refer to the specific protein fragments. The bioactive peptides act as sources of biological compounds (nitrogen and amino acids) and also have numerous potential physiological functions within the body. Some of the peptides may exhibit multifunctional properties like opioid, immunomodulatory, antibacterial, antithrombotic and antihypertensive activity (Kim, 2012). Bio functional peptides have a size range of 2 to 20 amino acid residues and are encrypted within the sequence of the parent protein and are released during fish processing. They can be formed either by acid or alkaline hydrolysis. The type of bioactive peptides formed is dependent on two factors: (a) the primary sequence of the protein substrate and (b) the specificity of the enzyme(s) used to generate such peptides. The major bioactivities of peptides are as follows: antihypertensive (ACE inhibitory) activity, antioxidant activity, antimicrobial activity, antihypoallergenic activity, cell immunity

Peptide bioactivity	Marine resources
ACE inhibitory activity	Big eye tuna (muscle), Alaska pollock, sea bream, yellow fin sole, oyster, shrimp, clam and sea cucumber
Antioxidant activity	Big eye tuna (muscle), Alaska pollock, yellow fin sole, horse mackerel (skin), croaker (skin), conger eel, hoki fish (skin), squid, oyster, mussel,
Antimicrobial activity	Oyster, American lobster, shrimp and sea urchin
Antihypoallergenic activity	Big eye tuna (muscle), seaweed, pipe fish (muscle) and sea cucumber
Cell immunity	Oyster

Proteins isolated from *Dunaliella*, *Phaeodactylum tricornutum* and *Arthrospira platensis* are having potent antioxidant and anti-inflammatory activity which can be effectively used in aquaculture practices. Similarly, enzymes (Superoxide dismutase and Carbonic anhydrase) derived from *Porphyridium*, *Anabaena*, *I. galbana* and *Amphidinium carterae* can also play an important role in regulating the metabolite waste (CO<sub>2</sub>).

## VII. Vitamins

Commercially produced cod liver oil is rich in vitamins A and D. Marine microalgae are also known to have good amount of alpha-carotene. Microalgae like, *Arthrospira*, *I. galbana*, *P. cruentum* and *Tetraselmis* are rich in vitamin C, K, A, E and alpha-carotene which possess strong antioxidant activity. Vitamin A (particularly provitamin A, alpha-carotene) and E (particularly alpha-tocopherol) serve as excellent antioxidants and free radical scavengers that protect cells from damage by oxidants. Research has shown that vitamin E has a number of extraordinary beneficial effects as a specific antioxidant, acting together with vitamin C and alpha-carotene, in improving antioxidant defenses in the body. Fat soluble vitamin K isolated from *Pavlova* helps in blood clotting or coagulation. The role of antioxidant vitamins in health and disease control has been well documented. These antioxidants may also be defined as substances which interfere with normal oxidation processes in oils and fats and delay their oxidation.

### Marine Sources as Healthy Foods or Reservoirs of Functional Ingredients

Marine sources are known for their phenomenal biodiversity, which offers a strong basis for their use as a natural source of healthy food as well as of many novel functional food ingredients with biological properties. Crustaceans, macroalgae (seaweeds) or microalgae, fish, and fish by-products, as well as bacteria and fungi are the most representative groups of organisms of potential interest as healthy food or as a source of functional ingredients, which include polysaccharides, chitin, proteins and peptides, lipids, pigments, vitamins, minerals.

