Omega-3 Fatty Acid and Cardiovascular Disease

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Abstract: ***Cardioceuticals are nutritional supplements that contain all the essential nutrients including vitamins, minerals, omega-3-fatty acids and other antioxidants like a-lipoic acid and coenzyme Q10 in the right proportion that provide all round protection to the heart by reducing the most common risks associated with the cardiovascular disease including high low-density lipoprotein cholesterol and triglyceride levels and factors that contribute to coagulation of blood. Omega-3 fatty acids have been shown to significantly reduce the risk for sudden death caused by cardiac arrhythmias and all-cause mortality in patients with known coronary heart disease. Omega-3 fatty acids are also used to treat hyperlipidemia and hypertension. There are no significant drug interactions with omega-3 fatty acids. The American Heart Association recommends consumption of two servings of fish per week for persons with no history of coronary heart disease and at least one serving of fish daily for those with known coronary heart disease. Approximately 1 g/day of eicosapentaenoic acid plus docosahexaenoic acid is recommended for cardio protection. Higher dosages of omega-3 fatty acids are required to reduce elevated triglyceride levels (2-4 g/day). Modest decreases in blood pressure occur with significantly higher dosages of omega-3 fatty acids. Lifestyle intervention such as consistent aerobic exercise and a diet high in fruits and vegetables promotes cardiovascular health. A heart-healthy lifestyle decreases the risk of coronary heart disease and heart attack. Although it may seem intuitive that dietary fat is bad for the heart and that it must be avoided, certain unsaturated fats are heart healthy, and other saturated fats are not good for the heart. These heart-healthy unsaturated fats are known as omega-3 fatty acids. The 3 main omega-3 fatty acids that are beneficial for cardiovascular health are α-linoleic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). ALA is primarily found in plant-based foods such as olive, soybean, canola, walnut, and flaxseed oils, and in walnuts and flaxseeds, as well. EPA and DHA are primarily found in marine-based foods that include the variety of fatty fish, such as tuna, salmon, mackerel, herring, trout, halibut, and cod. This Cardiology Patient Page will present the beneficial effects of omega-3 fatty acids on cardiovascular health, explain the possible mechanisms for these effects, and offer recommendations that can be implemented into a healthy lifestyle to further promote good cardiovascular health.***

Keywords: omega-3 fatty acids, CVD, CHD, triglycerides levels, lipoprotein

1. Introduction

Omega-3 fatty acids are polyunsaturated fatty acids which have a double bond (C=C) at the third carbon atom from the end of the carbon chain. It is a group of fatty acids which have the first unsaturated bond in the third position from the omega carbon. **[1]**

Omega-3 Fatty Acids are believed to prevent insulin resistance, reduce serum triglycerides, prolong bleeding times, improve lipid profile, decrease platelet adhesiveness, and reduce platelet counts. The fatty acids have two ends, the carboxylic acid (-COOH) end, which is considered the beginning of the chain, thus "alpha", and the methyl (CH_3) end, which is considered the tail of the chain, thus "omega". The molecular formula of Omega-3 Fatty Acid is $C_{60}H_{92}O_6$ with a molecular weight of 909.39 g/mol. Omega-3 Fatty Acids are often of marine origin. Marine algae and phytoplankton are the primary sources of omega-3 fatty acids. **[2]**

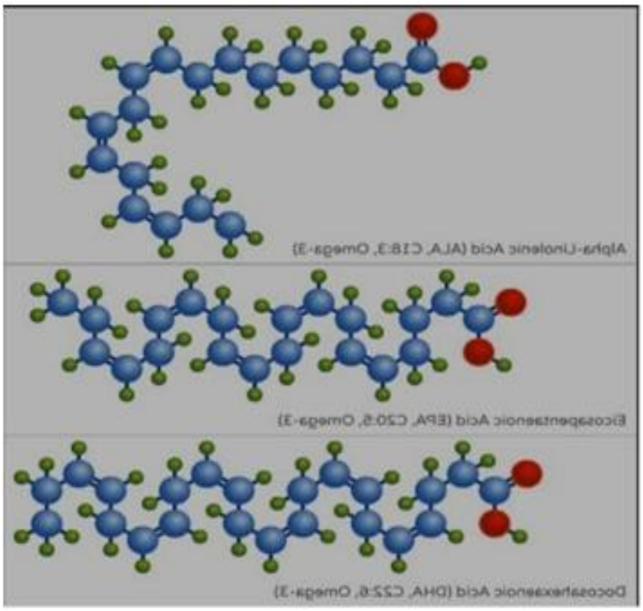

Diagram 1: Different types of omega-3 fatty acids

Sources of omega-3 fatty acids are – Chia seeds, Egg, Salmon, Mackerel, Walnuts, Soybean, Cod liver oil, Hemp seeds, Flaxseed, Broccoli, Kidney beans, Shrimp, Canola oil, Sprouts, Cauliflower, Paneer, Onion, Almonds, Peanuts, Blueberries etc. **[3]**

Today industrialized societies are characterized by–
1) An increase in energy intake and decrease in energy expenditure.
2) An increase in saturated fat, omega-6 fatty acids and trans fatty acids, and a decrease in omega-3 fatty acid intake.
3) A decrease in complex carbohydrates and fibre.

