# MARINE BIOMOLECULES: PRESENT & FUTURE PROSPECTIVE IN HUMAN HEALTH CARE

**Dr.Suseela Mathew**

HoD (i/c), Biochemistry & Nutrition Division

ICAR-Central Institute of Fisheries Technology, Kochi-29

## Introduction

Nutraceutical based research has shown continuous growth and the progressive approach owing to the increased awareness among the general public regarding its significance in consumption and overall well-being. Researchers across the globe are hence working on to explore the possibilities to extract and isolate bio-active compounds from both terrestrial and marine sources. Nutraceutical is 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 engineered designer foods, herbal products, processed foods, and Beverages). 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). The nutraceutical industry has identified a wide range of phytochemicals described as phytoestrogens, terpenoids, limonoids, glucosinolates phytosterols, polyphenols, carotenoids, flavonoids, isoflavonoids, and anthocyanidins having therapeutic effects on human health as antioxidants, anti-inflammatory, antibacterial, antiallergic, anti-fungal, chemopreventive, immunomodulatory etc., (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***

A dietary supplement, as defined by the Food and Drug Administration (FDA), is a product intended to supplement the diet by increasing the total daily intake, or an extract, metabolite, concentrate, constituent, or combination of at least one of the following dietary ingredients: vitamins, minerals, herbs or other botanicals, amino acids (FDA, 2022).The "Dietary constituents" can be 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***

The term "Functional foods have become popular in the scientific world, and mostly adopted in twenty first century by the food and nutritional researchers who are currently working on how to solve various crises arising from the degenerative diseases, 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, also known as deacetylated chitin, is a naturally occurring polycationic polysaccharide derived from partial deacetylation of chitin. 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. Chitosan 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***

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 to its 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 is a key component of the cartilage extracellular matrix (ECM). It is considered a member of the glycosaminoglycans (GAGs) family and is an unbranched sulphated, highly water-soluble anionic polysaccharide. Shark cartilage is found to be a good source of chondroitin sulphate. It has been shown that the incorporation of CS in scaffolds for cartilage tissue engineering induces the chondrogenic differentiation of mesenchymal stem cells (MSCs). CS provides a microenvironment that enhances clustering of cells (pre-cartilage condensation of mesenchymal cells), upregulates cartilage-specific genes, and provides cell-mediated degradable sites for the cell clusters to grow further and produce ECM. Studies have also demonstrated that CS increases the compressive stiffness of collagen scaffold (Rashidi et al., 2022).

***Hyaluronic acid (HA)***

Hyaluronic acid (HA) is a polysaccharide composed of alternating d-glucuronic acid and N-acetylglucosamine, which are naturally present in cartilage and synovial fluid. Compared with other polysaccharides, HA affects the regulation of cartilage function and repair of cartilage damage in many ways. Previous studies have demonstrated that HA can improve the lubricity of

cartilage boundaries, regulate inflammation at cartilage lesions, promote cell adhesion and proliferation, and ameliorate cartilage ECM deposition and cartilage regeneration, all of which have excellent application prospects in cartilage tissue engineering (Wang et al., 2022). 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 such as 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 hydroxyproline contents. (Mathew *et al*., 2017).

***Fish lipids***

Fish is considered as a good source of high quality, easily digestible protein rich in essential aminoacids (AHA 2012). Moreover, fats and oils from fish is an excellent dietary sources of long chain highly unsaturated fatty acids of omega-3 type such as EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) which are not contained in the fats of terrestrial animals or in vegetable oils. 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). The American Heart Association recommends adults eat fish (in particular fatty fish) at least two times per week.

***Squalene***

Squalene, a bioactive isoprenoid, have evoked an unparalleled interest in pharmaceutical, drug delivery, cosmeceutical and clinical arenas by virtue of its wide range of bioactivities such as antioxidant, chemopreventive, anticancerous, antilipidemic, membrane stabilizing properties, immune system enhancer, antiaging, detoxification etc. 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. 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.

