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Omega Fatty Acids in Health and Disease: A Review

Ramzi Abdulrashed Abdulkhaleq Gazem*, and Sharada A Chandrashekariah
Department of Biochemistry, Yuvaraja's College, University of Mysore, Mysore, 570005. Karnataka, India

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ABSTRACT

In the recent period there is renewed concern about dietary supplement of omega fatty acids for its beneficial effects on human health. Omega-3 (ω-3) and Omega-6 (ω-6) fatty acids are polyunsaturated fatty acids and both of them metabolically yield very long chain fatty acids which supports numerous physiological and development processes in the body. These are essential and must be obtained through the diet as they are not synthesized de novo in the human beings, The major dietary sources are plant seeds, nuts, fish oils and other sea foods, Many studies have revealed that omega fatty acids are potent molecules possessing anticancer, hypolipidemic, anti-inflammatory and anti diabetic activities and can reduce the risk of cardiovascular disease. Even though omega 6 fatty acid encompasses health benefits if not balanced with dietary supplement of omega 3 may cause detrimental effects Therefore the present article gives an account of chemistry, structure, and biological properties of ω -fatty acids and examines the importance of the ω-6/ω-3 balance in maintaining good health and its pivotal role in prevention of degenerative diseases and other inflammatory disorders.

KEYWORDS: Omega fatty acids, hypolipidemic, anti diabetic, anti-inflammatory, anticancer

1. INTRODUCTION:

Fatty acids (FAs) are the main constituents of oils and fats esterified to glycerol. Many fatty acids are known, but only 20 or less are encountered in significant amounts in the oils and fats of commercial importance and the most common are fatty acids with carbon chain length C_{16} and C_{18}.Carboxyl group and double bonds are the most reactive sites in fatty acids, methylenes neighboring to them are activated, increasing their reactivity[1].

Essential fatty acids (EFAs) can be outlined by classic definition, which defines that the fatty acids which are required for proper functioning of cells and are not synthesized by the body and, therefore, must be diet oriented. According to this definition, there are only two EFAs that is linoleic acid (LA, C18:2, ω-6) and alpha-linolenic acid (ALA, C18:3, ω-3). The proper definition of EFAs means that the fatty acids which can correct the symptoms produced by elimination of all EFAs from the diet. Thus, LA, Gamma-linolenic acid (GLA, C18:3, ω-6), and arachidonic acid (AA, C20:4, ω-6) can be included as EFAs of ω-6 family[2].

Plants and few marine species such as mussel, oyster, shrimp fish, were found to contain omega polyunsaturated fatty acids (ω-PUFAs) and are named as long chain PUFAs[3]. They are also present in a ample range of plant products such as nuts, especially walnuts, and seeds, namely sesame[4], flax seed, and vegetable oils such as canola, olive and soyabean[5]. ω-3 fatty acids, unlike saturated fatty acids, have various health benefits and are used in the treatment of rheumatoid arthritis[6] and coronary artery disease[7]. They were beneficial in improving blood pressure and preserving renal functions even in hypertensive heart transplant recipients[8]. The bioactive ω-3 PUFAs are effective against various cancers and also on other clinical disorders like rheumatoid arthritis, edema, cardiovascular disease and other closely associated disorders. Thus replacement of saturated fatty acids with ω-PUFAs gives the protection against metabolic disorders and diseases as ω-3 PUFAs have been considered as one of the cornerstones for healthy living and good nutrition.

This review attempts to convey collectively current information with respect to the biological activities, disease prevention and nutritional advantages of omega-Polyunsaturated fatty acids (PUFA).

***Corresponding author.**
Ramzi Abdulrashed Abdulkhaleq Gazem
Research Fellow, Department of Biochemistry,
Yuvaraja's College, University of Mysore
Mysore, 570005. Karnataka, India

2. Classification of Fatty Acids:

Fatty acids can be classified as saturated and unsaturated. Unsaturated FAs are further classified into two types namely monounsaturated and polyunsaturated, depending upon the number of double bonds present.

2.1. Saturated fatty acids (SFAs):

The most commonly found saturated fatty acids in animal and plant tissues are straight chain compounds with 14, 16 and 18 carbon atoms Examples are: myristic acid (14:0), palmitic acid (16:0) and stearic acid (18:0). In addition all possible odd- and even- numbered homologues containing 2 to 36 carbon atoms have been identified in nature in the esterified form[9].

2.2. Unsaturated fatty acids (USFAs):

The most common monounsaturated fatty acid identified in nature is oleic acid (18:1 ω-9) The most common double-bond position for monoenes is Δ9. However, few families of plants have also shown to contain unusual fatty acid patterns. For example, Eranthis seed oil contains Δ5 monoenes and non-methylene interrupted polyunsaturated fatty acids with Δ5 bonds[10]. Erucic acid (22:1ω-9) is present in higher concentration (40–50%) in plant seeds belonging to family Cruciferae such as rapeseed and mustard seeds. Canola oil is low in erucic acid content (<3% 22:1 ω-9). Polyunsaturated fatty acids (PUFAs) are best described in terms of families because of the metabolic pathway that allows only interconversion within, but not between, the families of PUFA. The essentiality of ω-6 fatty acids have been identified since 1920s and deficiency symptoms includes decreased growth, increased epidermal water loss, delayed wound healing, and impaired reproduction[11]. Early studies did not give clear evidence to affirm that ω-3 fatty acids are also essential. However in recent studies that is from 1970s, evidence has been accumulated clarifying the essentiality of the ω-3 PUFA. But all PUFAs are not EFAs, Plants can synthesize de novo and interconvert ω-3 and ω-6 fatty acid families by desaturases with specificity in Δ2 and Δ15 positions. Where as animals have only Δ5, Δ6, and Δ9 desaturase enzymes and hence are unable to synthesize de novo the ω-3 and ω-6 PUFAs.

2.2.1. Monounsaturated fatty acids (MUFAs):

Straight-chain, even-numbered fatty acids containing 10 to or more than 30 carbon atoms with one cis-double bond have been identified from natural sources. Cis-9-octadecenoic acid (18:1 ω-9), also designated as "Oleic acid." is the most abundant monounsaturated fatty acid in animal and plant tissues.

2.2.2. Polyunsaturated fatty acids (PUFAs):

Fatty acids containing two or more double bonds in their structure are referred as polyunsaturated fatty acids (PUFAs). There are two principal families of PUFAs, namely ω-3 and ω-6. The first double bond is located on the 3rd or 6th carbon-carbon bond, counting from the terminal methyl carbon (designated as n or ω) towards the carbonyl carbon, and double bonds are separated by one methylene unit. Humans cannot synthesize double bonds at 6 or lower positions hence ω-3 (n-3) and ω-6 (n-6) PUFAs must be obtained from the diet. The food sources of ω-3 are fishes and few varieties of plants, whereas ω-6 is mainly obtained from vegetable oils. Parent compound of the ω-6 family, linoleic aicd (LA) (18:2 ω-6) is profusely available in nature. Alpha-linolenic acid [ALA (18:3 ω-3)], the parent compound of the ω-3 family, is far less common. Both α-linolenic acid and linoleic acid can be elongated and desaturated to long-chain PUFAs in the human body.Linoleic acid is converted to arachidonic acid [AA, (20:4 ω–6)] and α-linolenic acid forms two types of products eicosapentaenoic acid [EPA, (20:5 ω-3)] and docosahexaenoic acid [DHA, (22:6 ω-3)]. The fatty acids are rarely found in free form but generally they form more complex molecules usually linked through ester bonds even other bonds like ether or amide bonds also exists[12].

3. Sources of Fatty Acids

Most of the commodity oils contain fatty acids with chain lengths ranging between C_{16} to C_{22}, and C_{18} fatty acids dominate in most plant oils. Laurel oils with medium-chain fatty acids are obtained from palm kernel and coconut. Fats of fish contain fatty acids with wider range of chain lengths and rape seeds are rich in C_{22} monoene acid **(Table 1)**.

