Fish Oil: Health Benefits and Quality Issues

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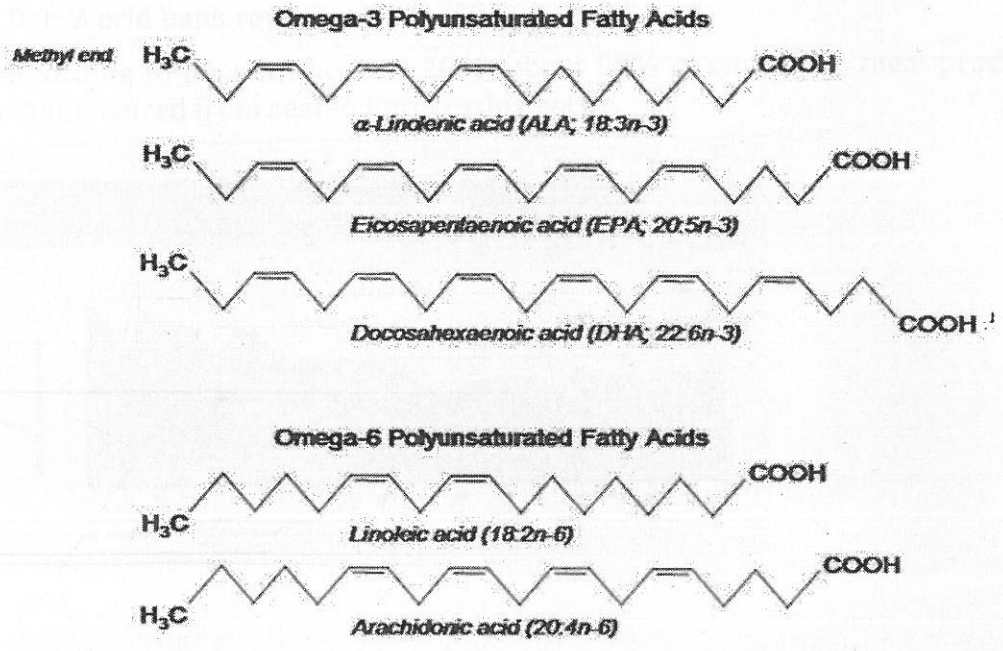
Introduction

Long chain omega-3 polyunsaturated fatty acids (LC PUFA) are reported to have a positive effect on human health. The main omega-3 LC PUFA are eicosapentaenoic acid (EPA C20:5) and docosahexaenoic acid (DHA C22:6). Fish oil is the main dietary source of these long chain omega-3 (n-3) polyunsaturated fatty acids (PUFA). Dietary fatty acids are considered as a primary energy source in humans. Apart from being a major dietary source, it is also reported to have extensive nutritional and health benefits, especially, n-3 polyunsaturated fatty acids. Omega-3 fatty acids are long chain polyunsaturated fatty acids containing methylene-separated double bonds starting from the third carbon atom counted from the methyl-terminus (Kralovec*et al.*, 2012). These fatty acids are required by humans, but cannot be synthesized endogenously and hence considered as essential fatty acids. Therefore, the requirements for these fatty acids must be obtained from the diet. There are several sources recognized for n-3 polyunsaturated fatty acids such as olive oil, rice bran and fish oil etc.

Fish oil is being widely recognized as an excellent dietary source of n-3 polyunsaturated fatty acids such as EPA and DHA. Researchers have shown that the fish oil supplementation is highly beneficial as it is having many health attributes such as the prevention of coronary heart disease, rheumatoid arthritis, hypertension, Crohn's disease, Type 2 diabetes etc.(Šimopoulos, 1999, Tur,et.al,2012). Fatty fishes like sardine and mackerel are considered as better sources of n-3 fatty acids like EPA and DHA (Gunstone 1996). However, the fatty acid profile of fishes might vary according to the species, the environment in which it grows, season, diet, stage of sexual maturity and sex also. The structure of important omega-3 fatty acids are shown in fig.1



