Role of Omega-3 Fatty Acids in Cardiovascular Diseases

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Abstract

Despite making slow headway in prevention and treatment technologies, the plague of cardiovascular disease (CVD)—the leading cause of death in much of the world—is not abating. For many years, omega 3 fatty acids, especially docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), have been studied as to their heart benefit. Widespread interest in their supplementation was sparked by early large-scale trials that demonstrated their beneficial effect on lowering the risk of CVD. Recent randomized controlled trials (RCTs), however, have produced contradictory results, casting doubt on their effectiveness in modern cardiovascular treatment. The significant advancements in CVD management over the past few decades, such as the widespread use of statins, antihypertensive medications, sophisticated revascularization techniques, and better eating habits, such as consuming more fish, may be the cause of these disparities. These advancements make it more difficult to pinpoint the precise function played by omega-3 fatty acids towards preventing CVD. In the light of current medicines and dietary efforts in preventing CVDs, the chapter discusses the expanding literature regarding omega-3 fatty acids and their biological mechanisms and therapeutic potentials. To precisely define their contribution to contemporary cardiovascular health strategies, more research is required.

Keywords: Cardiovascular disease management**,** Omega-3 fatty acid, Docosahexaenoic acid (DHA), Eicosapentaenoic acid (EPA), Randomized controlled trials (RCTs), Cardiovascular treatment

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Introduction

The heart and blood vessels that make up the cardiovascular system are susceptible to many different diseases. Cardiovascular diseases (CVD) are the conditions that affect the blood circulatory system, i.e., the heart, which pumps the blood, and the vasculature, which transport it around the body. CVDs comprise both congenital and acquired diseases spanning multiple modalities and include a wide variety of clinical manifestations (Thiriet & Thiriet, 2018; Olvera Lopez et al., 2021).

According to the definition provided by the World Health Organization:

Coronary Heart Disease (CHD): The term commonly used is coronary artery disease especially to the blood vessels which supply heart muscle. Reduced blood flow to myocardium leads to myocardial infarction, angina, or congestive heart failure. About one third to one half of total CVD cases are blamed on CHD.

Cerebrovascular Disease: Stroke and transient ischemic attack (TIA) - both are the diseases that associate themselves with the blood vessels that feed the brain

Peripheral Arterial Disease: Disease of the arteries in the limbs, particularly in the arms and legs, leads to limping

Rheumatic Heart Disease: Rheumatic fever affects the heart valves and muscles and is caused by a streptococcal infection.

Congenital Heart Disease: Structural abnormalities of the heart existing at birth in which the normal development and function of the heart is affected.

Deep Vein Thrombosis (DVT) and Pulmonary Embolism: Rheumatic fever affects the heart valves and muscles and is caused by a streptococcal infection (Olvera Lopez et al., 2021; WHO, 2021).

Prevalence of Cardiovascular Diseases

Altogether, cardiovascular diseases (CVDs) constitute the major factor in mortality worldwide, significantly impacting health outcomes and increase health care expense (Vaduganathan et al., 2022). The World Health Organization (WHO) projects that in 2019 CVDs were behind

17.9 million or 32% of the worldwide fatalities. Among these, 85% resulted from heart attack and stroke. In 2019, CVDs contribute for 38% of the 17 million deaths (under 70 years) as a result of noncommunicable diseases (WHO, 2021). Far more people perish from cardiovascular diseases (CVDs) than any other illness, with over 75% of heart disease and stroke related mortalities transpiring in low and middle-income nations (World Health Organization, 2020). American heart association disclosed ≈19 million CVD-attributed deaths globally in 2020, marking a spike of 18.7% from 2010 (Tsao et al., 2022). Cardiovascular disease (CVD) is one of the most expensive diseases ever to exist. The costs associated with this disease exceed those associated with diabetes and Alzheimer's. As much as $237 billion indirect cost weight is estimated yearly and will reach up to $368 billion by 2035 (Dunbar et al., 2018). In consonance with projections, by 2030 CVD's will eclipse all other ailments as biggest tenet of death globally (Karageorgou et al., 2023). Expanding the prevention and treatment approaches is urgently needed to address this escalating crisis (Li et al., 2022).

