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Review Article

Synthesis and Functional Significance of Poly Unsaturated Fatty Acids (PUFA's) in Body

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Abstract

There are 2 types of polyunsaturated acids (PUFA's) namely omega 6 and omega 3 series. PUFA's possess amphipathic properties i.e. hydrophobic head and hydrophilic tail. Such structure besides other properties of unsaturated fatty acids cause biological action especially maintaining cell membrane fluidity inhibiting inflammatory processes, decreasing secretion of proinflammatory cytokines by monocytes and macrophages/reducing susceptibility to ventricular rhythm disorders of the heart, improving functions of the vascular endothelial cells, inhibiting blood platelet aggregation and reducing triglyceride synthesis in the liver. In an organism arachidonic acid (ARA) gets converted to prostanoid series (PGE2, PGI2, TXA2) and leukotrienes (LTB4, LTC4, LTD4) which have proinflammatory potential and can induce platelet aggregation and vasoconstriction. The metabolism of EPA and DHA gives prostanoid series (PGE3, PGI3, TXA3) and leukotriene series (LTB5, LTC5, LTD5), this group of eicosanoids show anti-inflammatory and antiarrhythmic properties.

Keywords: Polyunsaturated Acids (PUFA); Arachidonic Acid (ARA); EPA; Docosahexaenoic Acid (DHA)

Introduction

Fatty Acid-Structure

Lipids belong to a heterogenous group of compounds made up of carbon and hydrogen atoms having a similar number of oxygen containing functional groups. Lipids can be divided into simple and complex compounds. Simple ones are esters of fatty acids and different alcohols. In lipids glycerol is an alcohol which is made up of 3 hydroxyl groups at present Carbon atoms which according to stereoscopic numbering are as sn-1, sn2 and sn-3. As per the number of attached acids, mono i.e. 1 acid, di and triacyl glycerol's get formed. Simple triacylglycerol are characterized by the presence of one type of acid although there are 2 or 3 types of acids in mixed triacyl glycerols. Fatty acids are the main part of membrane lipids and mostly contain 12-24 C atoms. They may be represented by saturated (without double bonds), monounsaturated (one double bond) and polyunsaturated acids having 2 or more double bonds. Figure 1 shows polyunsaturated fatty acids of omega 3 and omega 6 series [1-3]. Fatty acids mostly occurring in nature have usual names like palmitic acid, linoleic acid, arachidonic acid but because of different forms and number of possibilities of conversions, some rules as per nomenclature have been used. Order by which numbering C atoms in aliphatic fatty acids is done starts from the carboxyl group, C in this group (COOH) is referred to as C1 and future numbering continues like C2, C3 etc. According to a separate classification, C attached to the carboxyl group i.e. C2 is named by the Greek letter alpha-α, C3-β, C4-γ etc. and the C atom which is furthest from the COOH group is defined by the letter omega-ω. Once one starts counting from C ω to the first double bond between C atoms in the hydrocarbon chain (C-C), we can find out the affiliation of the acid to series of omega 3, omega 6 or omega 9 fatty acids. To present the chemical structure of fatty acid we use the number of C atoms (e.g. C22), the number of double bonds and the group ω e.g. docosahexaenoic acid (DHA) is defined as C22:6ω-3, which means that it has 22 C atoms, 6 double bonds when we count from the end at the 3rd C atom [1-3].

Fatty Acid Metabolism

Saturated fatty acids like palmitic acid (C16:0) or stearic acid (C18:0) which give energy are produced In humans and other mammals. The formation of malonyl coenzyme A (CoA) and acetyl CoA is the basic step of fatty acid synthesis. For elongation to take place fatty acid synthase is required. However some mammals including *Homo Sapiens* do not possess the enzymes (or possess them in slight amounts) capable of creating double bonds in fatty acid chains at a place distant than at C9. Human being is not capable of producing linoleic acid (LA:C18:2ω-6), and α-linolenic acid (ALA:C18:3ω-3), in sufficient quantities to meet the requirement for these compounds, hence they are termed exogenous acids. These 2 compounds give rise to the others and all of them constitute a group of essential fatty acids having high physiological significance (Figure 1). Human beings have the ability to elongate these 2 exogenous acids to a slight but insufficient degree, however their requirements is > than the endogenous supply [1-3].