Health benefits of n-3 PUFA

1. Role in inflammation

Inflammation, which is body's response to infection and cellular injuries, is mainly manifested by the production of several inflammatory mediators such as cytokines, reactive oxygen species, expression of adhesion molecules and arachidonic acid derived eicosanoids. However, studies have shown that the increased consumption of n-3 polyunsaturated fatty acids inhibits the arachidonic acid metabolism by competing with arachidonic acid for the enzymes for eicosanoid production. This process results in an increased production of n-3 derived eicosanoids which is having anti-inflammatory effects. Apart from the production of anti-inflammatory eicosanoids, some studies have also reported the production of certain mediator compounds from EPA and DHA which is also having anti-inflammatory actions. For instance, E-series resolvins and D-series resolvins, docosatrienes and neuroprotectins formed from EPA and DHA respectively is reported to have anti-inflammatory properties. Bouwens, et al., (2009) have studied the effect of fish oil supplementation in inducing anti-inflammatory gene expression profiles in human blood mononuclear cells. The study has reported that the supplementation of EPA and DHA resulted in a decreased expression of genes which are mainly involved in inflammatory- and atherogenic-related pathways

Role in prevention of cardiovascular diseases

Several studies have reported the association of fish oil consumption and reduction in the risk of cardiovascular diseases. The relationship between weekly fish consumption and the reduced risk factors of cardiovascular diseases such as obesity, hypertension, glycohemoglobin has been reported by Mizushima *et al.* and Burr *et al.* have studied the effect of n-3 supplementation (either fish oil capsules of fatty fish twice in a week) on patients with a recent myocardial infarction for a period of 2 years. They have observed 29% reduction in total mortality and in deaths from coronary heart diseases in the group administered with an increased intake of n-3 PUFA. Taking into consideration the cardioprotective effects of fish oil, American Heart Association recommended that adults should eat fish at least two times per week (Kris-Etherton, 2003). The International Society for the Study of Fatty Acids and Lipids (ISSFAL) also recommended an adequate intake of 0.65 g of DHA plus EPA per person per day (0.22 g of each).

3. Role in prevention of thrombosis

The antithrombotic effect of fish oil was first reported in an epidemiological study of Greenland Eskimo by Dyerberg and Bang (1979) and Dyerberg (1986) suggested the relation between a low incidence of heart diseases and seafood consumption. It was later found that the consumption of fish resulted in increased levels of tissue plasminogen activator (TPA) and decreased concentrations of plasminogen activator inhibitor. One of the possible mechanisms of anti-thrombotic effect of omega-3 fatty acids is that it inhibits platelet TXA2 synthesis and acts as antagonists of the pro-aggregatory TXA2/PG H2 receptor in human platelets in vitro.

4. Role in prevention of Rheumatoid arthritis

Kremer et al. (1995) have studied the effect of fish oil supplementation on rheumatoid arthritis and found that patients taking dietary supplements of fish oil exhibited

significant improvements. Fish oil consumption resulted in a significant decrease levels of IL-1 beta from baseline. Even, some patients who take the fish oil on a daily basis were able to discontinue the non-steroidal drugs. Some patients who take fish oil are able to discontinue NSAIDs without experiencing a disease flare. Caughey, et al., 2010 studied the combined effect of fish oil and paracetamol on the anti-inflammatory effect in patients with rheumatoid arthritis and found out that there has been a significant suppression of COX-2 generated prostaglandin PGE2 synthesis.

5. Role in the treatment of ulcerative colitis

Ulcerative colitis is a disease condition which is characterized by the influx and accumulation of neutrophils in the colonic mucosa. The presence of leukotriene B4, a potent chemotactic factor, was observed in high levels in inflamed colonic mucosa and was reported to have a pivotal role in the accumulation of neutrophils in the affected region. Hence, treatments which will reduce the synthesis of leukotriene B4 will be beneficial in controlling the incidence of ulcerative colitis. Diets containing high levels of w-3 fatty acids, such as eicosapentaenoic acid and docosahexaenoic acid, are known to modify leukotriene production. Eicosapentaenoic acid levels in cell membranes rise, with an increase in eicosapentaenoic acid derived lipoxygenase products, such as leukotriene B56, which has markedly reduced chemotactic potency compared with leukotriene B4. In addition synthesis of lipoxygenase products derived from arachidonicacid is reduced as a result of diminished substrate (Barbosa et al 2003).