Potential new oil crops with unusual unsaturation or with additional functions are under development. Compilations of the fatty acid composition of oils and fats[13] and less-common fatty acids[14] are conspicuously available (**Table 2)**.

Table 1. Fatty Acids and Their Significant Sources1

Fatty Acids	Sources
4:00	butter, dairy fats
6:00	coconut, palm kernel
8:00	coconut, palm kernel
10:00	coconut, palm kernel
12:00	coconut, palm kernel
14:00	coconut, palm kernel
16:00	cottonseed, palm
18:00	cocoa butter, tallow
18:1 9C	cottonseed, olive, palm, rape
18:2 9C, 12C	corn, sesame, soybean, sunflower
18:3 9C, 12C, 15C	Linseed/ Flaxseed
22:1 13C high erucic	rape
20:5 5C, 8C, 11C, 14C, 17C	fish and animal fats
22:6 4C, 7C, 10C, 13C, 16C, 19C	fish and animal fats

3.1. Sources of PUFAs:

Long chain PUFAs (C_{18}, C_{20} and C_{22}) especially ω-3 [ALA, 18:3] and

Table 2. Fatty Acid Content of the Major Commodity oils (wt%)[13].

Source	16:0 (wt%)	18:1 (wt%)	18:2 (wt%)	18:3 (wt%)	Other [Fatty acid (wt%)]
Butter	28	14	1	1	4:0 (9); 6:0–12:0 (18); 14:0 (14)+↑odd chain and trans
Castor	1	3	4	-	18:1(OH) (90)
Coconut	9	6	2	-	8:0 (8); 10:0 (7); 12:0 (48); 14:0 (18)
Corn	13	31	52	1	
Cottonseed	24	19	53	-	
Fish	14	22	1	-	16:1 n-7 (12); 20:1 n-9 (12); 22:1 n-11 (11);20:5 ω-3 (7); 22:6 ω-3 (7)
Groundnut (Peanut)	13	37	41	-	C_{20}–C_{24} (7)
Lard	27	44	11	1	14:0 (2) 18:0 (11)↑ long and odd chain
Flaxseed	6	17	14	60	
Olive	10	78	7	-	
Palm	44	40	10	-	
Palm Kernel	9	15	2	-	8:0 (3); 10:0 (4); 12:0 (49); 14:0 (16)
Rape seed	4	56	26	10	
Sesame seed	9	38	45	-	18:0 (6)
Soybean	11	22	53	8	
Sunflower seed	6	18	69	-	18:0 (6)
Tallow	26	31	2	-	14:0 (6) 18:0 (31) ↑+long and odd chain

ω-6 fatty acids; [LA,18:2] are most commonly found in few types of fish species[15]. These two EFAs are the only sources for the production of important longer chain PUFAs termed as prostaglandins which control blood pressure and other biological activities. Arachidonic acid [AA, (20:4 ω-6)], a member of the ω-6 PUFA, is the source of prostaglandins (PG). Eicosapentaenoic acid [EPA, (20:5 ω-3)], ALA and docosahexaenoic acid [DHA (C22)] are the three PUFAs or ω-3 PUFAs belonging to ω-3 series[16]. In addition, dietary ALA can be converted into EPA and DHA. AA, ALA and LA are long chain fatty acids are truly essential, while C_{18} compounds, like oleic, stearic and palmitic acids, exist in animal fats and can be considered as conditionally essential[17].

3.1.1. Omega-3-Fatty Acids:

Omega-3 fatty acids are essential, polyunsaturated fatty acids (PUFAs), they cannot be synthesized in human body. There are several sources of omega-3-fatty acids and can be obtained from marine animals and plants. Fish oils, flaxseeds and nuts, are the best dietary source of these fatty acids. EPA and DHA are derived from α-linolenic acid[18] and the other food sources are illustrated in the table given below (**Table 3**).

Table 3. List of Some Common Foods as a Source of ω-3 Fatty Acids[19].

Food	Rating	Botanical Name	Family
Flaxseed	Excellent	*Linum usitatissimum*	Linaceae
Cloves, dried, Ground	very good	*Eugenia caryophyllata*	Myrtaceae
Walnuts	Excellent	*Juglans nigra*	Juglandaceae
Cauliflower, boiled	very good	*Brassica, oleracea*	Brassicaceae
Mustard seeds	very good	*Brassica juncea*	Brassicaceae
Broccoli, Steamed	very good	*Brassica oleraceae* L.	Cruciferae
Spinach, Boiled	good	*Spinacia oleracea*	Amaranthaceae
Soybeans, Cooked	good	*Glycine max*	Fabaceae
Turnip greens, Cooked	good	*Brassica rapa*	Brassicaceae
Strawberries	good	*Fragaria ananassa*	Rosaceae
Raspberries	good	*Rubus idaeus*L.	Rosaceae

3.1.2. Omega-6-Fatty Acids

Small traces of GLA is existing in many plants belonging to the families of Aceraceae, *Boraginaceae*,*Cannabinaceae*, *Liliaceae*, *Onagraceae*, *Ranunculaceae*, *Saxifragaceae*,and *Scrophulariaceae*. Kleiman et al.,[20] (1964) investigated 29 species of family *Borageniceae* for the presence of GLA and tetraenoic [stearidonic acid (SDA)] fatty acid. They observed 0–27% GLA, 0–56% ALA, and 0–17% SDA in seed oils from different plants of *Boraginaceae*. In similar study Janick et al., (1989) identified GLA in the seed oil of 32 plants which was more than 5% weight/weight (w/w) of total fatty acid content[21] (**Table 4**).

Table 4. Selected Plant Species High in a -Linolenic Acid[22].

Family Genus and Species	Total oil content of the seed (%)	GLA content (%) in oil	of seed
Boraginaceae			
Adelocaryum coelestinum	22	12	2.7
Alkanna orientalis	23	12	2.8
Anchusa azurea	21	13	2.7
Anchusa capensis	29	10	2.9
Anchusa hybrid	20	13	2.6
Borago offcinalis	28–38	17–25	5:0–8:4
Brunnera orientalis	27	15	4.2
Cerinthe minor	10	10	1
Cynoglossum amabile	23	11	2.5

Family Genus and Species	Total oil content of the seed (%)	GLA content (%) in oil	 of seed
Cynoglossum lanceolatum	25	13	3.3
Echium rubrum	15	14	2.1
Echium vulgare	22	11	2.4
Gastrocatyle hispida	28	16	4.5
Lithospermum arvense	17	14	2.4
Lithospermum			
purpureocaeruleum	14	18	2.5
Moltkia aurea	10	10	1
Moltkia coerules	10	11	1.1
Nonea macrosperma	39	13	5.1
Onosma sericeum	20	13	2.6
Onosmodium molle	17	20	3.4
Onosmodium occidentale	17	18	3.1
Paracarvum caelestinum	21	12	2.5
Pectocarva platycarpa	15	15	2.3
Symphaticum officinale	21.0.	27	0 5.6
Cannabaceae			
Cannabis sativa	38	3–6	1.1–2.3
Onagraceae			
Oenothera biennis	17–25	7–10	1.2–2.5
Oenothera grandifolia	4	9.3	0.3
Saxifragaceae			
Ribes alpinum	19	9	1.7
Ribes nigrum	30	15–19	4.6–5.8
Ribes rubrum	25	4–6	1.0–1.5
Ribes uva-crispa	18	10–12	1.8–2.2
Scrophulariaceae			
Scrophularia marilandica	38	10	3.6

4. Chemistry and Composition of Fatty Acid

4.1. Fatty Acids

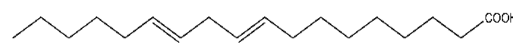
Most of the fatty acids are straight chain, aliphatic, carboxylic acids. The chain lengths of most natural fatty acids are C_4 to C_{22}, and C_{18} is the most common. All naturally occurring fatty acids share a common biosynthetic pathway.

