Fish Oil: Health Benefits and Issues

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Fish production is one of the global industries, with over 160–170 million tonnes of annual production, marine capture fisheries representing about 50%. Around 30% of fish landings are intended for direct human consumption in the form of fresh or chilled commodity, while the rest are typically processed before final sale (Soldo *et al.*, 2019). There is a great potential in marine bioprocess industry to convert and utilize fish and its byproducts as valuable products. Majority of fisheries byproducts are presently employed to produce fish oil, fishmeal, fertilizer, pet food and fish silage. However, most of the recycled products possess low economic value. Studies have identified a number of bioactive compounds from fish and fishery waste having high value. These bioactive compounds can be extracted and purified with technologies and it includes bioactive peptides, oligosaccharides, fatty acids, enzymes, water-soluble minerals and biopolymers. Furthermore, some of these bioactive compounds have been identified to possess nutraceutical potentials that are beneficial in human health promotion (Kim and Mendis, 2006).

According to Spinelli *et al*., 1987, fish oils comprise a complex mixture of fatty acid moieties, mostly straight chain with an even number of carbon atoms. The fatty acids, usually present as their glycerides, are either saturated or mono or polyunsaturated. Fish and marine mammal oils contain substantial amounts of fatty acids having four, five or six double bonds. In addition, fish and liver oils also contain numerous other substances such as cholesterol, cholesterol esters, wax esters, hydrocarbons like squalene, pigment like astaxanthin, amines, and phospholipids. It was observed that Green Land Eskimos, whose food intake comprises mainly fish and marine animals, exhibit unusually low incidences of cardiovascular diseases, and a number of chronic degenerative diseases such as arthritis, diabetes and ulcerative colitis

Fish oil is the primary natural longchain omega-3 fatty acid source containing two human health beneficial fatty acids, eicosapentaenoic acid (EPA)and docosahexaenoic acid (DHA) (Fig 1). Scientifically it is proven that EPA and DHA have a positive impact on human health as they reduce the chance of heart and vascular disease, cancer, diabetes, decrease the risk of depression, affect the immune system, and ensure the proper neural development. Fish oil accounts for about 2 % of world consumption of fats and oils.

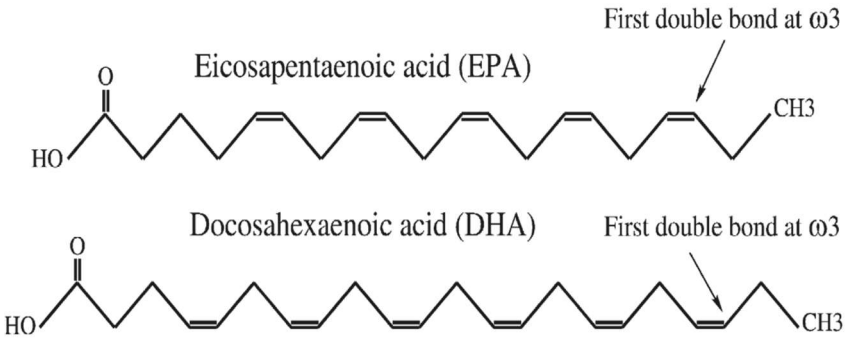

Fig 1. Structure of EPA and DHA

Traditionally, the fish oil is obtained as a by-product of the fish meal industry. But currently smaller fish with a relatively high fat content – anchovies, sardines, herring, eels are in the centre of attention as a raw material in the fish oil industry. Fish oil is mainly used in food and pharmaceutical industry, agriculture and aquaculture as a feed additive (Ivanovs and Blumberga, 2017). Human dietary intake of omega-3 oils is largely derived from the flesh of marine pelagic oily fish, such as mackerel, salmon, anchovy, sprat, pilchard and herring. EPA and DHA accumulate in the fish from the lipids obtained from marine algae, the primary producers. Omega-3 oils are also found in demersal white fish such as cod and tuna. Other marine fauna such as shrimp and krill will also provide a significant supply of omega-3. Fish oil plays a significant role in the human diet, and currently, the demand for fish oil is growing due to its curative properties.

Health benefits of fish oil

Effect on bones

Age-associated bone loss is a widespread, health burden among a fast-growing aging population. The supplementation with concentrated fish oil (CFO) with a high content of EPA and DHA is very efficient in maintaining bone mineral density in mice during aging. But the supplementation should be started at middle age rather than later stages. CFO protects bone loss during aging, primarily by inhibiting inflammation-associated with bone resorption. Thus, CFO may be beneficial in preventing bone loss during aging. (Abou Saleh *et al*., 2019).