6. Role in the treatment of diabetes

In streptozotocin-diabetic rats, long-term ω-3 PUFA supplementation has been shown to prevent diabetic heart muscle disease. In neonatal cardiomyocytes cells, arrhythmia caused by agents such as high extra cellular calcium, ouabain, isoproterenol or lysophosphatidylcholine was prevented by exogenous EPA in the free form (Calder, 2004). As removal of free EPA with added bovine serum albumin quickly reversed this protective effect (Leaf et al 1999), it was suggested that the free carboxylic group of ω-3 PUFA modulates ion channels, especially the calcium and sodium channels on the cardiomyocyte membrane to prevent arrhythmia (Calder, 2004). It is possible that through similar mechanisms, EPA could prevent calcium overload in the diabetic heart, which is known to induce mitochondrial pore transition leading to cytochrome c release and cardiomyocyte apoptosis (Oliveira et al.,2003). Interestingly, exogenous DHA supplementation has also been demonstrated to correct calcium homeostasis and mitochondrial dysfunction in diabetic cardiomyocytes.

7. PUFA and cancer

Many trials using fish oil in diet shows promising results in the area of cancer treatment. In rats, linoleic acid, a precursor of arachidonic acid in tissues, increases the size and number of tumours whereas EPA and DHA decrease both. It is suggested that the potential of n-3 fatty acids to prevent recurrence and metastases of mammary cancer when used in adjuvant therapy is associated with a (n-6) to (n-3) ratio < 2:1(Cowing and Saker, 2001). Adding fish oil to a diet containing adequate polyunsaturated fatty acids enhances azaserine- induced carcinogenesis in rats and N- nitrosobis(2 oxopropyl)amine- induced carcinogenesis in hamsters (Woutersen and Appel, 1999). A meta-analysis of experimental animal studies found that n-6 fatty acids strongly enhanced carcinogenesis, monounsaturated fatty acids had no effect, and n-3 fatty acids weakly (but notsignificantly) inhibited carcinogenesis (Fay *et al.,* 1997).

8. PUFA and liver disease

Liver disease must be one of the major causes of PUFA deficiency because long chain PUFA biosynthesis mostly occurs in the liver. PUFAs are synthesized from their essential precursors in the smooth endoplasmic reticulum, especially in the liver, by successive desaturation (i.e., oxidation with double bond formation) and elongation (i.e., lengthening of the chain with two methylene groups) reactions. PUFA deficiency is a well established feature of advanced cirrhosis mainly in plasma, erythrocytes and platelets (Owen *et al.,* 1982; Wilcox *et al.,* 1978). PUFA deficiency may decrease the fluidity of cell membranes and hence impair their biological functions. Decrease in fluidity has been reported either in red blood cells (Owen *et al.,* 1982) or hepatocytes (Schuller*et al.,* 1986) of patients with cirrhosis as compared with healthy controls. Arachidonate deficiency may lead to impaired platelet aggregation often occurring in advanced cirrhosis (CabreandGassull, 1996). It has been reported that changes in membrane lipid composition hamper the insulin receptor function in the erythrocytes of cirrhotic patients (Peterson et al., 1992) and that the infusion of polyunsaturated lecithin improves such a derangement (Cantafora*et al.,* 1992). Eicosapentaenoic acid (EPA; 20:5n-3) up-regulates the metabolic action of insulin and inhibits cell proliferation (Murata *et al.,*2001). It has been found that fish-oil rich in EPA inhibit DEN-induced hepatocarcinogenesis in rats (Sasagawa*et al.,* 2002). On the other hand, some experimental studies have reported that, in alcohol fed rats, a PUFA enriched diet leads to more severe liver injury than a diet enriched in saturated fatty acids (Nanji*et al.,* 1989; Nanji*et al.,* 1995).

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