Naturally occurring fatty acids predominantly contain even number of carbon atoms. The chain is built from two carbon units (2C) and cis double bonds are inserted by desaturase enzymes at specific positions from the carboxyl end. This result in even-chain-length fatty acids with a distinctive pattern of methylene interrupted with double bonds. In this pathway fatty acids of different chain length with various degree of unsaturation are synthesized.

Systematic names for fatty acids are too cumbersome for general use, and shorter alternatives are widely agreeable. The fatty acids are also represented by two numbers separated by a colon, indicating the chain length and number of double bonds example: octadecenoic acid with 18 carbons and 1 double bond is therefore 18:1. The position of double bonds is mentioned in a number of ways: clearly, defining the position and configuration; or locating double bonds from the methyl or carboxyl ends of the chain.

Double-bond position joined to the methyl end is shown as n-x or ω-x, wherein, x is the number of carbons from the methyl end. The n-system is now preferred, but both are widely used. The position of the first double bond from the carboxyl end is assigned as x. Common names (Table 1) may be historical, often conveying no structural information, or abbreviations of systematic names. Alternative impersonation of linoleic acid are 9cis, 12cis-octadecadienoic acid; 18:2; 9c, 12c ω-6 is given as under (**Figure 1**).

CH_3-$(CH_2)_4$-CH=CH-CH_2-CH =CH- $(CH_2)_7$-COOH

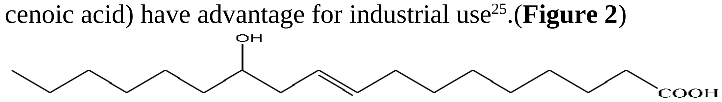


Data adapted from [25]

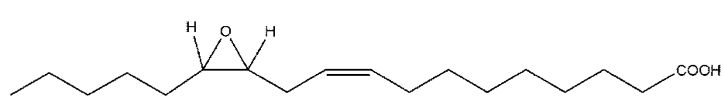
Figure 1. Chemical structure of linoleic acid precursor w**-6-fatty acids**

The terms cis and trans, are abbreviated as c and t, are used widely for double-bond geometry; as with only two substituent's, there is no perplexity that requires the systematic Z/E convention. An accurate discussion of fatty acids, lipid nomenclature and the structures are represented in the article by Akoh and Min[23] .

Around 1000 fatty acids are known, but 20 or less are encountered in significant amounts in the oils and fats of economical importance (Table 1). C_{16} and C_{18} are the most common fatty acids, below this range; they are classified as short or medium chain and above it as long-chain acids. Fatty acids with trans or non-methylene-interrupted unsaturation appear naturally or are formed during processing; for example, vaccenic acid (18:1 11t) and the conjugated linoleic acid (CLA) rumenic acid (18:2 9t11c) are found in dairy fats. Hydroxy, epoxy, cyclopropane, cyclopropene acetylenic, and methyl branched fatty acids are known, but only ricinoleic acid (12(R)-hydroxy-9Z-octadecenoic acid) from castor oil is used for oleochemical manufacture[24]. Oils containing vernolic acid (12(S), 13(R)-epoxy-9cis-octadecenoic acid) have advantage for industrial use[25].(**Figure 2**)



12-hydroxy-octadec-*cis*-9-enoic acid (Ricinoleic acid)



***cis*-12,13-epoxy-octadec-cis-9-enoic acid (Vernolic acid)**

Data adapted from 23

Figure 2. Chemical structure of epoxy and hydroxyl fatty acids found in nature

Typical fatty acid composition of the most widely traded commodity oils are shown in (**Table 5**).

Table 5. Fatty Acids in Commodity Oils and Fats. Nomenclature and Structure1

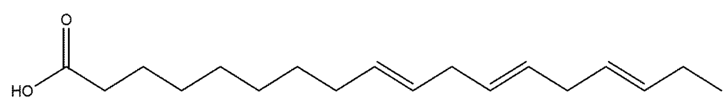
Fatty Acid	Common Name	Formula	Chain Length
4:00	Butyric	$CH_3(CH_2)_2COOH$	short
6:00	Caproic	$CH_3(CH_2)_4COOH$	short
8:00	Caprylic	$CH_3(CH_2)_6COOH$	short/ medium
10:00	Capric	$CH_3(CH_2)_8COOH$	
12:00	Lauric	$CH_3(CH_2)_{10}COOH$	
14:00	Myristic	$CH_3(CH_2)_{12}COOH$	
16:00	Palmitic	$CH_3(CH_2)_{14}COOH$	
18:00	Stearic	$CH_3(CH_2)_{16}COOH$	
18:1 9C	Oleic	$CH_3(CH_2)_7CH=CH(CH_2)_7$ COOH	medium
18:2 9C, 12C	Linoleic	$CH_3(CH_2)_4$-CH=CH-CH_2-CH=CH- $(CH_2)_7COOH$	medium
18:3 9C, 12C, 15C	α-Linolenic	CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-$(CH_2)_7COOH$	medium
22:1 13C	Erucic	CH_3-$(CH_2)_7$-CH=CH-$(CH_2)_{11}COOH$	long
20:5 5C, 8C, 11C, 14C, 17C	EPA	CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-$(CH_2)_3$-COOH	long
22:6 4C, 7C, 10C, 13C, 16C, 19C	DHA	CH_3-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-CH_2-CH=CH-$(CH_2)_2$-COOH	long

4.2. Omega-3-Fatty Acids

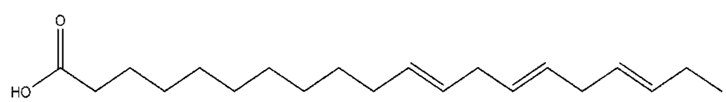
Among the several ω-3 fatty acids (**Table 6**) there are three ω-3 fatty acids which are nutritionally essential to humans which includes α-Linolenic acid (18:3.ALA), EPA(20:5), and DHA (22:6,) represented in Figure 3.These three polyunsaturated fatty acids have 3, 5 or 6 double bonds in a carbon chain of 18, 20 or 22 carbon atoms, respectively. All double bonds are in the *cis*-configuration; i.e the two hydrogen atoms are on the same side of the double bond. Fatty acids from plants or fish are in *cis* configuration and are more easily transformable. The *trans* configuration results in much more stable chains and are very difficult to further break or transform, forming longer chains that accumulate in tissues and they lack the necessary hydrophilic properties. Moreover, the ω-3 compounds are still more weak than ω-6 because the last double bond is geometrically and electrically more unstable, particularly in the natural *cis*-configuration. The ω-3 and ω-6 families categorized based on the position of the first double bond from the methyl end in the fatty acid chain. The biological activity of these molecules depends upon the position of the first double bond from the methyl end in fatty acid chain. Therefore, LA and ALA are regarded as the parent of ω-6 and ω-3 fatty acid series, respectively and the chemical structure of ω-3 fatty acids are shown in (**Figure 3)**.

Table 6. List of Most Common w-3 Fatty Acids Found in Nature[19].