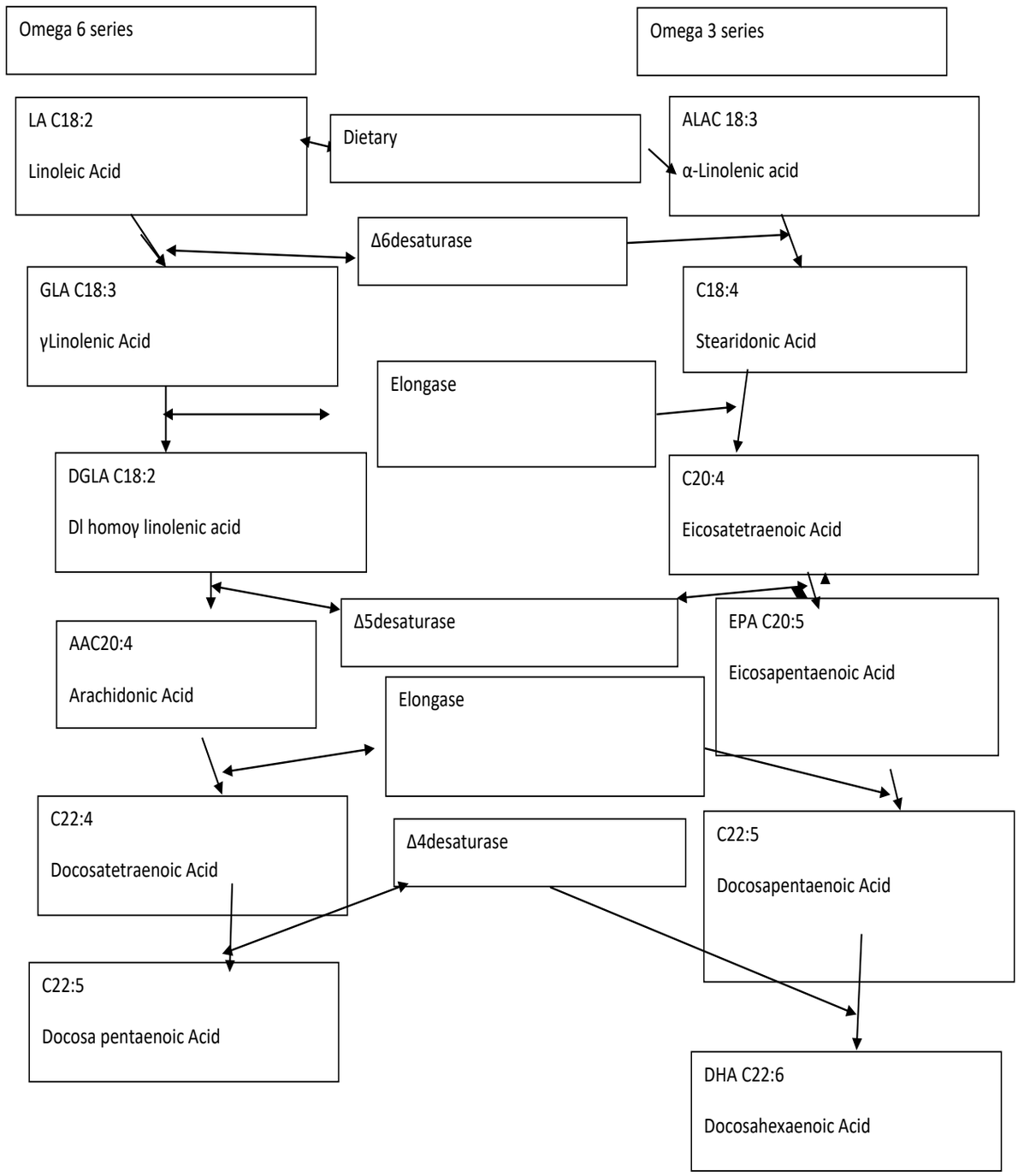

Figure 1: Pathways of biosynthesis of unsaturated fatty acids-omega6 and omega 3 series.