4) An increase in cereal grains and a decrease in fruits and vegetables.
5) A decrease in protein, antioxidants and calcium intake. [**4**]

The increase in trans fatty acids is detrimental to health as shown in diagram (2).

In addition, trans fatty acids interfere with the desaturation and elongation of both omega-6 and omega-3fatty acids, thus further decreasing the amount of arachidonic acid, eicosapentaenoic acid and docosahexaenoic acid availability for human metabolism. **[5]** The beneficial health effects of omega-3 fatty acids, eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) were described first in the Greenland

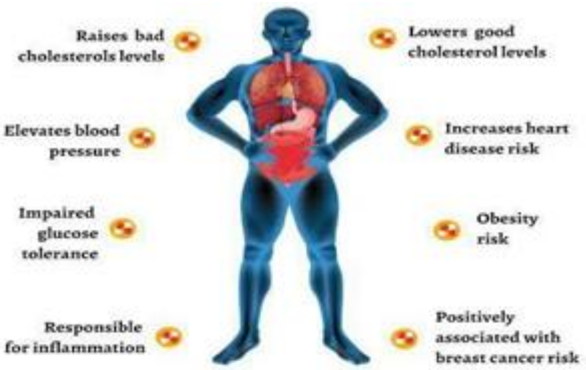

Diagram 2: Transfatty acids is detrimental

Eskimos who consumed a high seafood diet and had low rates of coronary heart disease, asthma, type 1 diabetes mellitus, and multiple sclerosis. Since that observation, the beneficial health effects of omega-3 fatty acids have been extended to include benefits related to cancer, inflammatory bowel disease, rheumatoid arthritis, and psoriasis. Whereas evolutionary maladaptation leads to reproductive restriction (or differential fertility), the rapid changes in our diet, particularly the last 150 years, are potent promoters of chronic diseases such as atherosclerosis, essential hypertension, obesity, diabetes, arthritis and other autoimmune diseases, and many cancers, especially cancer of the breast, colon, and prostate. In addition to diet, sedentary lifestyles and exposure to noxious substances interact with genetically controlled biochemical processes leading to chronic disease. In this review, I discuss the importance of the balance of omega-6 and omega-3 essential fatty acids in the
prevention and treatment of coronary artery disease, hypertension, diabetes, arthritis, osteoporosis, other inflammatory and autoimmune disorders, cancer and mental health, and the mechanisms involved. **[6]**

Omega 3 fatty acids can be obtained from several sources, and should be added to the daily diet to enjoy a good health and to prevent many diseases. The European Food Safety Agency (EFSA) proposed a recommended daily intake of 250 mg/eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) for adults, because this intake is negatively related to cardiovascular diseases (CVD) risk in a dose-dependent way up to 250 mg/d (1–2 servings/week of oily fish) in healthy subjects. The American Heart Association (AHA) recommended for the general population a consumption offish, at least twice a week, estimating a consumption of one portion (125 g) of oily fish (2 g/100 g EPA and DHA) and one portion of lean fish (0·2 g/100 g), which results in anmean intake of 3 g/week or 430 mg/d of DHA and EPA. AHA also established intakes of 1 g of EPA and DHA from fish or fish oils for subjects with clinical history of CVD and a 2–4 gsupplement for subjects with high blood triacyl glycerides. To achieve recommended alpha-linoleic acid (ALA) intakes, food sources including flaxseed and flaxseed oil, walnuts and walnut oil, and canola oil are recommended. The consumption of 500 mL/d for 6 wk of an enriched semi skimmed milk (400 mg of EPA and DHA) decreased TAG and increased HDL-cholesterol serum levels. A standard egg contains a ratio of n-3 LC-PUFAs to total fatless than 1 %. By feeding laying hens with grains, soybean and flaxseed rich in ALA, n-3 LC-PUFAs content per egg can be increased to 6 times than the standard eggs. **[7]**

Hence the study aims at knowing the different sources of Omega-3 fatty acid and the beneficial role of disease prevention in diet.

Microencapsulation is one approach used to protect those oils from oxidative deterioration and to improve their ingredient properties (e. g., handling and sensory). Spray drying is the most commonly used technique to develop microcapsules. The preparation of protein-stabilized emulsions is a fundamental step in the process in order to produce microcapsules with good physical properties, effective protection and controlled release behaviours. This review describes types of emulsions prepared by animal and plant proteins, discusses the relationship between emulsion properties and microcapsule properties, and identifies key parameters to evaluate physical properties (e. g., moisture content, water activity, particle size, surface oil and entrapment efficiency), oxidative stability and release behaviour of spray-dried microcapsules for industrial application. **[8]**

2. Aims and Objectives

- As evidences suggested a positive Association between omega-3 fatty acid consumption and CVD prevention the aim of this review study was to
- Exploring the source of omega-3 fatty acid in different functional food and also as nutraceutical
- Exploring the mechanism how omega-3 fatty acid helps in CVD therapy.
- Recent advances in research with omega-3 fatty acid.

