# Chapter 5

## Nutraceuticals from Fish and Fish Wastes: Scopes and Innovations

**Suseela Mathew and Tejpal.C.S**
Biochemistry and Nutrition Division,
ICAR-Central Institute of Fisheries Technology, Cochin
Email:suseela1962@gmail.com

Bio-active compounds having health beneficial effect on human beingsfrom terrestrial and marine sources are considered as “Nutraceuticals”. Nutraceuticals from marine origin are proved to have wide range of therapeutic effects*viz.*,anti-obesity, immune enhancement, natural antioxidant, cardio protective, anti-diabetic, anti-inflammatory effects.These natural products do not have any side effects contradictory to many medicines available today, hence have attracted global market. Microencapsulation technique has been considered as one of the unique methods to encapsulate the bio-active compounds for target delivery. Importance and application of nutraceuticals from marine origin are highlighted.

**Introduction**

World over in the recent past, research in nutraceuticals has shown continuous growth and the progressive approach is aimed at identifying the potential nutraceutical compounds which are having health benefits in human beings. Awareness among the people is the prime reason for the growing demandfor nutraceuticals.Today people are more aware about the nutrition and related health problems. Recently, researchers across the globe are exploring the possibilities to extract and isolate bio-active compounds from both terrestrial and marine sources.

Nutraceuticalis a combination of two words, “nutrition” and “pharmaceutical,” and the word nutraceutical was coined by Stephen L. DeFelice in 1989 (Wildman *et al*., 2006). Nutraceuticals are food products of natural origin from both terrestrial and marine sources having healthcare importance. The word nutraceuticals comprise of variety of products derived from terrestrial and marine sources (isolated nutrients, dietary supplements, and genetically engineereddesigner foods, herbal products, processed foods, andBeverages). Recent report says that nutraceuticals provides a positive healthcare approach with tremendous therapeutic impacts on human body (Das *et al*., 2012; Bagchi*et al*., 2015). A wide range of phytochemicals described as phytoestrogens, terpenoids, limonoids, glucosinolatesphytosterols, polyphenols, carotenoids, flavonoids, isoflavonoids, and anthocyanidins having therapeutic effects on human health as antioxidants, anti-inflammatory, antibacterial, anti-allergic, etc. are identified (Gupta and Prakash, 2014; Karwande and Borade, 2015).

**Classification of Nutraceuticals**

Based on the bio-functional properties of bioactive compounds from terrestrial and marine sources are classified into following –

1. Dietary Supplements
2. Functional foods
3. Medicinal food

**Dietary Supplements**

According to the Dietary Supplement Health and Education Act (DSHEA), 1994 in USA, dietary supplements are defined as products comprised of “dietary constituents” and orally administered to supplement the nutritional requirement of diet. The “Dietary constituents” refers to bioactive components comprising of amino acids, vitamins, minerals, fibres, important metabolites, and certain enzymes. The dietary supplements also include extracts available in tablets, capsules, powders, liquids, and in any other dosage form (Radhika *et al*., 2011).

**Functional Food**

Functional foods are foods derived from natural origin enriched in nutrients and are being fortified with essential nutrients (Jones, 2002). As per the Health Canada, functional food defines a regular food with an ingredient having specific therapeutic effect along with nutritional value (Wildman *et al*., 2006). Whereas in Japan, functional foods are assessed on the basis of three important standards: (1) functional foods must be derived from natural sources and consumed in their native state instead of processed in different dosage forms like tablet, capsule, or powder; (2) consumed regularly as a part of daily diet; and (3) exert a dual role in prevention and management of disease and contribute in biological processes (Arai, 1996).

**Medicinal food**

Medical foods are foods that are specially formulated to be consumed internally under the supervision of a physician, which is intended for the dietary management of particular disease that has distinctive nutritional needs that cannot be met by normal diet alone. Dietary supplements and functional foods do not meet these criteria and are not classified as medical food (Radhika *et al*., 2011).