Elongation of Linoleic Acid and Linolenic Acid

Omega 6 series is made from Linoleic Acid and constitutes arachidonic acid (AA or ARA; C20:4ω-6), the last being docosapentaenoic acid (DPA-C22:5ω-6). Giving α-linoleic acid into the body helps to form omega 3 fatty acid series like eicosapentaenoic acid (EPA:C20:5ω-3) and docosahexaenoic acid (DHA:C22:6ω-3). For synthesis of these acids (Δ6, Δ5 desaturases i.e. enzymes which form double bonds) and elongase (elong a long hydrocarbon chain are required which takes place in the endoplasmic reticulum. The last stage of conversion i.e. β oxidase) needs translocation of substrates to peroxisomes. Omega 9 series of fatty acids also compete for the same enzymes and these reactions result in a final formation of eicosatrienoic acid (C20:3ω-9) from oleic acid (C18:1ω-9), which is not so important as the remaining 2 series since it can be totally synthesized by humans from saturated stearic acid. Further a high concentration of eicosatrienoic acid, which normally occurs in trace amounts indicates deficiency of substrates for the synthesis of omega 3 and omega 6 series of polyunsaturated fatty acids, this value may have a diagnostic importance. The same enzymes take part in conversion of fatty acids of all 3 series showing functional connections between metabolic pathways of omega 3, 6 and 9 acids, which depend on competing for enzymes and regulating a given stage of transformation based on a negative feedback through a direct or indirect product [1,2,4].

Eicosanoid Synthesis

Because of external conversion of omega 3 and omega 6 families of fatty acids like arachidonic acid (ARA), DHA, EPA get formed, which are precursors of mediators of a lot of compounds having importance physiologically (Figure 2). Eicosanoids i.e. prostaglandins and leukotrienes are products of the ARA and EPA metabolism, their names get derived from the Greek word eikos i.e. 20 as their precursors is made up of 20 C atoms, ARA, affected by cyclooxygenase (COX) undergoes conversion into prostaglandin E2, which is an inflammatory mediator, prostacyclin I2 (PGI2), responsible for blood vessel dilation and thromboxane A2 (TXA2), activating blood platelet aggregation and vasospasm. Due to lipoxygenase (LOX) action 4 series of leukotrienes get formed which have an important role in the development and maintenance of the inflammatory response EPA (C20:5ω-3), get mobilized in a similar manner with the involvement of the same enzymes i.e. cyclooxygenase and lipoxygenase, however its metabolic products are different i.e. 3 series of prostanoids and 5 series of leukotrienes of different properties mainly anti-inflammatory (PGE3, LTA5, LTB5, LTC5, LTD5), antiaggregatory (TXA3) and vasodilative (PGI3) [1,4-6].

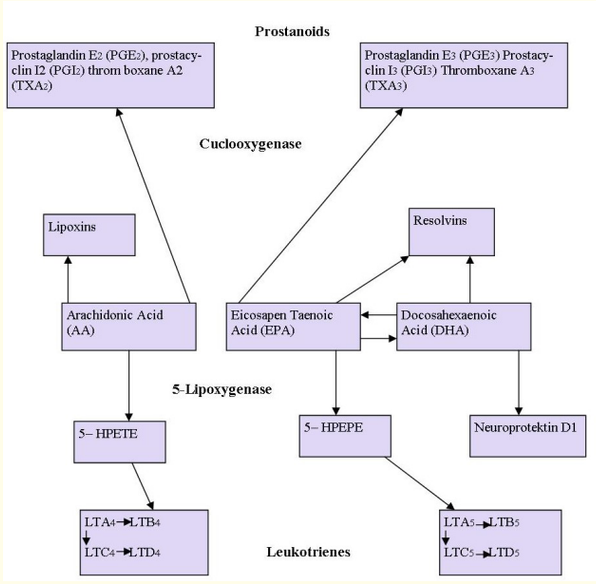

Figure 2: Metabolic pathway of a polyunsaturated fatty acid omega-6 and omega-3 series.