Effect on Brain

Brain cell membranes of vertebrates have high concentrations of long-chain polyunsaturated fatty acids, mainly DHA and arachidonic acid. The accretion of DHA during perinatal development is considered to be essential for the proper functioning of the mammalian central nervous system, especially in primates. The functional role of DHA has been mainly investigated in animal models, mainly rodents, deprived of any dietary source of n-3 PUFAs during perinatal development. Dietary deficiency of n-3 PUFAs leads to decreased brain content of DHA, which is accompanied by severe learning, memory, and anxiety impairments that have been linked to changes in neurotransmission processes

(Alessandri *et al*., 2004). In a study conducted by Pifferi *et. al.* (2015),increased long chain n-3 polyunsaturated fatty acid intake at an early age may help to prevent or correct the glucose hypometabolism observed during aging and age-related cognitive decline. Lemurs supplemented with n-3 PUFA had higher brain glucose uptake and cerebral metabolic rate of glucose compared with controls in all brain regions.

Effect on Cardiovascular system

According to Goel *et al*. (2018), fish and commercially available fish oil preparations are rich sources of long-chain omega-3 polyunsaturated fatty acids. EPA and DHA are the most important fatty acids in fish oil. Following dietary intake, these fatty acids get incorporated into the cell membrane phospholipids throughout the body, especially in the heart and brain. Many experimental studies and some clinical trials have documented the benefits of fish oil supplementation in decreasing the incidence and progression of atherosclerosis, myocardial infarction, heart failure, arrhythmias, and stroke. Possible mechanisms include reduction in triglycerides, alteration in membrane fluidity, modulation of cardiac ion channels, and anti-inflammatory, anti-thrombotic, and anti-arrhythmic effects. Fish oil supplements are generally safe, and the risk of toxicity with methylmercury, an environmental toxin found in fish, is minimal. Dietary eicosapentaenoic acid, a main component of fish oil, has been proved to reduce the risk of cardiovascular disease. Ling Yu Zhang *et. al*., (2019) investigated the anti-atherosclerosis effect of fish oil enriched with EPA partially relied on its chemical groups at the sn-3 position. EPA incorporated into phospholipids (EPA-PL) or triglycerides (EPA-TG) was used in the study and compared with the model group, a decrease in the area of atherosclerosis lesions at the aorta was observed in both EPA-treated groups, in which EPA-PL was superior to EPA-TG. EPA-PL was superior to EPA-TG in reducing lesion progression by modulating the hepatic lipid metabolism, as well as decreasing the inflammation in the artery wall and circulatory system, which might be attributed to their structural differences.

Anti-cancer effect

Docosahexaenoic acid is rich in fish oil with many pharmacological impacts such as anti-inflammation and anti-cancer activities. Low doses of DHA effectively inhibit metastasis in prostatic cancer cell line (Wu *et a*l., 2019). Epidemiological studies confirm high fish oil consumption with decreased risk of breast cancer. The literature suggests that DHA has a greater anti-cancer effect in triple negative breast cancer. In estrogen positive breast cancer, DHA has a greater effect on cell viability, while both fatty acids have similar effects on apoptosis and proliferation (Vander Sluis *et al.,* 2017).

Pancreatic cancer is a highly aggressive malignant tumour of the digestive system. Dietary fish oil supplementation has shown to suppress pancreatic cancer development in animal models. Experimental studies revealed that several hallmarks of cancer involved in the pathogenesis of pancreatic cancer, such as the resistance to apoptosis, hyper-proliferation with abnormal Wnt/β-catenin signaling, expression of pro-angiogenic growth

factors, and invasion. DHA shows anti-cancer activity by inducing oxidative stress and apoptosis, inhibiting Wnt/β-catenin signalling, and decreasing extracellular matrix degradation and expression of pro-angiogenic factors in pancreatic cancer cells (Park and Kim, 2017).Omega-3 polyunsaturated fatty acids and atorvastatin, besides having anti-inflammatory properties, proved a chemopreventive effect against bladder cancer, which nominates them to be used as adjuvant therapy with other chemotherapeutics (El-Ashmawy *et al*., 2017). DHA can promote cervical carcinoma cell apoptosis by down-regulating the anti-apoptotic proteins and suppress cell invasion by decreasing MMP-9 and VEGF expressions (Yang *et* al., 2016).

Dyslipidemia

Dietary fish oil has proved to be effective in lowering plasma triacylglycerol and lipoprotein concentrations in experimental animals and in normal as well as hyper triglyceridemic men thereby being attributed a role in preventing cardiovascular disease. These dietary fatty acids are capable of inhibiting the formation of VLDL by the liver via a number of mechanisms, including a decrease in lipogenic enzymes activities, increased fatty acid oxidation, decreased Apo-B secretion, impaired VLDL assembly, decreased activities of enzymes responsible for esterification of fatty acids, or a combination of them. Lombardo *et al*., 1996). Fish oil supplementation may partially correct the dyslipidemia of type 2 diabetic patients. However, the putative very important aspect of diabetic dyslipidemia the predominance of small dense LDL particles was unaffected by fish oil (Petersen*et al*., 2002). Erkkilä and Lankinen (2016) confirmed that fish oils decrease VLDL size and the number of large VLDL particles. Fatty fish intake has not consistently been associated with VLDL particles, possibly due to lower n–3 PUFA intake it supplies compared to fish oil supplementation. The observed VLDL effects may reflect increased clearance of triglyceride-rich lipoprotein particles. Fatty fish and fish oil increase both the HDL size and the number of large HDL particles. These effects are regarded as beneficial as large HDL particle number and HDL size have been inversely associated with cardiovascular events.

