A Review into the benefits of Omega-3 fatty acids

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ABSTRACT

Essential fatty acids are long-chain polyunsaturated fatty acids. Linolenic acid (LNA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are omega-3 series whereas linoleic acid (LA) and arachidonic acid (AA) are omega-6 series of essential fatty acids. Omega-3 fatty acids are present in meat, fish, poultry, flaxseed etc. Foods fortified with omega-3 fatty acids are protected and stabilized by antioxidants like carotenoids, flavonoids, anthocyanins and vitamin E which prevent oxidative damage. Mechanisms that prevent oxidative damage are radical scavenging, metal chelation, and oxygen depletion. The absence of enzyme omega-6 desaturase in mammalian cells prevents conversion of omega-6 to omega-3 fatty acids. The ideal omega-6/omega-3 (ω-6/ω-3 ratio) is 1:1. This ratio should be maintained and adjusted depending upon the disease conditions, dietary factors, genetic factors and geographical habitat which varies the need of these nutrients. The risk of contaminants of omega-3 fatty acids in dietary brands can be avoided by stringent checks on quality, purity and certification. There are side-effects of excessive consumption of omega-3 fatty acids in very large quantities; like bleeding from gastrointestinal tract, diarrhea, nausea, vomiting and loss of appetite. Benefits of omega-3 fatty acids in inflammation, obesity, pregnancy, eye health, metabolic syndrome, brain function and performance of athletes are focused in this review. Futuristically proactive measures are recommended to maintain the quality as well as zero-contamination of foods fortified with omega-3 fatty acids to maintain human health globally.

Fatty acids are compounds made up of carbon and hydrogen atoms. Fatty acids are classified as saturated and unsaturated [1]. Saturated fat affects human health deleteriously [2]. It increases the risk of coronary heart disease [3][4][5][6]. Unsaturated fatty acids include both monounsaturated and polyunsaturated fatty acids. Monounsaturated fatty acids are characterized by presence of one double bond [1], whereas polyunsaturated fatty acids possess two or more double bonds [7][8].

The overall fat intake adequately meets the fatty acids requirement by human beings. Due to lack of necessary enzymes some fatty acids are not synthesized in the human body. Therefore, it becomes necessary to consume appropriate dietary sources of such fatty acids. These fatty acids are known as essential fatty acids (EFA’s) [9]. Essential fatty acids of omega-6 series (which includes linoleic acid [LA] and arachidonic acid [AA]) and omega-3 series (especially linolenic acid [LNA], eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) are necessary for growth and development. They have major role in counteracting against coronary disease, hypertension, diabetes and autoimmune conditions [10][11][12].

Sea food products especially their oils contain high contents of long-chain polyunsaturated fatty acids. Fishes are good sources of omega-3 fatty acids. Long-chain polyunsaturated fatty acids such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are prevalent in fishes. Variations in size, reproductive time and geographical locations of habitat have effects on the fat content in fishes [13]. Meat, fish, poultry are rich in omega-3 fatty acids [14]; soya bean oil, flaxseeds, margarine, walnuts are other important sources of omega-3 fatty acids [15].

Platelet aggregation, inhibition of epinephrine, reduction in thromboxane A2, reduction in whole blood viscosity and increase in fluidity of erythrocyte membrane may result due to ingestion of fish and fish oils [16][17][18][19]. A balance needs to be maintained in the consumption of omega-6 and omega-3 fatty acids. Linoleic...
add (LA) and linolenic acid (LNA) are important constituents of cell membranes of both animals and plants. When fish and fish oils are consumed by humans, the EPA and DHA intake replaces the omega-6 fatty acids especially AA in the cell membranes of platelets, erythrocytes, neutrophils, monocytes and liver cells [20].

In normal healthy humans the omega-6/omega-3 ratio optimally should be 1:1 to 1:4[8]. The balance between omega-6 and omega-3 fatty acids contribute to the flexibility as well as fluidity of the cell membranes for neural impulse transmission, physical and mental well-being. There is consensus on the view that the ratio must be maintained as well as adjusted according to the requirements in certain diseases and dietary factors, which alter the need of these nutrients [14]. During evolution as a result of increased intake of omega-6 fatty acids as compared to omega-3 fatty acids in the western countries, the ω-6/ω-3 ratio has shifted from 1:1 to 20:1. In the South Asian countries due to excessive intake of sunflower, corn oil and soya bean oils, there is marked rise in the ω-6/ω-3 ratio to 45:1 [21].