Synthesis of Compounds with Extinction of Inflammatory Processes Capacity

Inflammation mobilizes Prostanoids and leukotrienes, which are damage stimuli. Acute inflammation which tests for a relatively short time is a beneficial process in which threatening factors get removed and functions as tissue structure gets restored. Inflammatory resolution/extinction is an important active stage, which is mediated by small molecules which are the products of the omega 6 and omega 3 metabolites. Under the influence of lipoxygenases (LOX; LOX5-LOX15 and LOX12) ARA, EPA and DHA acids undergo conversion into lipid mediators actively extinguishing the inflammation process like lipoxin A4 and B4, LPXA4, LPXB4, arising from ARA. E series resolvins (RvE1 and RvE3), generated from eicosapentaenoic acid and D series resolvins (RvD1, RvD2, RvD3 and RvD4 generated from docosahexaenoic acid [7,8]. Also atleast 2 oxylipins get formed from DPA-ω6acid, which also have property extinguishing inflammation. At the same time, an involvement of acetyl salicylic acid (ASA), commonly named aspirin/poloprin has been observed which acetylates COX2 and ASA-COX2, in turn metabolizes ARA, EPA and DHA acids into intermediate products which next form lipoxins and E and D series resolvins with participation of lipoxygenases. COX2 acetylation inhibits formation of this enzyme, however it maintains the ability to synthesize 15R hydroxy eicosatetraenoic acid which is next converted to resolvins by activated inflammatory cells. Importance of ASA is the initiation of those conversions achieved are preceded by symbol AT-derived from aspirin triggered: aspirin triggered lipoxins-ATL, aspirin triggered resolvins-ATRvE or aspirin triggered resolvin D-ATRvD [9-11]. The roles described above for ESA functions highlights importance of this drug as an anti-inflammatory agent which not only inhibits the initiation of the inflammatory process but participates in the extinction of ongoing inflammation as well.

DHA influenced by lipoxygenases (LOX) is also converted into other compounds with protective potentials i.e. protectins, PD1 (D1 indicates derivation from DHA and no.1 defined the first compound in this series). The protectin which gets formed in the CNS is termed neuroprotectins, NPD1, which has neuroprotective properties. NPD1 occurs in photoreceptors and retinal pigment epithelium (RPE), it is responsible for the inhibition of expression and activity of proinflammatory factors and proapoptotic caspase3 as well as for the stimulation of antiapoptotic factors (i.e. proteins of Bcl2 family) [12-17].

There is still another path of the DHA conversion affected by lipoxygenases, which =.> formation of the next group of compounds, maresins having anti-inflammatory activity. Until now only one compound from the group MaR1 has been determined. The term maresin derives from the initial letters of the macrophages, resolution, inflammation, which describes the site of formation of this compound and its biological functions. Biological activity of MaR1 includes multidirectional interactions which => the limitation of polynuclear leukocyte aggregation in the area of inflammation resulting from the stimulation of phagocytic activity of macrophages [11,18,19].

Oxidation of polyunsaturated Fatty acids

Because of double bond (-C=C-) PUFA's are susceptible to oxidation by radicals produced by increased amounts during the oxidative stress (haemostatic disorders causing increased production of ROS which are not sufficiently deactivated by antioxidants). Lipid peroxidation without the enzyme involvement comprises the process namely initiation, propagation and termination processes of initiation depends on the OH* reaction with PUFA as a result of which a lipid radical is produced which in reaction with O_2 provides LOO* (a radical of lipid peroxide) having the ability to detach