#### 1. Seaweeds

Considering their great taxonomic diversity, algae or seaweeds, are a very interesting source of healthy food as well as a natural source of compounds with biological activity that could be used as functional ingredients. There are about 10,000 identified species of algae and about 5% of them are used as food especially in Asian countries as sea vegetables. Seaweeds when incorporated in diets are low in calories that can help in reducing obesity and blood pressure and also are known to help to overcome free radical stress. Seaweeds are rich in polysaccharides, minerals, vitamins, proteins, steroids, and dietary fibers in addition to possessing several biological properties such as antibacterial, antioxidant, anti-inflammatory, anticoagulant, antiviral and/or apoptotic activities. Presence of pigments such as carotenoids, phycobilins, chlorophylls, and phenolic compounds make them strongly antioxidant in nature. Some algae thrive in complex habitats exposed to extreme conditions. To adapt and survive, they produce a wide variety of biologically active secondary metabolites like acetogenins, terpenes, derivatives of aminoacids, phenols, and polyphenols, which are often halogenated. Algae are generally classified as: brown macroalgae (phylum Ochrophyta), red macroalgae (phylum Rhodophyta), or green macroalgae (phylum Chlorophyta). Brown algae owe their color to the presence of the carotenoid

fucoxanthin. Food reserves of brown algae are characteristically complex polysaccharides including laminarins, fucans, and cellulose, as well as higher alcohols; many bioactive metabolites with different pharmacological activities such as antioxidant, anti-inflammatory, antitumor, cytotoxic antifungal, and nematocidal activities, have been isolated from these algae. Green algae owe their color to the dominant presence of chlorophylls a and b, and the main polysaccharides present are normally ulvans. In turn, red algae, which are also considered an important source of many biologically active metabolites possess phycoerythrin and phycocyanin as the main pigments, and the primary polysaccharides are agars and carrageenans.

## **2. Microalgae**

Microalgae or phytoplankton are microscopic marine organisms that can be found in benthic and littoral habitats in the ocean comprising blue-green algae (phylum Cyanobacteria, class Cyanophyceae), diatoms (phylum Ochrophyta class Bacillariophyceae), dinoflagellates (phylum Myzozoa, class Dinophyceae), as well as green and yellow-brown flagellates (chlorophyta, prasinophyta, prymnesiophyta, cryptophyta, and others). Microalgae play a key role in the productivity of oceans, constituting the basis of the marine food chain and are considered important producers of some highly bioactive compounds. Microalgae have abundance of PUFAs and pigments such as carotenoids and chlorophylls -chlorophyll a, phycocyanins, and phycoerythrin (phycobilins) are the pigments of interest found in blue-green algae. These compounds exhibit biological properties such as anticancer, antifungal, antibacterial, and immuno-suppressive properties. Diatoms are photosynthetic organisms that dominate the phytoplankton of cold and nutrient rich waters. They produce PUFAs such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and other omega-3 FAs, antioxidants fucoxanthin and chlorophyll. Dinoflagellates eukaryotic primary producers are rich in chlorophyll and carotenoids as well as PUFAs [42,38].

## **3. Fish and Fish By-Products**

Several million tons of fish and fish by-products are discarded as waste, representing a large environmental problem. However fish and fish by-products are known sources of potential bioactive ingredients such as fish oils rich in PUFAs from fish livers, calcium from fish bones, protein hydrolysates of high biological value, peptides with biological properties such as antihypertensive activity, amino acids such as taurine, which have antioxidant activity and positive effects on cardiovascular system, as well as vitamins and minerals. Fish heads, viscera, skin tails, blood, and seafood shells possess a plethora of compounds with the potential to be used as functional food ingredients. Bioactive compounds from marine processing by-products can be obtained by extraction and purification procedures enabling the isolation of bioactive peptides, oligosaccharides, as well as FAs suitable for biotechnological applications

## **4. Crustaceans**

Chitin is extractable from crustaceans shell, being the second most abundant natural polymer. Chitosan is a biodegradable and biocompatible polymer chitin derivative. Its ability to absorb fat is exploited in applications as an anticholesterol agent. Chitosan and chito oligosaccharides are reported to have several biological activities (antioxidant, antitumor, anticancer, hypocholesterolemic, immunity-enhancing, antimicrobial) and hence finds application in food and health industries.