Risk Factors Associated with Cardiovascular Diseases

It has been shown in epidemiological, genomic and population based studies that high low density lipoprotein cholesterol (LDL-C) is an important risk factor for cardiovascular disease (CVD). Indeed, even when LDL-C reaches a healthy level, there is still some risk of cardiovascular disease (Li et al., 2022). However, the sources of cardiovascular risk have not yet been investigated, and the remaining cardiovascular risk is largely due to lipid and nonlipid changes (Li, 2022).

Hypertension, diabetes and inflammation are the main determinants of non-lipid factors, whereas the main determinants of lipid factors are whether Low Density Lipoprotein Cholesterol (LDL-C) are under control. They were also assessed by circulating levels of TG) lipoprotein (TRL), cholesterol (TRL-C), and lipoprotein 1(Dhindsa et al., 2020; Zhao, 2021). It has been demonstrated that high TGRL-C levels are a new genetic and epidemiological marker of risk of cardiovascular disease and all deaths (Prevention 2019; Sherratt et al., 2023).

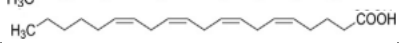
Role of Omega-3 Fatty Acids in CVD's

Because treatment of heart disease is highly personalized, heart disease patients should receive intensive education about the importance of secondary prevention — risk modification and livelihoods (Olvera Lopez et al., 2021). Preventing that heart disease is prevented by when people follow a healthy diet with fruits and vegetables and doing regular aerobic exercise. They help prevent heart disease and stroke. While too much fat in the diet may not be good for the heart, a few unsaturated fats are good for the heart, some are bad. According to the theory, unsaturated fats, sometimes called omega-3 fatty acids, are good for the heart too (Chaddha & Eagle, 2015).

Omega-3 Fatty Acids

Hydrocarbon chain fatty acids where the end groups are attached to a carboxyl and a methyl group respectively, except that which is straight chain. How saturated or polyunsaturated they are, and sometimes how many double bonds they have depends. PUFAs greater than two double bonds in a chain are called long chain PUFAs (LC-PUFAs). Following that, the arrangement of the primary bond to the methyl culminations provides the two major types of nutraceutical PUFAs, which are omega 3 (n-3) and omega 6 (n-6) fatty acids. These include α-linolenic acid (ALA, C18:3n-3), eicosapentaenoic acid (EPA; C20:5n-3), docosahexaenoic acid (DHA; C22:6n-3), and most millimoles per kilogram of all other fatty acids are listed in table 1. Omega-6 fatty acids such as γ-linolenic acid (GLA, C18:3n-6), linoleic acid (LA, C18:2n-6), and arachidonic acid (ARA, C20:4n-6) (Summarized in Table 1) (Tocher et al., 2019; Karageorgou et al., 2023).

Table 1: Biochemical data of Omega-3 PUFAs and Omega-6 PUFAs (Weinberg et al., 2021).

Name	Number of carbon atoms	Number of double bonds	Double bond position from methyl terminal of the fatty acid	Chemical structure
Omega-3 PUFAs				
Alpha-linolenic acid	18	3	n-3	
Eicosapentaenoic acid	20	5	n-3	
Docosahexaenoic acid	22	6	n-3	
Omega-6 PUFAs				
Linoleic acid	18	2	n-6	
Arachidonic acid	20	4	n-6	

The Omega 3 fatty acids are necessary to provide the body with sustainable normal cellular function. They are different from EPA and DHA (obtained from marine sources such as krill, squid & highly efficient fatty fish or tuna, salmon, mackerel, herring, trout, halibut & cod) which are a plant based source (olive, soybean, canola, walnut & flaxseed oil) known as ALA (alpha linoleic acid) (Chadda & Eagle, 2015; Saini & Keum, 2018; Barry & Dixon, 2021). Table 2 summarizes the sources of food items with Omega-3 polyunsaturated fatty acids.