hydrogen from other molecules and to generate subsequent radicals L*. These radicals undergo conversion into alcoxylic radicals LO* in the presence of iron Fe^{2+}, and next into peroxylic radicals which are decomposed into reactive aldehydes; 4 hydroxynonenal 4 hydroxy hexanal malonic dialdehyde and acroleins defined as secondary toxic transmitters. Omega 6 series fatty acid like linoleic or arachidonic acid are mainly converted into 4 hydroxy 2 nonenal (HNE) and omega 3 acids (EPA, DHA) into 4 hydroxy 2 hexanal (HHE) [20-22]. Monoperoxides are always primary products of PUFA's which are defined as lipid peroxides with an additional group LOOH. The no. of monoperoxides which can be generated from unsaturated fatty acids depends on the number of double bonds (n) and can be represented by the formula: 2n-2, which means that monoperoxides with OOH group will generate from linoleic acid (18:2) at the 9th and 13th C atom (9-OOH, 13-OOH), on the basis of this formula 6 different monoperoxides are produced from arachidonic acid (20:4)-8 from EPA (20:5) and 10 from DHA (22:6). As a consequence of PUFA oxidation changes in the physical properties of the cell membrane) a decrease in electric potential difference on both sides of the membrane) occur which => loss of functioning and structural integrity of the cell membrane [19-26]. Lipids are attacked by free radicals in a special way. The conversion described alone which occurs under the influence ROS which are not the only ones, because Morrow., *et al.* [21] in 1990 discovered isoprostanes which are the compounds resembling prostaglandins which get generated from arachidonic acid. Because of ROS oxidation irrespective of COX. Further studies showed that because of peroxylic transformations, isoprostanes of various types can arise both *in vivo* as well as *in vitro* from omega 3 series of PUFA's like EPA and DHA [24,25]. Isoprostanes derived from DHA within the tissues of the CNS are called neuroprostanes-it is of interest that there are more of them as compared to other isoprostanes [26]. In *in vivo* conditions in the presence of increased partial pressure of O_2 from arachidonic acid, extra compound of the isofuran structure and DHA structurally similar compounds called nitrofuran get formed [27]. In cerebral cortex of animals which are used as a model of Alzheimer's disease higher concentration of these has been found [28]. The first report regarding free radical formation of isoprostanes from arachidonic acid suggested that these compounds might be mediators of oxidative stress. This hypothesis has been confirmed by future research on free radical formation of isofurans and neurofurans in biological fluids like urine, blood or CSF. Hence the measurement of iso/neurofuran concentration can be used as a reliable biomarker for intensity of oxidative stress and lipid peroxidation in the cells/tissue/organism and a biomarker of an advanced stage of neurodegeneration in the CNS [25,27]. Supplementation of fish oil having high amounts of EPA provides anti-inflammatory properties which results in marked reduction of forming isoprostanes (F2-IsoPs) from arachidonic acid with strong proinflammatory activity [28].

Fatty Acid Functions

Omega 3 and omega 6 fatty acids play definite functions in the organisms and their neurofunctions are still being discovered. On the basis of unsaturated fatty acids conversions in the human body, their role in forming prostanoids and leukotrienes have been seen. When they arise from ARA like PGE2, PGD2 or 4 series leukotrienes, they exhibit proinflammatory activity which is commonly known and described in the reports which discuss the mechanism of nonsteroidal anti-inflammatory drug action. Basic studies have shown that DHA and EPA are beneficial for the human body exerting these biological actions [29].

Namely

1. Maintaining cell membrane fluidity
2. Inhibiting inflammatory processes
3. Reducing secretion of proinflammatory cytokines by monocytes/macrophages
4. Reducing susceptibility to ventricular rhythm disorders of the heart
5. Improving functions of vascular endothelial cells
6. Inhibiting blood platelet aggregation
7. Decreasing triglyceride synthesis in the liver.

Omega 3 fatty acid and cell membrane fluidity

Cellular elements constitute the membrane of the cell as well as of mitochondrion, which are built up of proteins and lipids, which contain saturated and unsaturated fatty acids. Saturated fatty acids have simple tails as they do not possess double bonds. They are densely packed so there is no space between the chains => rigid membrane. The presence of unsaturated fatty acids with various double bonds (which occur in nature in the cis confirmation) causes tail hydrocarbon chain bending which in turn => forming free spaces and affects membrane fluidity and elasticity. Polyunsaturated DHA usually occurs in cellular and plasma membranes of the organism. Its high amount has been especially found in the brain tissue and retina (upto 50% and 60 - 80% membrane phospholipids respectively). DHA may occur in the free state or combine with phosphatidyl ethanolamine (PEA) and phosphatidyl choline (PC) as well as in the phosphatidyl serine (PS) [3,30]. DHA in the cell membranes (membrane rafts) are especially rich in DHA) exerts influence on their physical properties-ensures proper fluidity and also affects the proper functioning of membrane receptors, ion channels and transporting proteins, i.e. elements involved in adequate cell reactivity, its ability to reach to stimuli and in inter cellular communication [31].