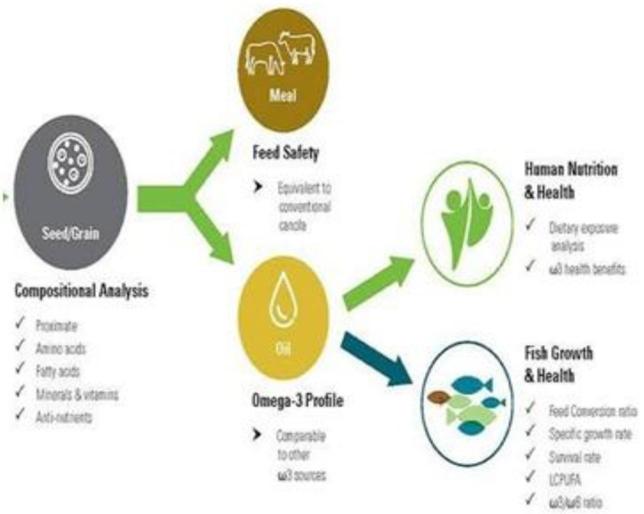

Diagram 3: Different Aims & Objectives Of Reference with Omega-3 fatty acids.

3. Review of Literature

1) **R. Preston Mason** et al discussed about new insights into mechanism of action for Omega-3 Fatty Acids in atherothrombotic Cardiovascular disease, to reduce markers of inflammation, cholesterol crystal formation, endothelial dysfunction and oxidative modification of various ApoB-containing lipoprotein particles as well as increasing functionality of HDL. [**9**]
2) **Alex Pizzini** et al discussed about the role of Omega-3 Fatty Acids in Reverse Cholesterol Transport and possible beneficial effects of n-3 PUFAs which have a positive impact on atherosclerosis and CVD, a major concern of today's health care system. [**10**]
3) **Yasuhiro Watanabe** et al discussed about the Omega-3 polyunsaturated Fatty acids for Cardiovascular diseases, improvement in lipid metabolism, lowering blood pressure and heart rare, counteract arrhythmia, improvement in vascular endothelial function and counteract clotting and inflammation. [**11**]
4) **R. Preston Mason** et al discussed about the emerging mechanism of Cardiovascular Protection for the Omega-3 Fatty Acid and Eicosapentaenoic Acid which has a more stable and extended structure and that contributes to membrane stability as well as inhibition of lipid oxidation and cholesterol domain formation. [**12**]
5) **John H. Lee** et al discussed about the Omega-3 fatty acids: Cardiovascular benefits and sustainability which help to be achieved a long-term Cardiovascular risk reduction at the population level. **[13]**
6) **Tewodros Shibabaw** et al discussed about the Omega-3 polyunsaturated Fatty acids: anti-inflammatory and anti-hyperglyceridaemia mechanisms in Cardiovascular disease, atherosclerosis, plaque rupture, and Cardiovascular related mortality. [**14]**
7) **P. JAIN** etal discussed about the Omega-3 fatty acids and Cardiovascular disease as well in the treatment of atherosclerotic, arrhythmia and primary myocardial disorders, coronary heart disease and heart failure. [**15]**
8) **Mateusz M. Wilczek** et al discussed about Trans – Fatty Acids and Cardiovascular disease: Urgent need for legislation and there is more than enough convincing evidence that a high iTFA intake is detrimental to Cardiovascular health. **[16]**
9) **HaroldE Bays** et al discussed about the prescription omega-3 fatty acids and their lipid effects: physiologic mechanism of action and clinical implications on triglycerides lowering mechanisms, reduced VLDL-TG synthesis by Omega fatty acids, Enhanced TG clearance by Omega-3 fatty acids. **[17]**
10) **Peter L. McLennan** et al discussed about the cardiac physiology and clinical efficacy of dietary fish oil clarified through cellular mechanisms of Omega-3 polyunsaturated Fatty acids which preventing cardiac arrhythmia, lowering heart rate and preconditioning the heart to resist a variety of insults. **[18]**
11) **Magnus Back** et al discussed about the Omega-3 fatty acids, Cardiovascular risk, and the resolution of inflammation in Cardiovascular prevention. [**19]**
12) **Julia C. Kuszewski**et al discussed about the effects of long omega-3 polyunsaturated fatty acids on endothelial vasodilator function and cognition, beneficial effects on systemic endothelial function, improvements in cerebral vasodilator function. [**20]**
13) **Yuji Ueno** et al discussed about the effect on Omega-3 polyunsaturated fatty acids on stroke burden and mortality, which may offer a potential candidate for public health benefit to prevent stroke as well as Cardiovascular disease. [**21]**
14) **William S. Harris** et al discussed about the Omega-3 fatty acids and coronary heart disease risk and it's clinical and mechanistic perspectives, effects in lowering triglycerides, clearance of triglycerides from the plasma. **[22]**
15) **Georges Khoueiry**et al discussed about that do omega-3 polyunsaturated fatty acids reduce risk of sudden cardiac death and ventricular arrhythmias? A meta-analysis of randomized trials which shows that the protective effect of Omega-3 PUFA against life threatening arrhythmias might be confined to patients with recent myocardial ischemia. **[23]**