Historical Background of Omega-3 Fatty Acid and CVD Risk

Studies have been conducted on Greenlandic Inuit, a traditional people subsisting on a diet rich in whales, seals, seabirds and fish, who have a low incidence of ischemic heart disease and omega-3 fatty acids, which appear to be beneficial for the heart, are increasingly popular. Benefits include reduced atherogenic lipid profile, reduced platelet count, increased omega-3 content in platelet membranes and prolonged platelet activation time, all of which are related to the anti-inflammatory properties of marine EPA and DHA. Though Sinclair's 1944 report on rare coronary heart disease among Eskimos started things off, there were decades of research on Inuit after that, including Sinclair's finding in 1944 that cholesterol, triglyceride and myocardial infarction risk were less among Eskimos than among whites; Bang and Dyerberg's discovery (Sinclair, 1953; Bang & Dyerberg, 1972; Dyerberg & Bang, 1995).

The Omega-3 fatty acids -- these are essential nutrients that can be consumed in foods and supplements -- are of interest and curiosity to the public (Jain et al., 2015). OTC dietary supplement and prescription grade formulations of omega-3 products are divided according to the composition, purity and dose. OTC products are regulated as dietary supplements for regulation, composition, purity, efficacy and safety and are not interchangeable with prescription grade omega-3s (Prestson Mason, 2019; Li et al., 2022).

Table 2: Content of Omega-3 PUFAs in selected food (According to US Food Data Central) (Weinberg et al., 2021).

Food Source	Omega-3 PUFAs (g/100g)		
	ALA	EPA	DHA
Fish			
Herring, Atlantic	0.10	0.71	0.86
Salmon, Atlantic farmed	0.15	0.86	1.10
Salmon, Atlantic wild	0.30	0.32	1.11
Anchovy, canned	0.02	0.76	1.29
Sardines, canned	0.50	0.47	0.51
Trout	0.16	0.20	0.53
Snapper	-	0.05	0.26
Mackerel	0.16	0.90	1.40
Cod, Atlantic	-	0.06	0.12
Flounder	0.02	0.14	0.11
Tuna, yellowfin	-	0.01	0.09
Tuna, canned (water)	-	0.03	0.20
Fish oil			
Menhaden	1.49	13.17	8.56
Salmon	1.06	13.02	18.23
Sardine	1.33	10.14	10.66
Cod liver	0.94	6.90	10.97
Herring	0.76	6.27	4.21
Oil			
Canola	7.45	-	-
Flaxseed	53.37	-	-
Soybean	6.79	-	-
Corn	1.04	-	-
Olive	0.76	-	-
Seeds			
Chia	22.81	-	-
Walnuts	9.08	-	-
Flax	22.81	-	-

Intake of omega-3 from such a variety of OTC supplements and concentrated pharmaceutical grade EPA and DHA formulations is also possible from dietary sources and commercial products. Four prescription dose formulations of omega-3 PUFA are now approved for use by the U.S. FDA (Barry & Dixon 2021). EPA and DHA contents of selected pharmaceutical preparations are shown in Table 3.

Table 3: Pharmaceutical Omega-3 fatty acids and their EPA and DHA content (Innes & Calder, 2020; Weinberg et al., 2021;Kurpa et al., 2024).

Drug name	EPA (g/1g capsule)	DHA (g/1g capsule)	EPA+DHA content per gram of oil	Daily dose	Form
Omacor/Lovaza	~0.465	~0.375	460 mg EPA + 380 mg DHA	2 g twice a day or 4 g once a day	In ethyl ester form
Omtryg	~0.375	~0.465	465 mg EPA + 375 mg DHA	2 g twice a day or 4 g once a day	In ethyl ester form
Epanova	0.55	0.2	550 mg EPA + 200 mg DHA	2 g twice a day or 4 g once a day	In free fatty acid/carboxylic acids
Vascepa/icosapent ethyl	1.0	0	900 mg EPA	2 g twice a day	In ethyl ester form