**Nutraceuticals from marine sources**

**Chitin and chitosan**

Chitin,a cationic amino polysaccharide,is a natural biopolymer composed of *N*-acetyl-d-glucosamine with β (1 → 4) glycosidic linkages. The term chitosan is used when nitrogen content of chitin is more than 7% by weight or the degree of deacetylation is more than 60% (Peter *et al*., 1986; Gagne and Simpson 1993). Chitosan is a biopolymer and it consists of d-glucosamine units obtained during the deacetylation of chitin by adopting hot alkali treatment. Chitin and chitosan can be obtained from the bio-waste generated from both terrestrial and marine sources. Chitin is abundant in the marine organisms like lobster, crab, krill, cuttlefish, shrimp, and prawn. The extraction of chitin form marine source comprises of thee-steps: deproteinization (DP), demineralization (DM), and decolorization (DC). Further, chitin has to undergo a de-acetylation process to obtain chitosan. Chitin is known for its unique properties like, biodegradability, nontoxicity, physiological inertness, antibacterial properties, hydrophilicity, gel-forming properties (Se-Kwon, 2010). In India, a few entrepreneurs are producing chitin and chitosan on a commercial scale under the technical guidance of the ICAR-Central Institute of Fisheries Technology, Cochin. In-line with chitin, chitosan also finds extensive application in multidimensional sectors, such as in food and nutrition, biotechnology, material science, drugs and pharmaceuticals, agriculture and environmental protection, dental and surgical appliances,removal of toxic heavy metals, wine clarification, industrial effluent treatment, etc. (Se-Kwon, 2010).

**Glucosamine Hydrochloride**

Generally, glucosamine is obtained from the crustacean waste (Xu and Wang, 2004; Tahami, 1994). Glucosamine is part of the structural polysaccharides such as chitosan and chitin, which is present in the exoskeletons of crustacean and other arthropods. Though, glucosamine was discovered long back, market for glucosamine has gained popular interest due toits health benefits. Dietary supplementation of glucosamine (glucosamine sulphate, glucosamine hydrochloride, or N-acetyl-glucosamine) is proven to promising biomolecule for the treatment of osteoarthritis, knee pain, and back pain (Houpt*et al*., 1999; Luo *et al*., 2005). It is also known for its unique properties like anti-cancer, anti-inflammatory and antibacterial effects (Nagaoka *et al*., 2011).

**Chondroitin sulphate**

Chondroitin sulphate (CS) consists of repeated disaccharide units of glucuronic acid (GlcA) and *N*-acetylgalactosamine (GalNAc) linked by β-(1→3) glycosidic bonds and sulfated in different carbon positions (CS no-sulfated is CS-O). Shark cartilage is found to be a good source of chondroitin sulpahte. Chondroitin sulfate plays various roles in biological processes such as the function and elasticity of the articular cartilage, hemostasis, inflammation, cell development, cell adhesion, proliferation and differentiation by being an essential element of extracellular matrix of connective tissues (Schiraldi*et al*., 2010).

**Hyaluronic acid (HA)**

HA can be obtained from the bio-waste like fish eyeball and it is also present in the cartilage matrix of fishes. HA finds several biomedical applications *viz.*viscosupplementation in osteoarthritis treatment, as aid in eye surgery and wound regeneration. Further, hyaluronic acid finds its applications in drug delivery, tissue engineering applications, gene delivery applications, targeted drug delivery, tumor treatment, environmental applications and sensors (Mathew *et al*., 2017).

**Collagen, gelatin and collagen peptides**

Fish skin and scales which constitutes about 30% and 5% of the total seafood processing discards respectively are considered as the richest source for collagen and gelatin. Collagen derived from marine sources is finding wide applications in various sectors due to its biocompatibility, biodegradability, high cell adhesion properties and weak antigenicity (Yamada *et al*., 2014). Another major application of collagen is to act as a source for extraction of collagen hydrolysates, peptides, gelatin and gelatin peptides. Collagen peptides are reported to have bioactive properties like antioxidant, antimicrobial, antihypertensive, metal chelating, tyrosinase inhibitory, immunomodulatory, neuroprotective, antifreeze, wound healing, cell-proliferation, activities (Zhuang *et al*., 2009; Chi *et al*., 2014).

Gelatin, the denatured form of collagen, by virtue of its surface active properties finds extensive applications in food, pharmaceutical and biomedical industries. Gelatin peptides are reported to have antihypertensive, antioxidant properties. The major difference between fish and mammalian gelatin lies in the iminoacid composition, viz, proline and hydroxyprolinecontents. (Mathew *et al*., 2017).