## 5. Marine Fungi and Bacteria

Marine bacteria and fungi have drawn increasing attention from researchers from all over the world since they are considered as sources of new marine natural compounds. Marine extremophilic bacteria, for example, are of particular interest since they have metabolic pathways adapted to various extreme marine environments. Many microbial enzymes and exopolysaccharides from extremophiles have unique properties. Bacteria derived from intestinal tracts of marine organisms such as fish have also been researched with interest, since these strains may be new probiotics or have additional functions such as antibacterial activity. For example, it was observed that *Lactococcus lactis* isolates from the intestinal tract of freshwater fish possess different phenotypic properties, suggesting additional functions in comparison to those derived from a cheese starter. Much interest has also been focused on marine fungi, which have been studied for their metabolites. A unicellular marine fungus with high concentration of  $\gamma$ -amino-butyric acid (GABA), which is a promising functional and healthy food ingredient. In addition, marine fungi are a promising source of novel bioactive compounds with anticancer, antibacterial, antiplasmodial, anti-inflammatory, and antiviral properties.

### Functional Foods Incorporating Marine-Derived Ingredients

Marine resources are a source of high value-added compounds with biological properties to be used as functional food ingredients. Several types of polysaccharides, such as sulfated polysaccharides, chitin or chitosan, proteins and protein hydrolysates, peptides, amino acids such as taurine, omega-3 oils, carotenoids, and other bioactive compounds are examples of compounds that can be added at different stages, from processing to storage, of the food production process. Since dairy products are widely accepted by consumers, the use of this type of product to deliver bioactive compounds has received attention from the food industry in the last years. Functional foods and natural health products are an emerging field in food science due to their increasing popularity with health-conscious consumers and are a source of new opportunities for the agri-food sector. Food products containing marine-derived chitin, chitosan, as well as oils rich in omega-3 fatty acids, are some food products that are being commercialized in several markets around the world including Japan, the USA, and some European countries.

The consumption of functional foods can provide various nutritional/health benefits, with diet controls and modulates many functions of the body, maintaining good health and homeostasis. Enhancement of immunity and antioxidant effect are most studied health benefits. Nowadays, marine-derived functional ingredients such as fish oils, fish proteins, and seaweeds themselves have found application in bakery, dairy, confectionary, and pasta products. They are added as fortificants and nutritional enrichments in food, to form functional foods. More concerted efforts in research and design of novel marine ingredients-based functional foods are needed to contribute to the reduction of health problems through diet. Despite the scientific progress in the use of marine-derived food ingredients, there still are various challenges ahead that have to be overcome:

- i) Efficient extraction methods and purification steps, to obtain food grade validated extracts or purified compounds with biological properties (antioxidant, antibacterial, prebiotic, and others). Isolated functional ingredients should rely upon food methods compatible with economically viable yields. Hence, different extraction methods must

be applied in order to maximize the extraction efficiency of functional ingredients with biological properties.

ii) To design functional foods based on the incorporation of marine-derived functional ingredients upon biological validation. Consumers are more inclined to buy functional foods with physiological health claims.

iii) Foods should have good sensorial characteristics in order to be accepted by the consumer. In general consumers do not compromise taste for health. This is, in fact, one of the most important challenges to overcome in the use of some of the marine compounds, for example, fish oil.

### **Conclusions**

In the present scenario people are very health cautious and prefer to consume organic food stuff which are free from antibiotics, pesticides, hormones and other contaminants. The ban on usage of antibiotics, pesticides and hormones in aquaculture industry improved the farmed fish quality but still it needs certain value addition to enhance health benefits of consumers. Similarly, to mitigate the stress in culture condition (present intensive farming practices), in addition to feed, certain compounds are desired by cultured fish. Now, the industry is looking for alternative products which are derived from nature (organic) and having the nutritional and health benefits. Marine nutraceuticals are naturally available organic substances which are having greater health promoting factors and are derived from seaweeds, marine micro algae, marine lipids, etc. So, directly or indirectly, marine nutraceuticals help in near future, to gratify everyone's (fish farmers and consumers) necessity of the aquaculture industry and overall enhance the aquaculture production.

\*\*\*\*\*