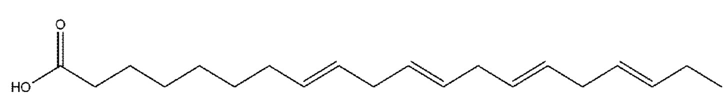
Common Name	Lipid Name	Chemical Name
Hexadecatrienoic acid (HTA)	16:3 (ω-3)	*all-cis*-7,10,13-hexadecatrienoic acid
α -Linolenic aicd (ALA)	18:3 (ω-3)	*all-cis*-9,12,15-octadecatrienoic acid
Stearidonic acid (SDA)	18:4 (ω-3)	*all-cis*-6,9,12,15-octadecatetraenoic acid
Eicosatrienoic acid (ETE)	20:3 (ω-3)	*all-cis*-11,14,17-eicosatrienoic acid
Eicosatetraenoic acid (ETA)	20:4 (ω-3)	*all-cis*-8,11,14,17-eicosatetraenoic acid
Eicosapentaenoic acid (EPA)	20:5 (ω-3)	*all-cis*-5,8,11,14,17-eicosapentaenoic acid
Docosapentaenoic acid (DPA), Clupanodonic acid	22:5 (ω-3)	*all-cis*-7,10,13,16,19-docosapentaenoic
Docosahexaenoic acid (DHA)	22:6 (ω-3)	*all-cis*-4,7,10,13,16,19-docosahexaenoic
Tetracosapentaenoic acid	24:5 (ω-3)	*all-cis*-9,12,15,18,21-docosahexaenoic acid
Tetracosahexaenoic acid (Nisinic acid)	24:6 (ω-3)	*all-cis*-6,9,12,15,18,21-tetracosenoic acid



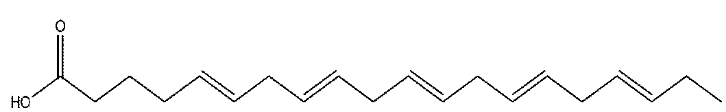
a**-Linolenic acid (ALA)**



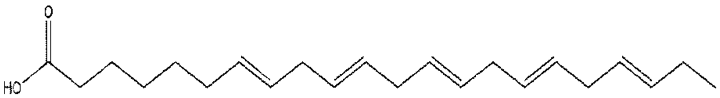
Eicosatrienoic acid (ETE)



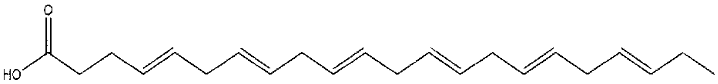
Eicosatetraenoic acid ETA



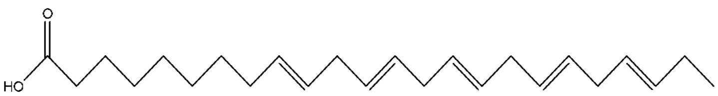
Eicosapentaenoic acid (EPA)



Docosapentaenoic acid (DPA)
Clupanodonic acid



Docosahexaenoic acid (DHA)



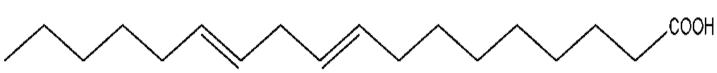
Tetracosapentaenoic acid (TPA)

Data adapted from[19]

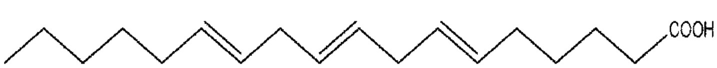
Figure 3. Chemical structure of omega-3- PUFA found in nature

4.3. Omega 6- Fatty Acids:

GLA is an 18-carbon polyunsaturated fatty acid containing three double bonds and its IUPAC name is cis-6, cis-9, cis-12-octadecatrienoic acid. It is produced in the body from desaturation of LA catalyzed by enzyme delta-6-desaturase (D-6-D). GLA is rapidly extended to DGLA (dihomo gamma linolenic acid) by elongase enzyme. DGLA can be acetylated and incorporated into membrane phospholipids. A small amount can be converted into AA, and is used for the synthesis of prostaglandins PGE1, PGE2, PGI2 and Thromboxane A2 (TXA2), 15-hydroxy eicosatrienoic acid (15-HETrE) and Leukotriene B4 (LTB4) and the reaction is catalyzed by the enzyme delta-5-desaturase. In animal species each tissue varies in their capacity to convert DGLA to AA. A considerable amount of DGLA is converted to AA in rats whereas humans and other species possess limited capacity to form AA from DGLA, chemical structure of ω-3 fatty acids are shown in (**Figure 4)**.



18:2 w**-6 Linoleic acid**



18:3 w**-6** g**-linolenic acid**

20:3 w**-6 Dihomo-**g**-linolenic acid**

20: 4 w**-6 Arachidonic acid**

Data adapted from[9]

Figure 4. Chemical structure of some Omega-6- PUFA found in nature.

The slowest reaction in the metabolic pathway of LA considered as a rate-limiting step is catalyzed by D-6-D enzyme[26]. Studies have shown that activity of this enzyme decreases with age especially in disease conditions, such as diabetes, hypertension, eczema, arthritis, psoriasis, and so on. Further life style factors like stress, smoking, excessive consumption of alcohol, and consumption of saturated and trans-fatty acids, nutritional deficiencies of Vitamin B6, zinc, magnesium also decreases the activity of desaturase enzyme[27]. As a result of limitations of *in vivo* production of GLA, dietary supplementation is becoming important. This has led to interest in development and commercialization of the sources rich in GLA[28]. (**Table 7**)

Table 7. List of Most Common w**-6 Fatty Acids Found in Nature[13]**

Common Name	Lipid Name	Chemical Name
Linoleic acid	18:2 (ω-6)	*all-cis*-9,12-octadecadienoic acid
γ-Linolenic acid (GLA)	18:3 (ω-6)	*all-cis*-6,9,12-octadecatrienoic acid
Eicosadienoic acid	20:2 (ω-6)	*all-cis*-11,14-eicosadienoic acid
Dihomo-γ-linolenic acid (DGLA)	20:3 (ω-6)	*all-cis*-8,11,14-eicosatrienoic acid
Arachidonic acid (AA)	20:4 (ω-6)	*all-cis*-5,8,11,14-eicosatetraenoic acid
Docosadienoic acid	22:2 (ω-6)	*all-cis*-13,16-docosadienoic acid
Adrenic acid	22:4 (ω-6)	*all-cis*-7,10,13,16-docosatetraenoic acid
Docosapentaenoic acid (Osbond acid)	22:5 (ω-6)	*all-cis*-4,7,10,13,16-docosapentaenoic acid
Tetracosatetraenoic acid	24:4 (ω-6)	*all-cis*-9,12,15,18-tetracosatetraenoic acid
Tetracosapentaenoic acid	24:5 (ω-6)	*all-cis*-6,9,12,15,18-tetracosapentaenoic acid

5. Extraction, Isolation and Purification of Fatty Acids (Table 8)

6. Mechanism of Action of Omega-3 and Omega-6 Fatty Acids

The physiological roles of the essential fatty acids are discussed in the article by Aaes-Jorgensen[48] (1961) and Holman[49] (1968). Both ω-3 and ω-6 fatty acids support the normal growth and development and further studies has helped in understanding of the various important actions of eicosanoids[50]. The ω-6 fatty acids are regarded as essential fatty acids[49], by many scientists and in contrast few investigations also gave quantitative evidence for the physiological efficacy of ω-3 fatty acids[51].. A major review evaluating the activities of ω-3 fatty acids did not give much evidence for any of the unique action of the ω-3 fatty acids that could not be met by ω-6 fatty acids[52]. Some of

Table 8. Summary of methods to obtain Omega fatty acids from animals and plants sources.