Effect of Omega-3 fatty acid on Cardiovascular Diseases

Past studies have suggested that foods high in EPA, such as fish or omega 3, may lower the risk of heart disease such as coronary heart disease (Julvez et al., 2021). Also omega-3's in foods like ALA in walnuts, canola, flaxseed are linked with reduced mortality, lower risk of heart disease and less sudden cardiac arrest, especially with age (Innes & Calder 2020).Elevated triglyceride levels is an important target in treatment of atherosclerotic cardiovascular disease. However, if lifestyle changes do not reduce triglycerides to <2.3 mmol/L (<200 mg/dL), the following measures are recommended: non-HDL drugs and LDL (Karageorgou et al., 2023). As ethyl ester, EPA and DHA carboxylic acids, or a purified EPA (IPE), Omega 3s when prescribed (4 g./day) reduce very high triglycerides but only by normalizing the lipid profile and lowering of VLDL concentrations (Virani et al., 2021). Thus, according to the American Heart Association first of all, it is safe to supplement with omega-3 and lowers deaths from heart disease and, indeed, deaths from heart disease and especially myocardial infarction. Omega-3 recommended for people with heart disease (Siscovick et al., 2017).

Mechanisms of Cardio-Protection by Omega-3 Fatty Acids

Although recent study provides new understanding, many of the ways by which omega 3 fatty acid consumption confers CVD advantage are still unclear (Elagizi et al., 2018). These overall effects are mainly attributed to the following mechanisms by which omega-3 fatty acids may reduce the incidence of cardiovascular events. Anti-arrhythmic actions:

1. Anti-inflammatory actions
2. Anti-thrombotic effect
3. Pro-resolving mediators
4. Lowering of Triglyceride rich lipoproteins
5. Membrane Stabilizing Effect
6. Alter prostaglandin synthesis

1. Anti-arrhythmic Actions

The electropharmacology of omega-3 fatty acids is due to a stabilization of electrical activity in cardiac myocytes and prolongation of a relative refractory period through action at sarcolemmal ion channels (Jain et al., 2015). When ingested, omega 3 fatty acids stabilize mitochondrial and plasma membranes to prevent oxidation and to protect against arrhythmias (Mason et al., 2020).

2. Anti-inflammatory Actions

The ability to modulate inflammation is a primary function of Omega PUFAs, with EPA and DHA giving special importance. Thus, they influence leukocyte chemotaxis, adhesion molecule expression, leukocyte endothehelial interaction, and proinflammatory eicosanoids and cytokines production. EPA and DHA also generate anti-inflammatory mediators: The biopotency of lemurin, fennel, and malathion is lower than that of EPA and EPA-derived arachidonic acid eicosanoic acid, but the biopotency of such eicosanoic acids derived from EPA is generally lower than that of arachidonic acid derived from eicosanoic tetraenoic acid. The mechanisms by which they affect cells include altering cell membrane phospholipids, disrupting lipid raft, inhibiting proinflammatory transcription factors, and activating anti-inflammatory pathways such as PPARγ. These properties make EPA, DHA and related fatty acids therapeutically useful in pain management (Calder, 2017; Weinberg et al., 2021).

3. Anti-thrombotic effect

Omega-3 fatty acids can prevent thrombosis and vasospasm by increasing the synthesis of antiaggregatory and vasodilatory prostanoids (Mason et al., 2020).

4. Pro-resolving Mediators

Omega 3 has also been a source of some prostaglandins with anti-inflammatory properties. In particular, omega-3 fatty acids may give people a head start in finding specific solutions which can prevent the disease and also prevent from interfering with immune control, when compared to vaccines (Mason et al., 2020).