Effects of omega 3 Fatty acids on anti-inflammatory activity

Omega 3 and omega 6 PUFA's are incorporated into cell membrane. They are released from membrane phospholipids and constitute substrates for eicosanoid synthesis and prostaglandins, prostacyclins, thromboxanes and leukotrienes. Eicosanoids arising from arachidonic acid (omega 6) induce an inflammatory response by 2 series prostanoid synthesis by PGE2 may also influence anti-inflammatory effect by increasing lipoxin production by inducing 15LOX (lipoxygenase) [17]. Arachidonic acid derived eicosanoids are responsible for proaggregation and vasoconstriction effect (TXA2 and TXB2) and proliferation of cancer cells (specially by breast, colorectal, prostate cancers [5].

3 series prostanoids and 5 series leukotriene arising from fatty acids of omega 3 series (mainly from EPA) possess weaker inflammation inducing properties, which means factors inducing infection, impairment or inflammation depends on the composition of cell membranes. If there are favourable proportions of omega 3 PUFA's the response to inflammatory factors is weaker. Production of lipoxins, resolvins as well as oxylipins from both groups of polyunsaturated fatty acids allow to extinct the ongoing inflammation or excessive tissue damage and development of various diseases whose pathogenesis is associated with inflammatory diseases. Omega 3 acids derivatives may also have antithrombotic activities countering blood vessel narrowing and inhibiting carcinogenesis [32,33]. Omega 3 fatty acids have anti-inflammatory and antiallergic activity predominantly by the inhibition of excessive immune response competing for mutual enzymes with omega 6 fatty acids in the metabolic pathway. They reduce the synthesis of proinflammatory compounds (LTB4, PGE2, IL-1, TNF) as well as stimulates the synthesis of cytokines with anti-inflammatory actions (IL-2, TGF). Alleviation of inflammatory symptoms has been seen after administration of omega 3 acid preparations in case of autoimmune diseases like rheumatoid arthritis, ulcerative colitis, asthma, psoriasis and other autoimmune diseases. Also some reports show that they may alleviate the course of inflammatory processes of the bacterial or viral origin [6,34,35].

Effects of Omega 3 fatty acids on CVS

Omega 3 fatty acids help improving lipid metabolism, EPA, DHA decrease the triglyceride levels in plasma by 30% and in patients with hypertriglyceridemia even by 80%. They also reduce the levels of total and LDL fraction cholesterol while increasing HDL fraction levels [37,38]. DHA and EPA normalize BP by the rise in prostacyclins and endothelium derived factor (EDRF)-nitrogen oxide (NO) belonging to vasodilated factors as well as by reduction in levels of thromboxane A2 (TXA2), a strong vasoconstrictor and PGE2, which stimulates renin production and reversed Na reabsorption). Hypotensive activity can also be caused by beneficial changes in the lipid composition of cell membranes at the receptor site for vasoactive hormones and by the weakened response to them. A correlation has been found between the acid composition in the fatty tissue and the BP value, an increase in α-linolenic acid in the fatty tissue by 1% correlated with a decrease in systolic BP by 5 mmHg. 3 - 4 weeks of omega 3 fatty acid intake caused a complete hypotensive activity [34-38]. Omega 3 acids have antithrombotic activity. They prolong the bleeding time by reducing the platelets tendency towards adhesion and aggregation. This activity results from inhibiting the synthesis of prothrombotic compounds like TXA2, and platelet activating factor (PAF), decreasing fibrinogen, increasing prostacyclin levels and activity of tissue plasminogen activator as well as of angiotensinogen III [39-41]. Omega 3 PUFA besides potentiating platelet response to antiplatelet drugs, reduce thrombin formation. In coronary artery disease it was found that patients who received omega 3 PUFA's along with aspirin and clopidrogel fibrin clots had a less compact structure which made it less resistant to lysis [42,43]. Because of omega 3 fatty acids stabilization of the atheromatous plaque occurs. In subjects using omega 3 supplementation, thicker fibrous capsule of the plaque and lesser inflammation have been seen. Beneficial changes may occur even in old atheromatous plaques. Some reports can be found In literature, indicating that omega 3 fatty acids supplementation may help in decreasing the incidence of restenosis after coronary angioplasty and to decrease the incidence of vessel closure after coronary arterial bypass graft surgery [44,45]. Also omega 3 acids have an important roles in preventing sudden death induced by arrhythmias in patients with incidence of ischemic heart disease. They function as modulators affecting calcium flow via type L channels and control Ca release from the endoplasmic reticulum. Because the presence of omega fatty acids, elongation of the refraction period (by 150%) and increase in the threshold of cardiomyocyte excitability (the power of electrical stimulation required for inducing a functional potential increases by 50% has been noted. Long term administration of omega 3 fatty acids at dose of 1 g/day => decrease in rate of hospitalization and death risk due to heart rhythm disorders [46,47].