Sl. No.	Method	Technique	Interests	Sources	References
1	Application of Urea Complexes in the Purification of Fatty Acids, Esters, and Alcohols		Saturated and Monounsaturated Fatty acids	Animals and Plants	(Swern and Parker, 1951)
2	Urea Complexes			Animals and Plants	(Smith,1952; Han et al.,1987)
3	A Simple Methods for the Isolation and Purification of Total Lipids	Extraction and Measurement of Total Lipids	Total lipid	Animals and Plants	(Folch et al., 1957)
4	Preparation and Properties of Methyl Arachidoniate from Pork Liver		PUFA	Animals and Plants	(Privett et al., 1959)
5	Separation of PUFA	Techniques of Separation: A. Distillation, Salt Solubility, Low Temperature Crystallization	PUFA	Animals and Plants	(Markley, 1964)
6	Enzymatic methods	Lipase-catalysed hydrolysis, Lipase-catalysed esterification		Animals and Plants	(Bottino et al., 1967; Harnazaki et al., 1982)
7	Distillation method	This method takes advantage of the differences in the boiling point and molecular weight of fatty acids under reduced pressure	FFA	Animals and Plants	(Berger R, Mcpherson,1979; Brown and Klob, 1955)
8	Method of Extraction and Purification of Polyunsaturated Fatty Acids from Natural Sources (Patent)		PUFA	Animals and Plants	(Rubin and Rubin, 1985)
9	Chromatographic methods	High performance liquid chromatography (HPLC). Separation of polyunsaturated fatty acids by column chromatography on a silver nitrate-impregnated Silica Gel	PUFA	Animals and Plants	(Beebe et al., 1988)
		Solvent choice for separation of fatty acid esters depends on the desired purity of eluted fractions and their use			(Teshima et al., 1978)
		Fractionated methyl esters containing 29.1% EPA and 20.5% DHA into fractions of 87.7% into fractions of 87.7% EPA and 95.4% DHA with increasing amounts of acetonitrile (0-30%) in methanol.	Concentrates Fatty acids esters EPA and DHA		(Tokiwa et al., 1981; Adolf and Emiken, 1985)
10	Low temperature crystallization	Alkali salts of less unsaturated fatty acids crystallize more rapidly than those of PUFA containing four or more double bonds, when saponified solution is cooled. They also compared the cooling temperature and the rate of cooling on enrichment of ω-3 PUFA. Fatty acid composition of the prepared concentrates indicated that cooling rate and temperature had little influence on the yield and contents of EPA and DHA. Therefore, use of ambient temperatures would offer a practical choice for large-scale separation and production of ω-3 PUFA concentrates.	ω-3 PUFA	Animals and Plants	(Han et al., 1987)
		The solubility of fats in organic solvents decreases with increasing mean molecular weight and increases wit h increasing unsaturation	FFA	Animals and Plants	(Chawala and DeMan,1990)
		-Low-temperature crystallization was originally developed to separate certain fatty acids, TAG, esters and other lipids which are highly soluble in organic solvents at temperatures above 0°C, but become sparingly soluble at temperatures down to minus 80°C			(Brown and Klob,1955)
11	Supercritical fluid extraction	-Uses Co_2 -Uses propane		Animals and Plants	(Mishra et al., 1993)
12	Soxhlet	Extraction and Measurement of Total Lipids	Total lipid	Plants	(AOAC, 1995)

the physiological functions are better controlled with ω-6 fatty acids than ω-3 fatty acids. Hence dermal integrity, renal functions, and parturition appear to be maintained with less efficiency by ω-3 fatty acids than with ω-6 fatty acids[53, 48].

The rate of biosynthesis of prostaglandins was slower with 20: 5 ω-3 than with 20: 4 ω-6 led to a particular manifestation that ω-3 fatty acids competitively attenuate the rate of ω-6 eicosanoid formation[54]. This discovery was discussed in terms of the possible therapeutic effects in diminishing excessive ω-6 eicosanoid-mediated events. This concept of competition acquired greater significance and later it was discovered that the bio synthesis of ω-6 eicosanoid, thromboxane A2, was a rate-limiting step in the aggregation of platelets, which led to thrombosis[55]. Agents slowing the rate e.g., aspirin or the ω-3 PUFA in fish oil became subject of intense interest[56, 57]. Support to the concept of competition during eicosanoid formation intensified after the 1979 discovery of the biosynthesis of the leukotrienes which are rate limlting mediators of immune-inflammatory events[54]. A major study has been undertaken to interpret mechanisms for diminishing excessive formation and functions of ω-6 eicosanoids[56, 58].

The effect of ω-3 eicosanoids synthesized from 20: 5 ω-3 has less vigorous responses than ω-6 eicosanoids when bound to the specific receptors[59, 60]. GLA converted to PGE1, exhibited significant anti-inflammatory, antithrombotic, antiproliferative, and hypolipidemic potential. In similar manner smooth muscle relaxation and vasodilation was also enhanced. GLA as components of mitochondrial membrane phosoholipids increased the integrity and fluidity of the membrane[61].

6.1. Specific Activities/Roles and Corresponding Health Benefits of (w-3) PUFA:

Long-chain (ω-3) fatty acids are demonstrated to have a broad range of biological activities leading to certain health benefits and clinical impacts as summarized in the table 9. Increased intake of very long-chain (ω-3) fatty acids is associated with a reduced risk of cardiovascular morbidity and mortality[62, 63]. They are successfully used in treatment of rheumatoid arthritis[64] , Ininflammatory bowel disease[65] and bronchial asthma[66]. Dietary supplement of DHA in early life that is when the fetal brain and eye are developing is critically important to optimize visual and neurological functions[67, 68]. In another study ω-3 fatty acids improved childhood learning and behavioral capacity[69] lowered the burden of psychiatric illnesses in adults[70], and prevented neurodegenerative disease of ageing[71]. Plant (ω-3) PUFA that are precursors of EPA and DHA appear to share some of the biological and functional activities of very long-chain (ω-3) PUFA, These biochemical effects of the plant (ω-3) PUFA are attributed to the formation of bioactive EPA, The biological activity of the plant (ω-3) PUFA is less than that of the very long-chain (ω-3) PUFA from fish source[72]. (**Table 9**)

Table 9. Summary of Some Specific Activities, Roles and Potential Health Benefits of Very Long-Chain (w-3) Fatty Acids[73].

Physiological Role of Very Long-Chain (w-3) Fatty Acids	Potential Health Benefit	Disease Target
Regulation of blood pressure	Decrease blood pressure	Hypertension, CVD
Regulation of platelet function	Decrease likelihood of thrombosis	Thrombosis, CVD
Regulation of blood coagulation	Decrease likelihood of thrombosis	Thrombosis, CVD
Regulation of plasma TG concentrations	Decrease plasma TG concentrations	Hypertriglyceridemia, CVD
Regulation of vascular function	Improve vascular reactivity	CVD
Regulation of cardiac rhythm	Decrease cardiac arrhythmias	CVD
Regulation of heart rate	Regulation of heart rate	CVD
Regulation of inflammation	Decreased inflammation	Inflammatory diseases (arthritis, inflammatory bowel diseases, psoriasis, lupus, asthma, cystic fibrosis, dermatitis, neurodegeneration, etc.), CVD
Regulation of immune function	Improve immune function	Compromised immunity
Regulation of fatty acid and TG metabolism	Decrease TG synthesis and storage	Weight gain, weight loss, obesity
Regulation of bone turnover	Maintains bone mass	Osteoporosis
Regulation of insulin sensitivity	Improve insulin sensitivity	Type-2 diabetes
Regulation of tumor cell growth	Decrease tumor cell growth and survival	Some cancers
Regulation of visual signaling (via rhodopsin)	Optimize visual signaling	Poor infant visual development (especially preterm)
Structural component of brainand central nervous system	Optimize brain development leads to better cognitive and learning processes	Poor infant and childhood cognitive processes, learning, and behavior

7. Biological Activities of Omega-3 and Omega-6- FAs:

7.1. Anti-Hyperlipidemic Activities:

A major risk factor for the development of cardiovascular diseases is hyperlipidemia which includes hypercholesterolemia and hypertriglyceridemia conditions. The search for new drugs that are able to diminish and/or to regulate serum cholesterol and triacylglycerol levels has gained importance over a period of time[74]. PUFAs and monounsaturated fatty acids are important for normal growth, development and play a main role in modulation of cardiovascular inflammatory diseases and cancer[75, 76]. The approach of treatment with ω-3 PUFAs is intricately linked to the type of the fatty acid employed. For example, platelet aggregation inhibition is more effective with pure ethyl ester EPA than with fish oil extract. This is because of the easier absorption of the ethyl ester through the intestinal wall without requiring the enzyme lipase[77].