**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.

**References**


1. Arai, S., 1996. Studies on functional foods in Japan—state of the art. Biosci. Biotechnol. Biochem. 60, 9–15.
2. Bagchi, D., Preuss, H.G., Swaroop, A., 2015. Nutraceuticals and Functional Foods in Human Health and Disease Prevention. Taylor & Francis, USA.
3. Chi, C.F., Cao, Z.H., Wang, B., Hu, F.Y., Li, Z.R. and Zhang, B., 2014. Antioxidant and functional properties of collagen hydrolysates from Spanish mackerel skin as influenced by average molecular weight. *Molecules*, *19*(8), pp.11211-11230.
4. Cole, G.M., Ma, Q.L. and Frautschy, S.A., 2009. Omega-3 fatty acids and dementia. *Prostaglandins, Leukotrienes and Essential fatty acids*, *81*(2), pp.213-221.
5. Das, L., Bhaumik, E., Raychaudhuri, U., Chakraborty, R., 2012. Role of nutraceuticals in human health. J. Food Sci. Technol. 49, 173–183.
6. De Deckere, E.A.M., Korver, O., Verschuren, P.M. and Katan, M.B., 1998. Health Aspects of Fish and N-3 Pufa from Plant and Marine Origin: Summary of a Workshop.
7. Gagne, N. and Simpson, B.K., 1993. Use of proteolytic enzymes to facilitate the recovery of chitin from shrimp wastes. *Food Biotechnology*, *7*(3), pp.253-263.
8. Gupta, C., Prakash, D., 2014. Phytonutrients as therapeutic agents. J. Complement. Integr. Med. 11, 151–169.
9. Houpt, J.B., McMillan, R., Wein, C. and Paget-Dellio, S.D., 1999. Effect of glucosamine hydrochloride in the treatment of pain of osteoarthritis of the knee. *The Journal of rheumatology*, *26*(11), pp.2423-2430.
10. Jones, P.J., 2002. Clinical nutrition: 7. Functional foods—more than just nutrition. *Canadian Medical Association Journal*, *166*(12), pp.1555- 1563.

11. Karwande, V., Borade, R., 2015. Phytochemicals of Nutraceutical Importance. Scitus Academics LLC, New York, NY.
12. Mathew, S., Tejpal, C.S., Kumar, L.R., Zynudheen, A.A. and Ravishankar, C.N., 2017. Aquaceuticals for Developing High Value Noble Foods and Dietary Supplements. *Indian Journal of Agricultural Biochemistry*, *30*(1), pp.1-9.
13. Nagaoka, I., Igarashi, M., Hua, J., Ju, Y., Yomogida, S. and Sakamoto, K., 2011. Recent aspects of the anti-inflammatory actions of glucosamine. *Carbohydrate polymers*, *84*(2), pp.825-830.
14. Peter MG, Kegel G & Keller R (1986) In*: Chitin in Nature and Technology (RAA Muzzarelli, C Jeuniaux & GW Gooday, Editors) New York: Plenum Press*, pp. 21–28.
15. Radhika, P.R., Singh, R.B.M. and Sivakumar, T., 2011. Nutraceuticals: an area of tremendous scope. *Int. J. Res. Ayurveda Pharmacy*, *2*, pp.410- 415.
16. Rashidi, N., Tamaddon, M., Liu, C. and Czernuszka, J., 2022. Polymerization of chondroitin sulfate and its stimulatory effect on cartilage regeneration; a bioactive material for cartilage regeneration. Polymer Testing, 116, p.107796.
17. Se-Kwon K (2010) *Chitin, chitosan, oligosaccharides and their derivatives: Biological activities and applications; CRC Press-Taylor & Francis Group*: *Boca Raton.*
18. Tahami, M., 1994. "Synthesis of chitosan and Glucosamine from crustaceans wastes (Shrimp, Crab, Lobster)", Iranian Fisheries Journal, 3: 5-15.
19. Wang, M., Deng, Z., Guo, Y. and Xu, P., 2022. Designing functional hyaluronic acid-based hydrogels for cartilage tissue engineering. Materials Today Bio, p.100495.
20. Wildman, R.E.C., Wildman, R., Wallace, T.C., 2006. Handbook of Nutraceuticals and Functional Foods, second ed. CRC Press, Boca Raton, FL.
21. Xu, Y.S. and Y.M. Wang, 2004. "Preparation of D (+) glucosamine hydrochloride from crab shell", Chemistry Adhesion, pp: 4.
22. Yamada, S., Yamamoto, K., Ikeda, T., Yanagiguchi, K. and Hayashi, Y., 2014. Potency of fish collagen as a scaffold for regenerative medicine. *BioMed research international*, *2014*.

23. Zhuang, Y.L., Zhao, X. and Li, B.F., 2009. Optimization of antioxidant activity by response surface methodology in hydrolysates of jellyfish (Rhopilema esculentum) umbrella collagen. *Journal of Zhejiang University-Science B*, *10*(8), pp.572-579.