5. Lowering of Triglyceride Rich Lipoproteins

We do not know exactly how omega 3 fatty acids lower triglycerides (FDA approved). It's thought to lower triglycerides by following:

- **Suppressing Lipogenic Gene Expression**

By thwarting phosphatidic acid phosphatase, acyl-CoA: The expression of lipogenic genes is repressed in the presence of 1,2-diacylglycerol acyltranferase and with lowing expression of sterol regulatory element binding protein 1c by omega 3 fatty acids. Sterol regulatory element binding proteins (SREBPs) are membrane bound enzymes that cleave and enter the nucleus to transcribe enzymes that make fatty acids, cholesterol and LDL. In the presence of omega-3 fatty acid rich diet, negative feedback inhibits the ability of SREBPs to activate the SREBPs and their encoded enzymes, such as HMG-CoA reductase (3-hydroxy-3-methylglutaryl-coenzyme A reductase) and FPP synthase (farnesyl diphosphate synthase) (Krupa et al., 2024).

- **Increasing Beta Oxidation of Fatty Acids**

Practically all tissues in the body metabolize fat via the metabolic process known as beta-oxidation, and that fat is then turned into energy. As omega-3 fatty acids increase beta-oxidation mediated through regulation of CAT1 and ACC, the triacylglyceride concentrations in the body are reduced. Carnitine acetyltransferase modifies fatty acid substrates to allow them to be transported into inner mitochondrial membrane by carnitine-acylcarnitine translocation. It is converted to acyl CoA, a pre-cursor of acetyl CoA, which is used in different chemical pathways to ATP formation. In addition, through this delay in feedback inhibition EPA also increases beta oxidation. The enzyme which synthesizes malonyl-CoA, inhibitor of CAT1, is acetyl-CoA carboxylase, which is inactivated by EPA. CAT1 will be more aware and use more triacylglycerides for beta-oxidation if lesser malonyl-CoA forms (Backes et al., 2016; Krupa et al., 2024).

- **Increasing Expression of Lipoprotein-lipase (LPL)**

LDL, VLDL and chylomicrons triacylglycerol components are metabolized out of the circulation by the extracellular enzyme lipoprotein lipase (LPL), situated on the luminal surface of vascular endothelium. It is demonstrated that HSON omega-3 fatty acid diet increases the mRNA and subsequently the LPL lipoprotein lipase protein on endothelial lining of blood vessel and decreases the size of the chylomicrons. An increase in lipoprotein lipase levels and a reduction in LDL, VLDL, and chylomicron size may decrease triglyceride levels in hypertiglyceridemic patients (He et al., 2018; Pirahanchi et al., 2023; Krupa et al., 2024).

Influencing total body lipid Accretion

Omega-3 fatty acids can lower high triglycerides through impacting body lipid deposition. For any condition that requires omega-3 use for over six weeks, lean body mass is built, total body fat is reduced, while metabolic rate, fat loss, and basal metabolic rate are increased. This impact they claim is by the omega-3 stimulating the peroxisome proliferator-activated receptors (PPARs) that through genes regulation affect metabolisms of fatty acids and glucose. These changes enhance energy requirements and fat loss and therefore reduces blood triglyceride concentration (Logan & Spriet, 2015; Krupa et al., 2024).

One important blood lipid biomarker is TG, and high level of TG indicates the increased TRL-C. After exhibiting that TRL-C predicts CV events through directed analyses of LDL-C via therapeutic interventions, the prospective investigations and recent Mendelian randomization studies revealed that TRL-C directly forecasts residual CV risk based on prospective longitudinal observations (Li et al., 2022). According to the American Heart Association, the methods by which omega-3 has the ability to lower the TAG is through increased incorporation into cellular phospholipids rather than TAG because of phosphatidic acid phosphatase inhibition (Skulas-Ray et al., 2019). Furthermore, EPA and DHA is thought to accelerate the breakdown of apolipoprotein B and disrupt the formation plus secretion of very low-density lipoprotein (Weinberg et al., 2021). EPA's antiatherogenic qualities may be attributed to its further impact affecting lipoproteins and atherosclerotic plaque (Watanabe et al., 2017; Mason et al., 2020). Triglycerides are generally reduced by 20% to 30% using DHA and EPA (4 g/day), with greater decline in those suffering from severe hypertriglyceridemia (Skulas-Ray et al., 2019).