A study to determine the effects of omega-3 polyunsaturated fatty acids in combination with naproxen, a cyclooxygenase inhibitor, on dyslipidemia and gene expression in adipose tissue in humans suggested that combination showed effectiveness in reducing serum TG and favourably altering adipose tissue gene expression and plasma bile acid profile (Saraswathi et al., 2019). The effects of ω-3 polyunsaturated fatty acids in fish oil and fish oil in combination with vegetable oils on glucolipid metabolism in type 2 diabetic patients with dyslipidemia revealed that the effects of ω-3 PUFA from different sources on glucose metabolism in type 2 diabetic patients with dyslipidemia are similar and most of the lipid profile parameters decreased (Wang *et al.,*2019).

Hepatoprotection

The balance between n-3 and n-6 PUFAs is essential for metabolism and maintenance of the functions of liver. The availability of n-3 long chain PUFAs plays a major role in regulating both fat accumulation and its elimination by the liver. Derangement of hepatic n-6:n-3 PUFA ratio impacts on the histological pattern of fatty liver through modulation of the amount of intrahepatic lipids (El-Badry*et al*., 2007).
Fish oil contains n-3 polyunsaturated fatty acids such as eicosapentaenoic acid and docosahexaenoic acid. Fish oil is effective at preventing nonalcoholic fatty liver disease (NAFLD) induced by sucrose/fructose. Alcohol intake also causes an alcoholic fatty liver, which is decreased by fish oil consumption (Yamazaki *et al*., 2018).

Issues

Evidence from epidemiologic studies and clinical trials indicates that ω-3 polyunsaturated fatty acids has a preventive or therapeutic effect on allergy, although the results remain controversial. A study was conducted to investigate the association between intake of fish and ω-3 PUFAs with risk for lifetime prevalence of physician-diagnosed allergy.Fish and omega 3 PUFA intake were associated with increased risk for some allergic diseases in a Japanese population.(Huang *et al*., 2001).

As per European Food safety authority, oxidation occurs when unsaturated fats such as the omega-3 fatty acids EPA and DHA are exposed to heat, light, or oxygen. The greater the degree of unsaturation, the more susceptible the fatty acid is to oxidation. Polyunsaturated fats are more prone to oxidative damage than monounsaturated fats. Fish oil that has sufficiently oxidized will have a pungent odour and off-flavour. Oxidation of fish oil will give rise to the formation of free radicals, lipid hydroperoxides and secondary oxidation products (aldehydes, ketones, alcohols, hydrocarbons, core aldehydes). Only the secondary oxidation products are responsible for the undesirable changes in the aroma and flavour properties of foods caused by lipid oxidation.

Oxidation of the oil can limit the storage life of fishes more quickly than the protein changes that govern the extractable protein value. An important stage in the oxidation is the addition of oxygen to the fatty acid molecules to form hydroperoxides; the amount of these can be used as a measure of the extent of oxidation in the early stages. Increase in the peroxide value is most useful as an index of the earlier stages of oxidation; as oxidation proceeds the peroxide value can start to fall. Therefore, a single measurement of peroxide value can only be used as an index of current oxidation status if the peroxides formed are stable enough so that they do not decompose after formation. The anisidine test is a method commonly used in the oil industry as a measure of the level of secondary oxidation products. The principle of the anisidine test is that the compounds react with p-anisidine to form a coloured complex that absorbs at 350nm. The anisidine value is defined as the absorbance of a solution resulting from the reaction of 1 g fat in 100 mL of isooctane solvent and 0.25 % anisidine in glacial acetic acid (AOCS, 1994). The anisidine test measures the carbonyl

compounds that may contribute to off-flavour formation as a result of oxidation. Because of highly oxidative nature of fish oil, preservation of fish oil needs special care i.e. addition of antioxidant will cut off the exposure to atmospheric oxygen etc. Peroxidised fish oil if consumed can cause ill effects in human body than being beneficial.Melanson *et al.,* (2005) investigated for the presence of environmental toxins such as mercury, polychlorinated biphenyls, and organochlorine pesticides in fish oil. The levels of polychlorinated biphenyls and organochlorines were all below the detectable limit.

Conclusion

Fish oil has gained widespread use in the human nutrition and healthcare because of its curative properties. Fish oil supplementation has a substantial and highly clinically relevant beneficial impact on the human body because of its anticancer, lipid lowering properties and beneficial effects on brain, cardiovascular system and bones. Hence fish oil can be recommended as a nutraceutical as they have a role in nutrition as well as in medicine.

Suggested Readings

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