The health benefits of ω-3 and ω-6 fatty acids vary depending on the structural components of membrane phospholipids. Their metabolic products modulate the biosynthesis of active cellular mediators, the eicosanoids[78]. The ratio of ω-3 and ω-6 fatty acids required in the diet is important due to their competitive nature, diverse biological roles and to ensure the conversion of ALA to EPA and DHA[79]. Both ALA and LA in tissues can be converted into fatty acids of longer and more unsaturated chain by common pathway followed by alternate desaturation and elongation[80].

EPA/DHA can reduce accumulation of body fat by limiting both hypertrophy and hyperplasia of fat cells indicating antiadipogenic effect against obesity[81]. Omega-3 fatty acids, exhibited beneficial effects by lowering serum cholesterol and raising high-density lipoprotein, however the question about the optimal percentage of unsaturated fats in the diet still remain uncertain[82]. These results were comparable to the action of the drug simvastatin which increased the ratios of stearic to palmitic, gamma-linolenic to linoleic, and arachidonic to dihomo-gamma-linolenic acid in the body indicating the increased activities of fatty acid elongase and Delta-6- and Delta-5-desaturase enzymes[83].

The application of ω-3 LC-PUFA against obesity either alone or in combination with either caloric restriction or anti-obesity drugs has to be explored[84]. One of the natural sources of gamma-linolenic acid (GLA) is blackcurrant oil soft capsule (BOSC) and it was found to be effective in decreasing TC and TG levels and increasing the serum HDL-C level, especially in mildly hyperlipidemic patients and those with a lower BMI[85]. Omega-3 fatty acids and fenofibrate therapy amplified similar changes in triglycerides and endothelium-dependent dilation; However, fenofibrate therapy showed considerably better effects on lipoprotein metabolism in patients with hypertriglyceridemia[86]. Daily intake of plant sterols in combination with fish oil and B complex vitamins can alter the lipid profile of hypercholesterolemic children and adolescents[87]. Phang and Garj[88] (2014) reported that dietary supplementation of phytosterols and omega-3 fatty acids decreased hyperlipidemia and other cardiovascular diseases.

7.2. Anti-Diabetes Activities:

Diabetes may be due to inhibition of the activity of delta-6-desaturase which is the first enzyme in the metabolism of LA and ALA[89]. Treatment with GLA increased the content of GLA, DGLA, and AA in plasma phospholipids which is found to be reduced in diabetes[90]. The fatty acid compositions of plasma and liver microsomal lipids are not dependable indices of delta 6-desaturase activity in diabetes[91]. Alpha-lipoic acid and gamma-linolenic acid interact synergistically to improve NO-mediated neurogenic and endothelium-dependent relaxation of corpus cavernosum in experimental diabetes[92]. The combination of ALA, ascorbic acid-6-palmitate (AA6P), and fish oil (FO) has suppressed oxidative stress by enhancing the recycling of glutathione disulfide (GSSG) to reduced glutathione (GSH) in erythrocytes of diabetic rats [93]. Health benefits of consuming 1 to 2 g/day ω-3 LC-PUFA as part of lifestyle modification in insulin resistance was studied by Nettleton and Katz[94] (2005).

An increased activity of Delta9- and Delta6-desaturases, elongase, and a decreased C20:5 omega-3 content in phospholipids; followed by increase in brain triglyceride content; was observed in diabetic olueed rats[95]. Dietary intake of omega-3 fatty acids reduced the risk of islet autoimmunity (IA) in children with augmented genetic risk of type 1 diabetes[96]. The beneficial activities of ω-3 PUFA on T cell functions in type I diabetes could be attributed to their suppressive effect and modulation of cytokine secretion, and improvement of intracellular oxidative status[97]. Higher consumption of LCFAs and fish reduces the risk of type 2 diabetes mellitus[98].

The ω-6/ω-3 ratio of the maternal diet during gestation and lactation rather than that of offspring after weaning, strongly affects the development of overt diabetes in non-obese diabetic (NOD) mice[99]. An inverse association between fish and shellfish intake and T2D in women was found. However evidences about the detrimental effect of fish intake in this population were not seen[100]. A high dose of ω-3 PUFA could reduce insulin sensitivity (IS) but a lower dose of ω-3 PUFA positively influenced body composition and lipid metabolism[101]. Early treatment with ω-3 fatty acids led to improvement in all-cause mortality of patients with and without type 2 diabetes, against a background of contemporary cardiovascular risk–modifying treatments[102]. High concentrations of ω-3 or high ratio of ω-3/ω-6 have protective effects against renal function impairment in type 2 diabetic patients[103].

7.3. Anti-Inflammatory Activities:

Studies on the direct actions of ω-3 PUFA on *in vivo* neuroinflammation are lacking. However the therapeutic potential of ω-3 PUFA cannot be neglected as its bioactive metabolites may provide novel therapeutic targets for neurological disorders[104] Mice fed with diet containing ω-3 PUFA showed reduced expression of CD80, CTLA-4, IL-10, IL-18, CCL-5, CXCR3, IL-6, TNF-α and osteopontin mRNAs in kidney and/or spleen as compared to mice fed by ω-6 PUFA or ω-9 MUFA diets. It indicates that many of the genes are considered as biomarkers and/or biotherapeutic targets for SLE (systemic lupus erythematosus) and other autoimmune diseases.[105] This study clearly demonstrates that the beneficial effects on health are related to type of omega fatty acid ingested.

In animal models treatment of ω-3 fatty acids had beneficial effects and reduced the risk of rheumatoid arthritis (RA), inflammatory bowel disease (IBD) and asthma[106] Omega-3 and omega-6 polyunsaturated fatty acids (PUFA) are the precursors of biological lipid mediators, termed as eicosanoids, which play an important role in the regulation of inflammation, Eicosanoids derived from ω-6 PUFAs (e.g., arachidonic acid) have proinflammatory and immunoactive activities, in contrast eicosanoids derived from ω-3 PUFAs have anti-inflammatory properties attributed to their ability to inhibit the formation of ω-6 PUFA-derived eicosanoids[107] The western diet has a much greater ratio of ω-6 PUFAs compared with ω-3 PUFAs. Studies have shown that increasing the ratio of ω-3 to ω-6 fatty acids in the diet, favors the production of EPA in the body. Increasing the dietary intake of EPA and DHA through consumption of fatty fish or fish-oil supplements has led to reduction of many chronic diseases that involve inflammatory reactions like cardiovascular diseases, inflammatory bowel disease (IBD), cancer, and rheumatoid arthritis. Positive response was also seen even with psychiatric and neurodegenerative disease[108]

Many studies have discussed the novel mechanism(s) and bioactivities of omega-3 supplemented diet in inflammation, cancer, and vascular disorders[109] Mono and digalactosyldiacylglycerol galactolipids (MGDG and DGDG) with a high content of polyunsaturated fatty acids, mainly ω-3, are the most widespread non-phosphorous polar lipids in the biosphere and account for 80% of the membrane lipids that are found in green plant tissues, These lipids are also major constituents of the photosynthetic membranes of higher plants, algae and bacteria[110] Another study indicated that both acute inflammation and the response to an antiinflammatory drug were attenuated by ω-3 or ω-6 PUFA-rich diets[111] In animals, MGDG and DGDG are present at low concentration, particularly in the myelin sheath and in oligodendrocytes[112]

Arachidonic acid caused an increase in the secretion of corticosterone and PGE2, and induced anxiety-like behavior without enhancing the effects of IL-1 whereas; Ethyl-GLA antagonized IL-1 induced inflammatory changes[113]

Eicosanoids production is influenced by an intake of ω-3 LC PUFA and γ-linolenic acid suggesting a possible mode of action in therapy of chronic inflammatory diseases[114] ω-3 PUFAs regulates macrophage inflammation negatively by deacetylating NF-κB, which acts through activation of adenosine monophosphate-activated protein kinase/ sirtuin and regulation T1 (AMPK/SIRT1) pathway demonstrating the anti-inflammatory potential of ω-3 PUFAs[115] .