By consumption of omega-3 fatty acids, the risk associated with contaminants like methylmercury, polychlorinated biphenyl or dioxins will increase. These contaminants have prolonged half-lives within the human body. In dietary supplements EPA and DHA concentrations of up to 30% and variations in this value are found. To enable a regular supply of EPA and DHA, a stringent check on the concentrations of up to 30% and variations in this value are found. To within the human body. In dietary supplements EPA and DHA intake replaces the omega-6 fatty acids especially AA in the cell membranes of platelets, erythrocytes, neutrophils, monocytes and liver cells [20].

Figure1: Schematic representation of various Fatty Acids

Excessive dietary intake of omega-3 fatty acids in very large quantities cause unwanted side-effects. High risks of bleeding for e.g. in gastro-intestinal tract or stroke involving brain are associated side-effects. Diarrhea, nausea, vomiting and loss of appetite are significant gastro-intestinal symptoms. However, the pediatric populations differ in these symptoms when compared to the adult populations in the manifestation of clinical symptoms. The treatment recommended is consumption of fatty acids along with the regular diet. Although, chronic consumption of fatty acids may cause deficiency of vitamin E. It is advised to increase consumption of polyunsaturated fatty acids supplemented with vitamin E intake[22].

Role of Omega-3 fatty acids in Inflammatory Diseases

Inflammation caused in diseases such as diabetes, atherosclerosis, asthma and arthritis are decreased due to the anti-inflammatory mechanisms of omega-3 fatty acids. A cytosolic protein complex known as inflammasome becomes the major target for omega-3 fatty acids to exert their anti-inflammatory properties. Due to infections by pathogens or by a triggered mechanism, inflammasomes releases pro-inflammatory cytokines such as interleukin -1β (IL-1β), IL-18 and IL-33. Activation of inflammasome as well as caspase -1 and secretion of IL-1β is inhibited by the action of omega-3 fatty acids. G protein-coupled receptor 120 (GPR 120), GPR 40, β-arrestin-2 which is a downstream scaffold protein are involved in inflammasome inhibition. This is enabled by omega-3 fatty acids repressing the inflammasome, especially in ILN-β treatment provided for multiple sclerosis and nitric oxide regulator of inflammasome in lipopolysaccharide (LPS) induced septic shock are due to the anti-inflammatory properties of omega-3 fatty acids which are consumed in the diet [23].

Role of Omega-3 fatty acids in Cancer Treatment

Several in-vitro and animal models of cancer provide evidences suggesting the preventive and therapeutic role of omega-3 fatty acids in cancer. The antineoplastic action of omega-3 fatty acids are by three modes of action. Primary mode of action is by affecting the activity or expression as well as levels of cellular signaling molecules. Physical-chemical changes occur in the molecular lipid microenvironments (rafts) on the cellular surfaces. This event causes changes in the activity/expression of constituents of membranes and molecular pathways occurring downstream causing inhibition of cellular proliferation or even inducing apoptosis. Secondly peroxidative reactions make omega-3 fatty acids susceptible to reactions with oxidants within the cells. This has effects on the oxidative stress dependent molecular pathways associated with cell proliferation, apoptosis and inflammation. The third route of action involves the metabolic conversion of omega-3 fatty acids into bioactive molecules with anti-inflammatory activity. Receptors bind to these bioactive molecules as well as omega-3 fatty acids (e.g. peroxisome proliferator activated receptor γ (PPARγ), G protein coupled receptor GPR 120). The signaling originating from these receptors is translated downwards causing activation of specific molecular cellular pathways [24].
Effects of Omega-3 fatty acids on Obesity

Body metabolism can be improved in obesity by calorie restriction and increase in physical activity. In obesity, combining physical exercises with omega-3 fatty acids diet will prove more beneficial for the body than the results obtained by utilizing only physical exercises. The decrease in body weight as well as reduction in fat deposition is facilitated by multiple modes of action by omega-3 fatty acids [34]. Primarily through increase in post-prandial satiety that causes reduction in the intake of food [35]. Secondly, omega-3 fatty acids reduces body fats by enhancing lipid oxidation, by reducing efficiency of peroxisomal oxidation of lipids as well as mitochondrial substrate oxidation by increasing uncoupling proteins in liver; cardiac muscles, particularly skeletal muscles a major site for lipid metabolism [36], as well as lipid oxidation in the intestines [37]. This promotes lipid oxidation in the intestinal tissue, skeletal muscle, liver and heart, causing reduction in the metabolic efficiency of these tissues leading to decrease in the substrate availability for deposition in the adipose tissue. Initially omega-3 fatty acids promotes lipogenesis in the adipose tissue. There are alterations in gene expression due omega-3 fatty acids in the adipose tissue leading to enhanced lipid oxidation and decrease in lipid deposition [34].