4. Materials and Methods

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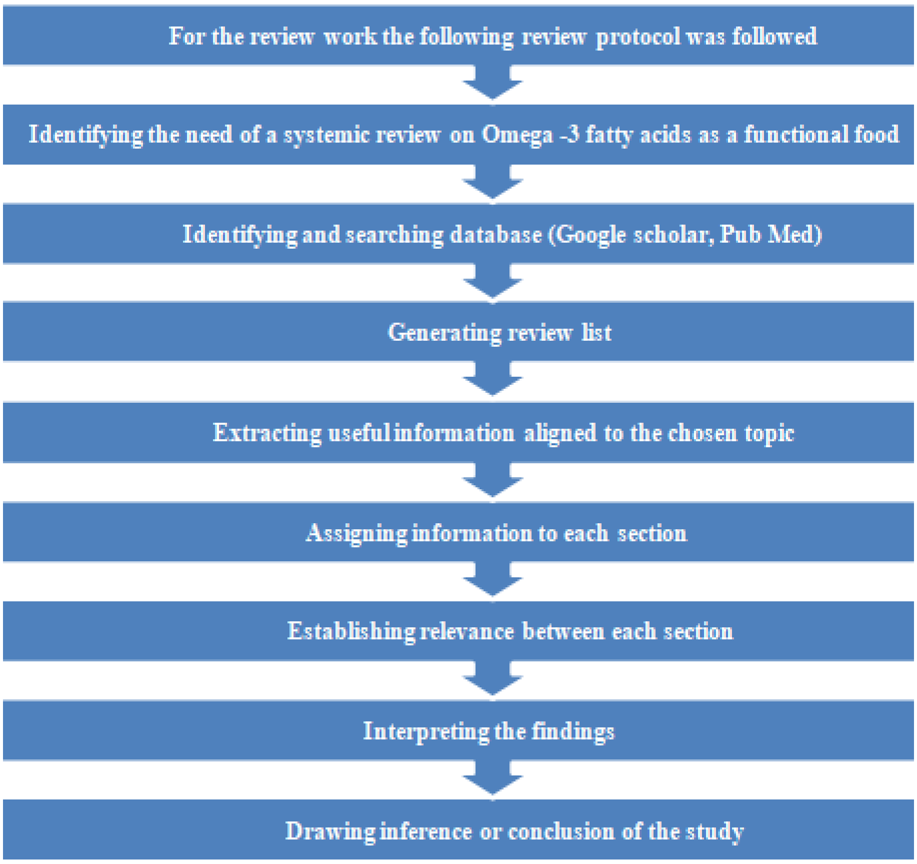

5. Discussions

Sources of omega 3 fatty acid in diet: [24]
The Following are the Sources of the Omega 3fatty acids.

Table 1

fatty acids per 100 g

Food item	EPA	DHA	ALA
Fish (Raw[a])			
Anchovy, European	0.6	0.9	-
Bass, Freshwater, Mixed Sp.	0.2	0.4	0.1
Bass, Striped	0.2	0.6	trace
Bluefish	0.2	0.5	-
Carp	0.2	0.1	0.3
Catfish, Channel	trace	0.2	0.1
Cod, Atlantic	trace	0.1	trace
Cod, Pacific	trace	0.1	trace
Eel, Mixed Sp.	trace	trace	0.4
Flounder & Sole Sp.	trace	0.1	trace
Grouper, Mixed Sp.	trace	0.2	trace
Haddock	trace	0.1	trace
Halibut, Atlantic and Pacific	trace	0.3	trace
Halibut, Greenland	0.5	0.4	trace
Herring, Atlantic	0.7	0.9	0.1
Herring, Pacific	1.0	0.7	trace
Mackerel, Atlantic	0.9	1.4	0.2
Mackerel, Pacific and Jack	0.6	0.9	trace
Mullet, Striped	0.2	0.1	trace
Ocean Perch, Atlantic	trace	0.2	trace
Pike, Northern	trace	trace	trace
Pike, Walleye	trace	0.2	trace
Pollock, Atlantic	trace	0.4	-
Pompano, Florida	0.2	0.4	-
Roughy, Orange	trace	-	trace
Salmon, Atlantic, Farmed	0.6	1.3	trace
Salmon, Atlantic, Wild	0.3	1.1	0.3
Salmon, Chinook	1.0	0.9	trace
Salmon, Chinook, Smoked[b]	0.2	0.3	-
Salmon, Chum	0.2	0.4	trace
Salmon, Coho, Farmed	0.4	0.8	trace
Salmon, Coho, Wild	0.4	0.7	0.2
Salmon, Pink	0.4	0.6	trace
Salmon, Pink, Canned[c]	0.9	0.8	trace
Salmon, Sockeye	0.6	0.7	trace
Sardine, Atlantic, Canned in Oil[d]	0.5	0.5	0.5
Seabass, Mixed Sp.	0.2	0.4	-
Seatrout, Mixed Sp.	0.2	0.2	trace
Shad, American	1.1	1.3	0.2
Shark, Mixed Sp.	0.3	0.5	trace
Snapper, Mixed Sp.	trace	0.3	trace
Swordfish	0.1	0.5	0.2
Trout, Mixed Sp.	0.2	0.5	0.2
Trout, Rainbow, Farmed	0.3	0.7	trace
Trout, Rainbow, Wild	0.2	0.4	0.1
Tuna, Fresh, Bluefin	0.3	0.9	-
Tuna, Fresh, Skipjack	trace	0.2	-