7.3.1. Activities of (Omega-3) Fatty Acids Mediated via Surface or Intracellular Fatty Acid Receptors or Sensors Involvement of PPAR:

Peroxisome proliferator-activated receptors (PPAR) are transcription factors which, is expressed mainly in the liver. It is involved in regulating hepatic responses to the availability of type of fatty acids or fatty acid metabolites, and other peroxisome proliferators. Further genes encoding for several key enzymes of ß-oxidation and lipoprotein metabolism are regulated by PPARα [116] It appears to be important in activating hepatic fatty acid oxidation (**Figure. 5A**). PPARα is expressed in adipose tissue where it regulates adipocyte differentiation and the metabolic responses of adipocytes in promoting insulin sensitivity. PPARα is also expressed in inflammatory cells, where it controls the production of mediators having anti-inflammatory actions[117] (**Figure. 5B**).

Further it has ability to lower fasting plasma TG concentrations, increase insulin sensitivity, and reduce inflammation (**Figure. 6**).

7.4. Anti-Cancer Activities:

Animal studies have shown that GLA,from borage oil inhibited mammary carcinoma by increasing the activity of ornithine decarboxylase in mammary tumors[119] *In vitro* studies also demonstrated that GLA, can enhance the effect of paclitaxel, a chemotherapy drug used for breast and ovarian cancers[120] The therapeutic potential of EPA as an anti-cancer agent is due to inhibition of pols and topos activities[121] GLA has been shown to be cytotoxic in superficial bladder cancer, with a response rate of 43%, indicating a cytotoxic effect against transitional cell carcinoma[122] Thus the use of fatty acids in breast cancer treatment could show a new avenue which would have impact on public health[123] GLA, DGLA, AA, EPA and DHA enhanced the

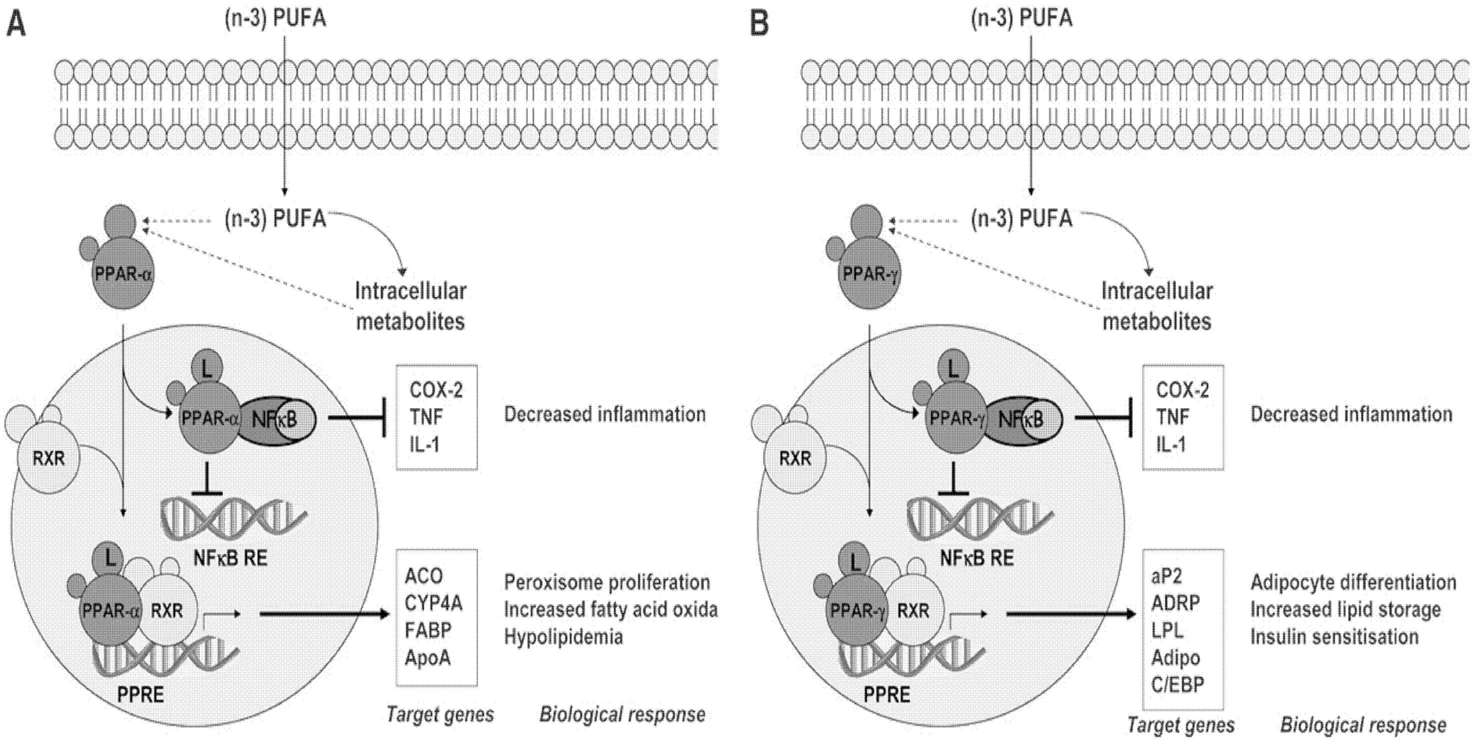
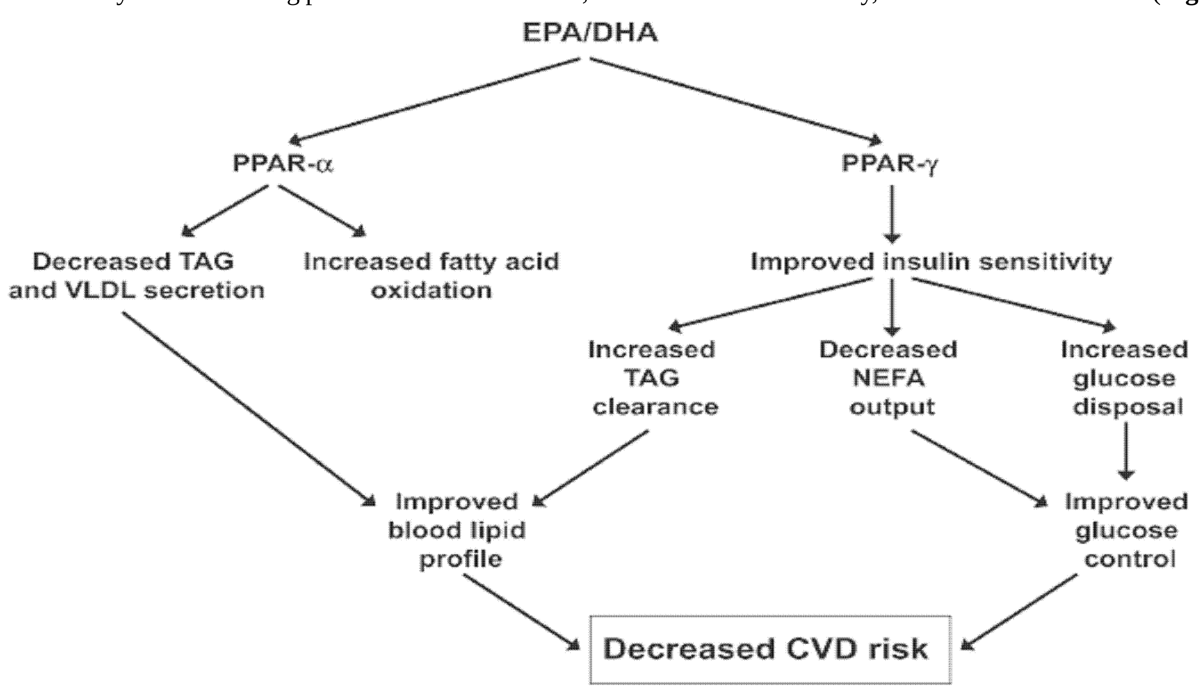