Role of Omega-3 fatty acids during Pregnancy

During pregnancy linoleic acid (omega-6) and linolenic acid (omega-3) are the essential fatty acids required in the diet for the formation and development of brain, eyes as well as eicosanoids in mother and foetus [38]. Deficiency of omega-3 fatty acids may result in lower intelligent quotient (IQ) scores as well as visual problems in infants, risk of depression in adults and potential risk of chronic diseases such as cardiac diseases involving inflammation [39][40][38]. There is deficiency of omega-3 fatty acids observed in pregnant women of western countries [41]. The reason being avoidance of sea foods a major source of omega-3 fatty acids in fear of mercury contamination. Intake of omega-3 fatty acids should be encouraged in women planning pregnancy, during pregnancy and lactation phase [42].

Effects of Omega-3 fatty acid on Eyes

Intake of omega-3 fatty acids prevents diseases of the eyes such as dry-eye syndrome, age-related macular degeneration (AMD) and cataract [43]. The lipid content of the outer membrane of the retinal photo receptor of the eyes consists of docosahexaenoic acid (DHA) which is a major omega-3 fatty acid. Alterations in permeability, fluidity, thickness, lipid contents of the membrane, retinal cell signaling molecular pathways involving retinal bound proteins, regeneration of rhodopsin and phototransduction are controlled by DHA. Inadequacy of DHA results in alteration of retinal function and deficiency in visual processing. Omega-3 fatty acids are essential for metabolic needs of photoreceptor cells in inflammation and diseases of the retina which are induced by age [44].

Role of Omega-3 Fatty Acids in Metabolic Syndrome

Glucose intolerance, central obesity, insulin resistance, risk factors for cardiovascular diseases, hypertension and gout are metabolic abnormalities in metabolic syndrome [45]. Ensuring satiety instead of polyphagia, balancing pro and anti-inflammatory transcription factors thereby balancing the hormones and even genetic control provides ultimate treatment for metabolic syndrome. Reduction in cellular inflammation can be induced by the diet. Genes involved in the cellular inflammation are silenced by the anti-inflammatory diet which has therapeutic benefit as compared to pharmacological drugs. Consumption of anti-inflammatory nutrients such as omega-3 fatty acids is a form of gene-silencing technology which silences the gene involved in cellular inflammation. Pharmacological drugs act downstream from the molecular target of cellular inflammation (NF-κB) whereas anti-inflammatory nutrients work upstream at the gene level to decrease the dietary factors that activate (NF-κB) to cause cellular inflammation [46]. In a recent study it has been reported that increased intake of omega-6 fatty acids without consideration for adequate omega-3 fatty acid may develop into metabolic syndrome with clinical manifestations which include hypertension, hypertriglyceridemia, hyperglycemia, low HDL and central obesity [45]. Omega-3 fatty acids controls leptin gene expression and levels of anandamines in the brain which further binds to endogenous cannabinoid receptors to regulate food intake, satiety and weight gain [47]. Deficiency of omega-3 fatty acids may lead to metabolic syndrome therefore maybe utilized for the prevention and management of metabolic syndrome. It is important to balance omega-6 :omega-3 ratio in the diet as well as decrease in consumption of refined carbohydrates and saturated fats [48] [49][50].