Food item	EPA	DHA	ALA
Fish, continued			
Tuna, Fresh, Yellowfin	trace	0.2	trace
Tuna, Light, Canned in Oil[e]	trace	0.1	trace
Tuna, Light, Canned in Water[e]	trace	0.2	trace
Tuna, White, Canned in Oil[e]	trace	0.2	0.2
Tuna, White, Canned in Water[e]	0.2	0.6	trace
Whitefish, Mixed Sp.	0.3	0.9	0.2
Whitefish, Mixed Sp., Smoked	trace	0.2	-
Wolffish, Atlantic	0.4	0.3	trace
Shellfish (Raw)			
Abalone, Mixed Sp.	trace	-	-
Clam, Mixed Sp.	trace	trace	trace
Crab, Blue	0.2	0.2	-
Crayfish, Mixed Sp., Farmed	trace	0.1	trace
Lobster, Northern	-	-	-
Mussel, Blue	0.2	0.3	trace
Oyster, Eastern, Farmed	0.2	0.2	trace
Oyster, Eastern, Wild	0.3	0.3	trace
Oyster, Pacific	0.4	0.3	trace
Scallop, Mixed Sp.	trace	0.1	-
Shrimp, Mixed Sp.	0.3	0.2	trace
Squid, Mixed Sp.	0.1	0.3	trace
Fish Oils			
Cod Liver Oil	6.9	11.0	0.9
Herring Oil	6.3	4.2	0.8
Menhaden Oil	13.2	8.6	1.5
Salmon Oil	13.0	18.2	1.1
Sardine Oil	10.1	10.7	1.3
Nuts and Seeds			
Butternuts, Dried	-	-	8.7
Flaxseed			18.1
Walnuts, English	-	-	9.1
Plant Oils			
Canola (Rapeseed)	-	-	9.3
Flaxseed Oil	-	-	53.3
Soybean Lecithin Oil	-	-	5.1
Soybean Oil	-	-	6.8
Walnut Oil	-	-	10.4
Wheatgerm Oil	-	-	6.9

Trace = <0.1; - = 0 or no data; Sp. = species; [a]Except as indicated; [b]Lox.; [c]Solids with bone and liquid; [d]Drained solids with bone; [e]Drained solids.

Role of Omega 3 Fatty Acid in CVD

1) n-3 PUFAs have the ability to respond to inflammation iatrogenesis through direct and indirect mechanisms. A direct mechanism through which n-3 PUFA decrease inflammation includes its rapid effect on the regulation of transcription factors, and indirect modes of actions include the production of three-and five series eicosanoids and inflammation-resolving lipid mediators and suppression of APRs (Table 2). **[25]**

Table 2: Anti-inflammatory role of omega-3 fatty acids

CARDIOVASCULAR EFFECT	MECHANISM
Antiarrhythmic	Improves membrane fluidity[23] Prevents atrial fibrillation[24]
Antithrombotic	Inhibits platelet aggregation[25]
Antiatherogenic	Inhibits intimal hyperplasia[26]
Anti-inflammatory	Reduces production of omega-6 proinflammatory eicosanoid (prostaglandin)[27] Reduces C-reactive protein[28]
Improves endothelial function	Direct effect on endothelial vasomotor function[29]
Lowers blood pressure	By the 3 previous cardiovascular effects[1,2]
Improves lipid parameters and cardiovascular risk parameters	Inhibits synthesis of hepatic triglycerides and very low-density lipoprotein resulting in lower triglyceride levels[30] Raises high-density lipoprotein levels[31] Lowers apolipoprotein B-100 levels[32]