Effect of Omega3 fatty acids on CNS

DHA plays an important role in proper functioning of the CNS of adults as well as its development during fetal life and childhood. It is one of the main constituents of phospholipids in neuron cell membranes especially in the synapse. Omega 3 fatty acids are also indirectly involved in the synthesis of dopamine and serotonin [48]. They seem to have a protective function in mood impairment. Some reports state that they may be useful for concentration and hyperreactivity in children with development of coordination disorders (DCD's) [49]. Also it is thought that use of omega fatty acids by patients with psychic disorders may provide health benefits not only due to their protective activity exerted on the nervous system but also due to alleviation of metabolic adverse effects of psychotropic medication and obesity frequently occurring in the group of pts [52]. DHA is also present in huge amounts in eye retina. The most important role performed by DHA in the eye is the role of a substrate for the earlier described compounds which have cytoprotective and anti-inflammatory activities involving neuroprotectin NPD1. DHA is involved in the structure of plasmic membrane of photoreceptors and especially their outer segment (POS). Moreover the presence of DHA in POS is essential for correct functioning of visual pigments (e.g. rhodopsin) [2]. However in certain situations like occurrence of oxidative stress DHA easily undergoes peroxidation and decomposes into smaller 7 carbon fragments from which immunogenic conjugates (adducts) arise after binding protein molecules (like albumin). Such molecules mobilize the immune system and can cause development of autoaggression reactions which in consequence may => age related macular degeneration (AMD). An e.g. of a 7C compound is 4 hydroxy 7oxohept-5enoic acid (HOHA) which is further converted into 2-(ω-carboxyethyl) pyrrole (CEP) and conjugated with the protein molecule (adduct CEP protein). Peroxidative fragmentation and fragmentation of immunogenic adducts or even all PUFA's consumed with food or in a form of diet supplementation. However free DHA oxidation where unfavourable action depends on local possibilities of their neutralization through antioxidative

protective systems [21,22]. This above situation demonstrates that PUFA' s are very important constituent for adequate functioning of the CNS or the vision organs, but due to their special susceptibility to oxidation they can give rise to molecules which exert side effects on the above mentioned structures and contribute to the development of various diseases. Therefore supplementation with DHA and other long chain PUFA's should be combined with antioxidant compounds like vitamin E and zeaxanthin the latter are usually recommended for subjects at risk of AMD development.