Role of omega-3 fatty acids in Brain

The following mechanisms have been suggested for the action of omega-3 fatty acids in brain functioning [51]

i) Omega-3 fatty acids have an inhibitory effect on the signaling pathways in the brain e.g. phosphoinositide 3-kinase (PI3K) and calmodulin dependent protein kinase C or cannabinoid receptors to regulate food intake, satiety and weight gain [47]. Deficiency of omega-3 fatty acids may lead to metabolic syndrome therefore maybe utilized for the prevention and management of metabolic syndrome. It is important to balance omega-6 :omega-3 ratio in the diet as well as decrease in consumption of refined carbohydrates and saturated fats [48] [49][50].

ii) Omega-3 fatty acids competes with arachidonic acid (AA) and its incorporation in the cell membrane decreases. Arachidonic acid is involved in the synthesis of pro-inflammatory eicosanoids like leukotriene B (LTB4), thromboxane-A2 (TXA2). Whereas anti-inflammatory eicosanoids such as prostaglandins-3 and prostaglandins 3α (PGF 3α and PGF 3β) are formed from EPA [22].
i) Oxidative degradation of DHA and EPA by lipooxygenases enzymes result into resolvin, docosatrienies and protectins [55] [56]. Resolvin are subclassified into D-series derived from DHA and E-series from EPA respectively [57]. Resolvin E1 function to decrease inflammation via suppression of the activity of transcription factor NF-kB [55]. Neuronal survival is enabled by the control over the pro or anti-apoptic genes by neuroprotectins [51]. Brain is protected from ischaemic damage by activities of resolvin [58].

ii) Omega -3 fatty acids regulates the brain energy metabolism [51], having control on both glucose uptake and glucosetransporter-1 [59]. Neuroimaging studies provide evidence about correlations between plasma fatty acids levels and cerebral metabolic rates for glucose in the brain [60].

iii) Omega -3 fatty acids also influences the blood supplies to the brain in a beneficial manner [61].

There is a trend in the Western population to consume omega-6 fatty acids in excess as compared to omega-3 fatty acid in the diet. This affects the omega 6/omega-3 ratio to shift from 1:1 to 15:1 which leads to disorders of the brain especially in such populations. Omega-3 fatty acid supplementation in diet may reduce the increased incidence of depression and other mood disorders in the Western population [62] [63].

**Effect of Omega -3 Fatty Acids on Athletic Performance**

Omega -3 fatty acids intake in the diet positively influences the mood, behavior and physical performances of athletes [64] [65]. Consumption of omega -3 fatty acids protects athletes from cardiovascular diseases [66] [67] and cardiac arrhythmias [67][69], improvement in lipid profile, lowers blood pressure, increases oxygen supply to the cardiac muscles during strenuous physical exercises [15]. Further, basal metabolic rate, oxidation of fatty acid and production of endogenous antioxidant enzymes are increased in athletes; this increases insulin utilization, lowers metabolic syndrome and platelet aggregation in them [70]. Amelioration of oxidative stress, decrease in inflammation and better lipid profile is observed in athletes consuming omega-3 fatty acids in diet [15]. Antioxidative benefits are provided by omega-3 fatty acids intake further reduces oxidative stress in athletes by inhibiting lipid peroxidation [70] [71]. In athletes and healthy adults muscular pain is a common side-effect of inflammation [15].

Resolvins E1 function to inhibit inflammation, sensitivity of the muscles, overcome discomfort during exercise sessions, better cell elasticity and reduced muscular lesions [64]. The pulmonary function in terms of pulmonary volumes, capacity, circulatory system, oxygen saturation, alveolar ventilation and partial pressure for oxygen are improved in athletes especially wrestlers consuming omega-3 fatty acids [73].

Training programs of high-intensity for athletes causes exercise-induced bronchoconstriction and decreases pulmonary function post-exercise. This may occur in elite athletes due to exercise induced hyperventilation, allergens or irritants, dehydration of airways causing production of histamines, neuropeptides, leukotrienes, prostaglandins, cytokines which result in contraction of smooth muscles of bronchi. These conditions and symptoms of exercise-induced bronchoconstriction are reversed by consumption of omega-3 fatty acids by these athletes in diet enabling anti-inflammation [69] [74].

**CONCLUSION**

Essential fatty acids are long-chained polyunsaturated fatty acids which consist of omega-3 and omega-6 fatty acids. A healthy, regular diet should ensure that the ideal ratio of omega-6/omega-3 is maintained. This provides protection against several harmful diseases. The influence of omega-3 fatty acids on inflammation, cancer, cardiac health, obesity, pregnancy, eye health, metabolic syndrome, brain function and athletic performance are reviewed focusing upon their beneficial roles.

Globally, in the contemporary scenario to maintain the health status of human beings, along with maintenance of quality and ensuring the zero contamination of dietary brands; the supplementation of foods with omega-3 fatty acids is a necessary proactive measure to be undertaken in future.

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