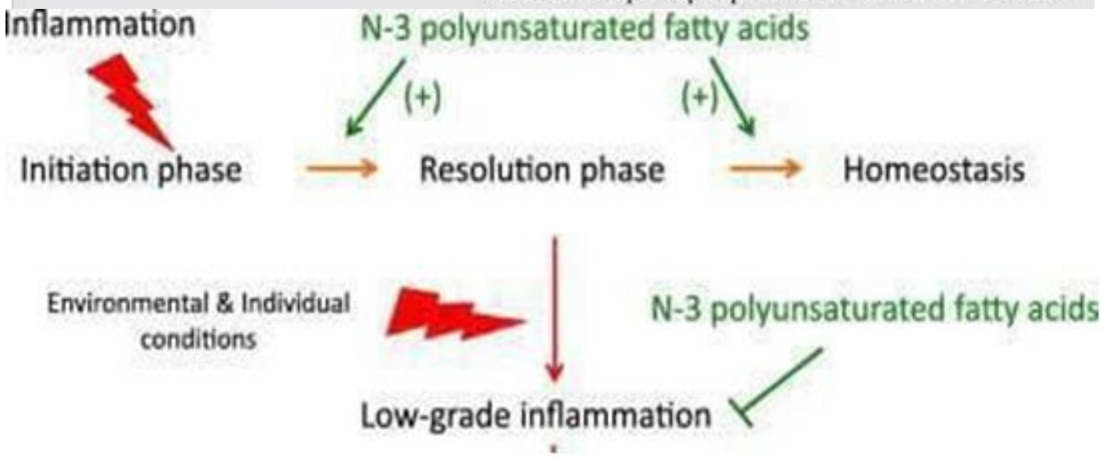

Diagram 5: Anti-inflammatory roles of omega-3 fatty acids

2) n-3 PUFA can alter plasma membrane microdomains called lipid rafts and caveolae that function as signalling platforms that regulate cholesterol transport, signal transduction and endocytosis. When n-3 PUFA is introduced, the microdomain lipid composition is altered: the sphingomyelin content in lipid rafts and the cholesterol and caveolin in caveolae are reduced. The effect of n-3 PUFA-induced cholesterol reduction is a result of poor incorporation of cholesterol into long-chain n-3 PUFA containing PL bilayer. [27]

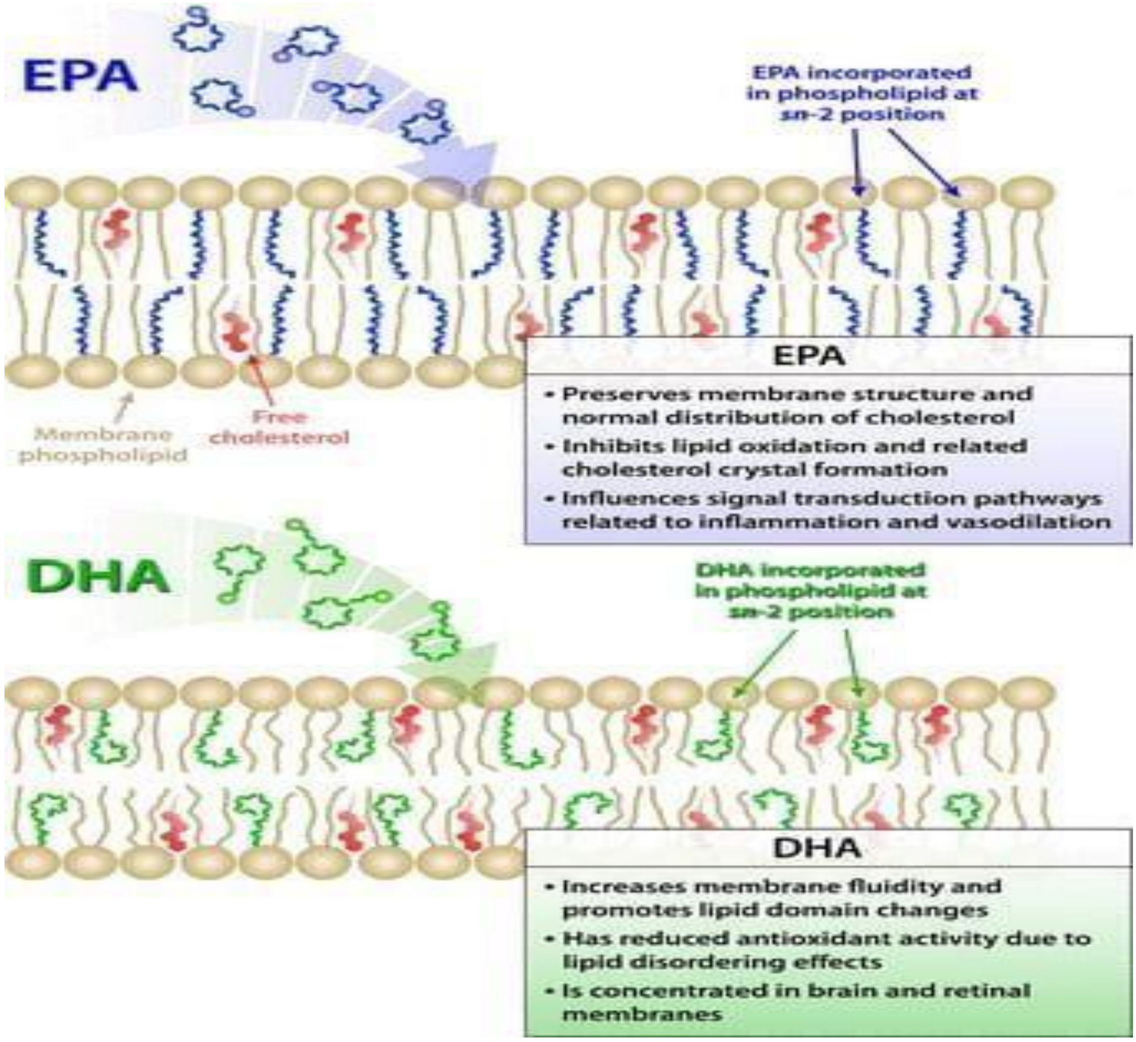

Diagram 6: Different role of EPA and DHA

3) Ultimately, the incorporation of n-3 PUFA can lead to changes in membrane properties, protein functionality and microdomain localization. Of signaling proteins, thus, resulting in the modulation of downstream cellular signaling pathways. [28]