**Fish lipids**

Across the globe the researchers have well documented the health beneficial effects of long chain omega-3 polyunsaturated fatty acids (PUFA) (Connor, 2000). The major omega-3 PUFA, such as eicosapentaenoic acid (EPA C20:5) and docosahexaenoic acid (DHA C22:6) are very much essential for human beings, and hence are considered as essential fatty acids. The intake of long chain omega-3 PUFA is promoted by many health organizations owing to the health benefits associated with it. An average intake of 0.2 g and 0.65g of EPA and DHA a day is recommended by the European Academy of Nutritional Sciences (EANS) and International Society for the Study of Fatty Acids and Lipids (ISSFAL) respectively (Dedeckere, *et al*., 1998). Fish oil remains as an excellent and economical source of omega-3 PUFA. Having high contents of fat soluble vitamins and lipids, especially EPA, cod liver has been exploited as an omega-3 PUFA source for development of nutraceuticals (Mondello*et al*., 2006). Dietary consumption of fish oil (omega-3 PUFA) in adequate quantities is reported to have health benefits in the treatment of cardiovascular diseases, cancer, hypertension, Alzheimer's disease, diabetes, arthritis, autoimmune disorders and to improve overall functioning of brain and retina (Cole *et al*., 2009).

**Squalene**

Squalene, a naturally occurring triterpenoid compound, is an intermediate in cholesterol synthesis. It is widely present in nature, such as wheat germ, rice bran, shark liver and olive oils and among all the sources identified, shark liver oil is considered to be the richest source accounting for about 40% of its weight. Recently, the squalene has gained attention due to its diverse bioactivities such as antioxidant, anti-lipidemic, membrane stabilizing, cardioprotective, chemopreventive, anti-cancerous, antiaging properties etc (Passi*et al*., 2002; Ko*et al*., 2002). Further, it is also reported to protect human skin surface from oxidation (Kabuto *et al*., 2013). Based on its diverse bio-active properties, squalene finds applications in field of biomedical, cosmetic, drug delivery systems and even in food industries.

**Minerals**

Marine organisms especially fish are considered as important source of minerals such as sodium, potassium, calcium, phosphorous and magnesium. Fish bone which is often discarded after the removal of protein is an excellent source of calcium and hydroxy apatite. Being rich in minerals, fish bone powder can be fortified into several food products. However, for fortification, the fish bone should be converted into an edible form by softening its structure by pre-treatment with hot water or hot acetic acid or superheated steam. Calcium powder processed from the backbone of tuna is a potential nutraceutical. It can be used to combat calcium deficiency in children. Fortification of calcium in foods helps consumers in meeting the calcium requirements and may reduce the risk of osteoporosis. Other than fish bone calcium, certain other minerals such as selenium, potassium, iodine, zinc, magnesium are more abundant in seafood than in meat. The higher intake of seafood diet will also ensure that adequate amount of iodine is obtained.

**Nutraceutical industry in India: Current scenario and future trends**

During the year 2015, global nutraceutical industry, valued at US$ 182.6 billion and is one of the fastest growing industries today and expected to grow at a Compound Annual Growth Rate (CAGR) of 7.3% from 2015 to 2021. As on today, the United States, Europe and Japan account for about 93% of the total global nutraceutical market and seems to have attained maturity in all three major regions. Hence, nutraceutical industries across the world are now showing their interest to emerging markets like India and China. Nutraceuticals industry in India is one of the rapid growing markets in the Asia-Pacific region. As per the record, the nutraceuticals industry in India is worth about US$ 2.2 billion and is expected to grow at 20% to US$ 6.1 billion by 2019-2020.

**Innovative work done at Central Institute of Fisheries Technology, Cochin**

By adopting grafting and micro-encapsulation technology, ICAR-Central Institute of Fisheries Technology, Cochin has developed some of the nutraceuticals products, such as thiamine and pyridoxine-loaded vanillic acid-grafted chitosan microspheres; sardine oil loaded vanillic acid grafted chitosan microparticles; microencapsulated squalene powder; vanillic acid and coumaric acid grafted chitosan derivatives; thiamine and pyridoxine loaded ferulic acid-grafted chitosan. These nutraceuticals products were shown to have health beneficial and immunomodulatory response in animal models.

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