Fatty Acids in Diet

Both omega 3 and omega 6 PUFA's are referred to as essential fatty acids (EFA) which emphasizes their important role in the functioning of the organism and the necessity for supporting with food. EFA's are absorbed in the digestive tract (diet supplementation, reach the liver, where they are esterified into Phospholipids and next they get released into blood stream as lipoproteins. EFA's are necessary for proper growth, development and functioning of all tissue organs, mainly the retina, brain and heart. Hence considering how important EFA's are especially omega 3 series the international health organization emphasizes on need for constant and regular consumption of about 200 mg of DHA/day by adults in the various forms of food rich in DPA and EPA or pharmacological preparations containing these acids [3,51]. Marine fish predators are the richest source of DHA and EPA. Other types of fish like salmons, herring, sardines, mackerel, tunas, halibuts, flounders and trout contain ω-3 series of fatty acids in slightly lower amounts. They also occur in different seafood and algae. Cultivated microalgae crypthecodinium cotinis, are one of ω-3 acid source, whose oil contains 40% of DHA (i.e. DHASCO) and DHA single cell oil the product which has obtained positive opinion in US FDA and is recommended to be given to infants and small children. Other recommended sources of fatty acids in the oil produced by microalgae *Schizochytrium* species, which contains upto 40% of DHA, 12.5% of EPA and additionally A 15% of Docosapentaenoic acid (DPA), which balances to ω-6 (DPA-ω-6) acids. It has been stated that bioequivalence and effectiveness by supplementation are similar to those achieved by taking capsules containing oils from both types of algae and don't differ from eating an equivalent portion of ready to eat salmon. In various countries, foods enriched with small amounts of fatty acids i.e. bread, milk products, margarine or juice has been produced. These products are treated as functional foods, which beneficially affect the human body of the presence of bioactive compounds (natural or added) regardless of its nutritional properties [52,53]. Various national and International health organizations which deal with protection of health specify regular consumption of atleast 50 μg/day of EPA and DHA [54]. Nationally experts recommend consumption/supplementation of diet with omega 3 fatty acids for adults to take fatty acid DHA and EPA from 0.5 - 1.5g (mean 1g)/day. To achieve beneficial health effects ratio of omega 6 to omega 3 fatty acids in the diet should be 4:1 [2,29]. Because omega 3 fatty acids reduce platelet aggregation in the blood, which prolongs the time of bleeding their simultaneous application with anticoagulant drugs may potentiate the response of these drugs [43,55,56]. Therefore in patients taking these drugs, an additional dose of omega 3 fatty acids should not exceed 1 g/day. This dose which may be covered by foods, exerts cardioprotective action. Patients having high risk of cancer, cardiac, rheumatoid and neurodegenerative disease, the EPA and DHA dose can be increased upto 1.5 g/day. For treating hypertriglyceridemia omega 3 fatty acids can be used as supplements under the physicians control at a dose of 2 - 4 g/day (capsule containing 265 mg of EPA and 375 mg of DHA in the form of ethylene esters) [57]. It is especially beneficial to consume omega 3 fatty acids in everyday diet combined with statin or fibrate treatment-this combination is especially useful for mixed dyslipidemias [58]. As per the FDA data consumption upto 3g of omega 3 fatty acids/day should not induce side effects, however higher doses should be reserved for special situations specified therapeutic implications) and used only under physicians supervisions [2,29]. Best solution for people who do not have any special indications for fatty acid supplementation seems to be the consumption of fatty acids rich natural products, e.g. a meal containing fatty sea fish twice a week, what corresponds to roughly 500 mg/day of EPA+DHA+DPA. The Europe food Safety Authority (EFSA) draws attention to the fact that growing environment pollution, unlimited meal consumption of meat of large fish predators (mainly tuna, shark, marlin and pike) may lead to increased exposure to mercury [59]. Because toxic activity of Hg compounds is most dangerous for fetuses, infants and small children, women planning pregnancy, breastfeeding mothers and younger children are advised to choose smaller fish which do not cumulate high amounts of these pollutants. In this group of people possibilities of supplementation with PUFA preparations should be considered.

Conclusions

Humans do not synthesize sufficient quantities of omega 6 and omega 3 series which must be provided in food. This is why they are referred to as essential. Sea fish oil is a source of DHA and EPA which limits their availability in the diet as compared to omega 6 fatty acids present in plants. But omega 3 series exhibit special beneficial effects on proper functioning of brain, CVS and eye retina. Because of presence of number of double bonds in the molecule. Double bond is sufficient for molecular properties, easily enter into reactions with radicals which promote their oxidation and changes their characteristics. At same time it is important to note that no significant side effects of these compounds has been observed. Also it should be noted that they can't replace a pharmacological therapy. But because of their involvement in maintaining health they should be supplied in proper balanced diet or as a pharmacological preparation as a diet supplement, which should also contain compounds possessing properties of lipophilic antioxidants like Vitamin E.

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