4) n-3 PUFAs have been shown to prevent arrhythmias through multiple mechanisms. One direct mechanism is that n-3 PUFA reduced membrane electrical excitability and activity of voltage-dependent Na+ channels in cardiomyocytes. [29]

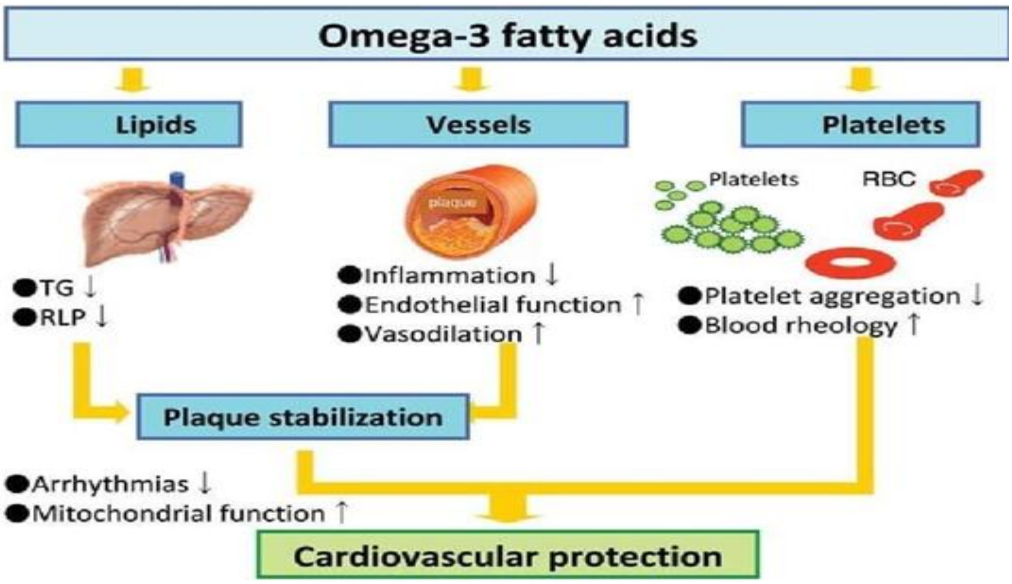

Diagram 7: Omega-3 fatty acids and atherosclerosis

5) A balance between the concentrations of vasoconstrictors (TXA2, PGH2, endothelin-1) and vasodilators (NO, endothelium-derived hyperpolarizing factor, PGI) that are produced by the endothelium determines the vascular tone. The vasorelaxant effect of DHA has been attributed to the decreases in Ca2+ influx in VSMCs. As discussed above, n-3 PUFA can modify eicosanoid production to favor vasodilation and antithrombotic actions. [30]
6) n-3 PUFA can also decrease TG concentration through the inhibition of hepatic very low-density lipoprotein (VLDL)-TG synthesis and secretion that is secondary to a decrease in TG synthesis. [31]

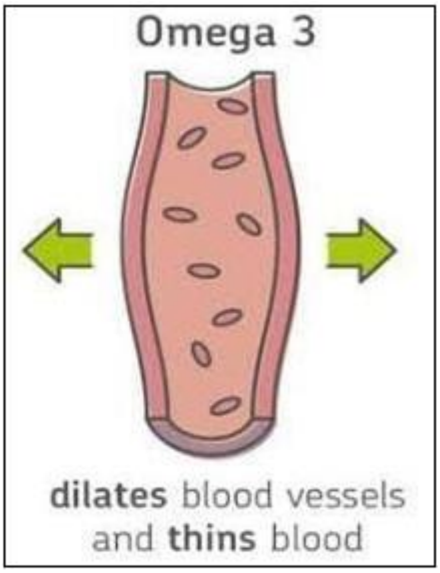

Diagram 8: Vasodilation by Omega-3 fatty acids

7) n-3 PUFA can also decrease TG concentration through the inhibition of hepatic very low-density lipoprotein (VLDL)-TG synthesis and secretion that is secondary to a decrease in TG synthesis. [31]

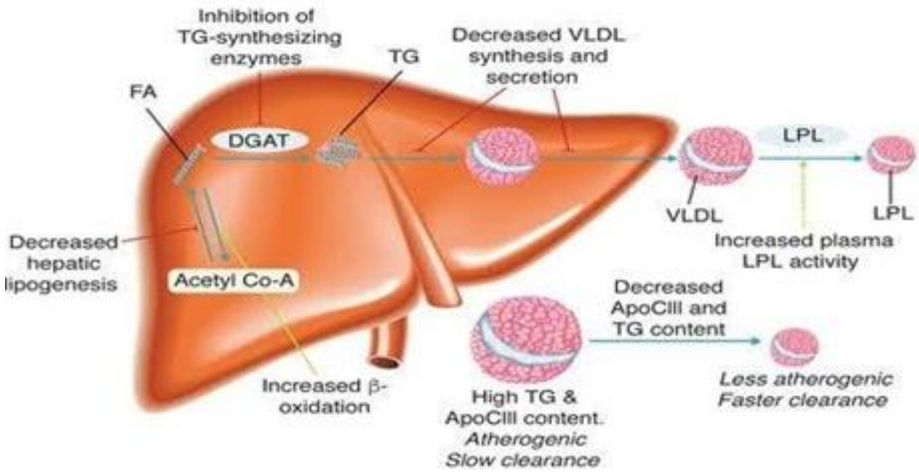

Diagram 9: Lipid Metabolism Moderation by Omega-3 fatty acids

Recent Advances in Studies of Omega 3fatty as a Functional Food Component / Nutraceutical to Prevent CVD