Figure 5. The PPARa and -g pathways. ACO, acyl CoA oxidase; Adipo, adiponectin; ADRP, adipose differentiation related protein; aP2, adipocyte protein2; ApoA, apolipoprotein A; C/EBP, CCAAT/enhancer-binding proteins;COX, cyclooxygenase; CYP4A, cytochrome P450 4A; FABP, fatty acid binding protein; L, ligand; LPL, lipoprotein lipase; RXR, retinoic acid

Data adapted from[118]

Furthermore it has ability to lower fasting plasma TG concentrations, increase insulin sensitivity, and reduce inflammation (**Figure. 6**).



DPA, docosapentaenoic acid; NEFA, nonesterified fatty acid; TAG, triglyceride.

Figure 6. Mechanisms by which (w-3) PUFA act via PPAR to improve blood lipids and glucose control. DPA, docosapentaenoic acid; NEFA, nonesterified fatty acid; TAG, triglyceride.

Data adapted from [118]

cytotoxic action of vincristine These results suggest that certain PUFAs have tumoricidal action and are capable of enhancing the cytotoxic effects of anti-cancer drugs alone or in combination[124]

Conjugated linolenic acids (CLnAs) were also found to possess preventive effect against tumor, A study by Shinohara et al., (2012) showed that Jacaric acid (JA) has antitumor effect *invivo* against adenocarcinoma (DLD-1) grown in nude mice[125]. Another study by Sato et al., [126] (2013) demonstrated that docosahexaenioc acid (DHA) supressed the growth of the cancer through Akt phosphorylation (protein kinase B) in conjunction with modulation of fatty acid metabolism. Migration, invasion and macrophage chemotaxis of PC-3 cells is induced by TAM-like M2-type macrophages and this process is reduced by EPA/DHA administration which may due to activation of PPAR-γ and decreased NF-κB p65 transcriptional activity[127]

The primary predisposing cause for cancer seems to be the fat component of the diet and an increased ratio of saturated fatty acids in the diet may lead to cancer. Many research studies have revealed the protective action of eicosanopentaenoic acid (as the main constituents of ω-3 PUFAs) against gastrointestinal and colorectal cancers[128] In another study supplementation of diet rich in ω-3 PUFAs to experimental tumour-bearing mice retarded the growth of different types of cancers such as lung, colon, mammary and prostate[129] An important outcome of these studies is that ω-3 PUFAs are significantly effective in reducing cancer risk[130]

Even in clinical studies dietary supplementation of ω–3 PUFAs - has shown potential effects by decreasing tumor formation in patients with pancreatic cancer[131] In contrast ω-6 PUFAs increased the risk of tumor promotion, indicating the advantages in the use of olive and canola oils, which are low in ω-6[132] Supplement of 3g flaxseed per day, which is a rich source of lignan and ω-3 PUFAs, resulted in decreased prostate specific antigen levels and proliferation of prostate cancer[133] In contrast high dietary LA (e.g. ω-6 PUFAs) raised oestrogen levels in pregnancy, altered mammary gland morphology, and expression of fat-and/or estrogen regulated genes and thereby increased the risk of breast cancer[134] An *in vitro* study demonstrated that GLA induces apoptosis in isolated B-cells cultured from patients with chronic lymphocytic leukemia[135] Geelen et al., [136] (2007), reported that ω-3 PUFAs inhibited colorectal carcinogenesis but they have concluded that data available is insufficient to substantiate the anticancer activity.

8. The Omega-6/Omega-3 EFA/PUFA Ratio

The change in human lifestyle and diet has occurred over few decades followed by revolution in the agricultural field which has introduced cereals and grains in the diet high in ω-6 FA. During the last 150 years, human population increased the consumption of vegetable seed oil rich in ω-6 FAs with a parallel decrease of ω-3 FAs intake. The result is that the actual ω-6/ω-3 FA ratio in the western diet ranges between 15:1 and 20:1[137, 138] .Previous accumulated data proves the importance of the ω-6/ω-3 FA ratio in the diet. As discussed above, the AA-derived eicosanoids if formed in large amounts increases the production of thrombus and atheromas, leading to allergic, inflammatory disorders with abnormal cell proliferation[139] . Several clinical studies support the view that decreasing the ω-6/ω-3 FA ratio results in an increased protection against degenerative diseases[140, 138]. The ω-6/ω-3 ratio (EFA/PUFA) is not only important in the pathogenesis of cardiovascular diseases, but also in cancer, inflammatory and autoimmune diseases. Hence very high ratio of ω-6/ω-3 is considered to be injurious for human health, in contrast low ratio is considered protective against degenerative disease and disorders. Simopoulos (1991) defined the importance of the ω-6 / ω-3 FA ratio[75]. For example, when corn oil (high in LA) was replaced with olive and canola oil (low in LA) to obtain a ratio of 4:1 of LA/ALA, a 70% decrease in total mortality was observed[141] A Mediterranean-style diet (serum ω-6/ω-3 FA ratio of 2.6:1), showed beneficial effects indicated by decrease in leukocytes, platelets and Vascular endothelial growth factor (VEGF) while the Swedish diet with a ω-6/ω-3 FA ratio of 4.72:1did not have any advantage[142] In similar studies 2.5:1 ω-6/3 FA ratio obtained by increasing fish oil intake suppressed rectal epithelial cell proliferation and PGE2 synthesis but 4:1 ratio did not have similar effect[138] In another study the differences in the percentage of deaths from CVD in Europe and United States versus Japan was 45% and 12%, respectively and, this significant variation was due to disparity in the concentration of EPA in the thrombocyte phospholipids (0.5% versus 1.6%), but the percentage of AA was similar in the both the groups (26% versus 21%)[138]. In another study Von sckacky and Harris, (2007) proposed the term' the ω-3 index' defined as the combined percentage of EPA + DHA of total fatty acids in erythrocyte membranes which reflect the ω-3 FA status in a given individual and can be identified as a new risk factor for sudden cardiac death. However further studies are needed to validate this novel biomarker for cardiovascular risk[143].

Finally FAO/WHO recommends a daily optimal intake of ω-6/ ω-3 as 5-10:1 this findings supports that EPA concentration gives the same effect as the ω-6/ω-3 FA ratio[144].

9- CONCLUSION:

Omega FAs appears to play vital role in disease prevention and health promotion. Combined use of omega fatty acids from different sources will have advantage and may reveal new pathways for excellent physiological and metabolic utilization of these FAs. Currently, there is enormous scientific information about the beneficial and protective activities of ω- PUFAs and their action against hyperlipidemia, obesity, diabetes, inflammation, cancer and heart diseases It is essential to increase the dietary uptake of PUFAs, or to enhance the ratio of ω-3 to ω-6 fatty acids in the diet, which will lead to decline of many chronic diseases and inflammatory disorders. However much more investigations are required to prove the therapeutic potential of omega fatty acids.

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