The omega 3 fatty acids are first extracted then characterized and finally studied for encapsulation techniques to deliver their benefits to humans, apart from consuming them from their direct dietary sources. [**32]**

Solvent based extraction techniques and additionally some greener techniques such as supercritical fluid-, enzyme-, microwave-, and ultrasound-assisted extraction methods have been under recent study. [**33]**

Different encapsulation methods are used to produce omega 3 fatty acid entrapped in beads such as: using spray-drying and freeze-drying, emulsification/internal gelation, extrusion, solvent evaporation etc. [**34]**

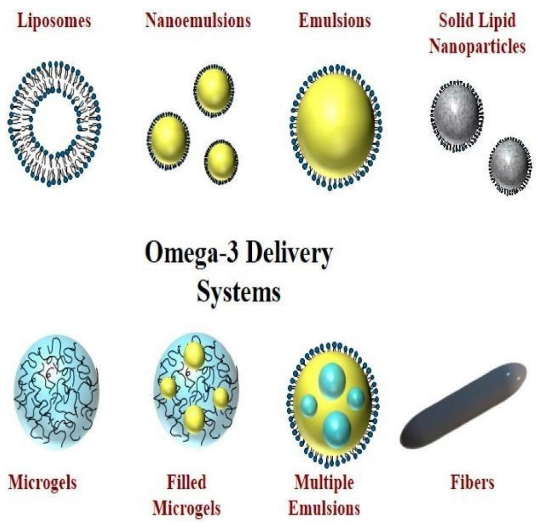

Diagram 10: Encapsulation techniques of Omega 3 fat

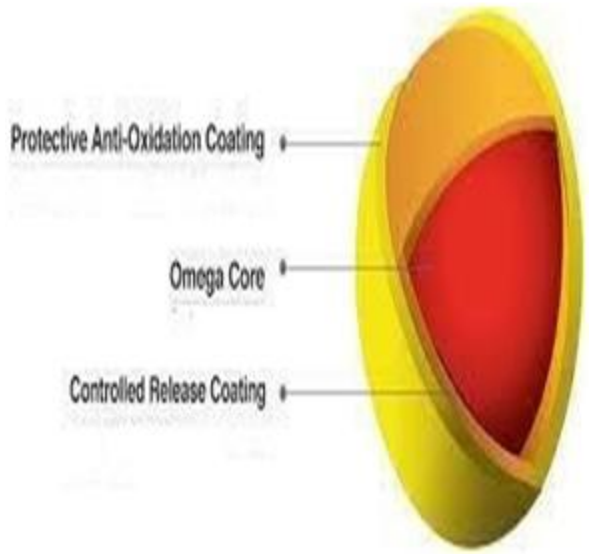

Diagram 11: Encapsulation of omega-3 fatty acid

Encapsulation is regularly used to increase the stability, handling, and application of fish oils, but it is significant that it does not unfavorably affect their bioavailability. Researchers have found that pectin and xanthan gum could increase the digestion of protein-coated fish oil droplets, the polysaccharide chitosan also increased the digestibility and bio availability of encapsulated Omega 3 Fatty acids. [**35**]

6. Summary and Conclusion

Randomized trials have convincingly documented that omega-3 fatty acids can significantly reduce the occurrence of CVD events in patients with coronary artery disease. The strongest evidence to date is from studies in which marine-derived omega-3 fatty acids have been consumed as supplements or fish. Additional clinical studies are needed to confirm the cardioprotective benefits of ALA. A food-based approach to increasing omega-3 fatty acids is preferable, although supplements are a suitable alternative. Additional clinical and mechanistic studies are needed to confirm and further define the health benefits of omega-3 fatty acids for both primary and secondary prevention.

Large-scale epidemiologic studies suggest that people at risk for coronary heart disease (CHD) benefit from consuming omega-3 fatty acids from plants and marine sources. Although the ideal amount to take is not firmly established, evidence from prospective secondary prevention studies suggests that intakes of EPA+DHA ranging from 0.5 to 1.8 grams per day (either as fatty fish or supplements) significantly reduce the number of deaths from heart disease and all causes. These data support the 2000 AHA Dietary Guidelines recommendation to include at least two servings of fish (particularly fatty fish) per week. For ALA, a total intake of 1.5 to 3 grams per day seems beneficial, although definitive data from prospective, randomized clinical trials are still needed. These are also available in nutraceutical and supplement forms, but dietary sources are always preferable.

Diagram 12: Cardio protection Role ofomega-3 fatty acid

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