Table 4: Summary Guideline Recommendation for Omega-3 fatty acids

No.	Organization	Population	Recommendation
1.	Academy of Nutrition and Dietetics (Vannice &Rasmussen, 2014)	Healthy adults	Consuming two or more portions of fatty fish in a week including 500mg of EPA plus DHA daily.
2.	2021 ADA CVD and Risk Management Guideline (Care, 2021)	ASCVD or other CVD patient	Patient using statin with target LDL- C but increased TG, the icosapent ethyl can reduce CVD threat.
3.	American Heart Association (Mosca et al., 2011; Bowen et al., 2016)	All adults Patients with coronary heart disease hypertriglyceridemia patients Women with hypercholesterolemia and/or hypertriglyceridemia	Fish at least two times a week. About 1g of EPA+ DHA in a day. EPA+ DHA 2–4g/ day in capsules Fish rich in omega-3 fatty or capsules (EPA 1800mg/day).
4.	2020 American Association of Clinical Endocrinologists/ American College of Endocrinology (AACE/ACE) Consensus Statement (Handelsman et al., 2020)	Patient with established ASCVD or diabetes	Icosapent ethyl should be prescribed to such patient requiring a statin and have elevated triglycerides of 135–499 mg/dL.
5.	2019 European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) Guideline (Mach et al., 2020)	High-risk, or above, patients with TG levels between 1.5– 5.6 mmol/L (135–499 mg/dL) despite statin therapy	Eicosapent ethyl 2 × 2 g/day of n−3 PUFAs together with a statin.
6.	2015 National Lipid Association (Jacobson et al., 2015)	Adults	≥2 servings (3.5–4oz.) of fish/seafood (preferably oily) per week
7.	2019 National Lipid Association Scientific Statement (Orringer et al., 2019)	Patients aged 45 years or older with clinical ASCVD	Patients requiring pharmacologic therapy, with fasting TGs 135-499 mg/dL, on a high- or maximally tolerated-intensity statin with or without ezetimibe, for ASCVD risk reduction, icosapent ethyl is recommended.
8.	2021 Canadian Cardiovascular Society Dyslipidemia Guideline (Pearson et al., 2021)	Patients with ASCVD, or with diabetes mellitus and ≥1 CVD risk factors	Icosapent ethyl is recommended to such patients with fasting TG level of 1.5– 5.6 mmol/L (135– 499 mg/dL) even after the optimized treatment of maximally tolerated statins.
9.	U.S. Food and Drug Administration (Krupa et al., 2024)	Adults (≥18) with hypertriglyceridemia (≥500 mg/dL) used in conjunction with diet and exercise	Icosapent capsules (4 g daily), usually two capsules of 2 g each taken with meals. Omega 3 ethyl esters are provided as 4 capsules/day or 2 capsules BID with meals. Daily dose of 2g / d (taken as 2 capsules or 4g / d d taken as 2 capsules taken once a day). Omega 3 acid ethyl ester (A) given as capsules of 4 g/d capsule, 4 capsules of 1 meal or 2 capsules into 2 meals.

6. Membrane Stabilizing Effect

Omega-3 PUFA has other actions in tissues including antioxidative, vascular, and electrophysiological ones and considered the ability to modulate the composition and functionality of cellular phospholipid membranes. The described characteristics allow outlining how omega-3 PUFAs act to support the heart and protect it. There are several ways that EPA and DHA bind to cellular membranes. The preclinical studies offer a hypothesis that can explain why EPA has shown CV improvements in randomized clinical trials (RCTs) while DHA has not:

the fatty acid has a stable extended molecular structure. This structure helps to increase the stability of membrane, decrease inflammation activity, and minimize the procedure of lipid peroxidation. By reducing the electrical excitability of cardiac myocytes EPA and DHA are first to decrease sudden cardiac mortality. An RCT involving fewer subjects but where omega-3 PUFA was administered in combination with a higher percentage of DHA was shown to reduce post-operative atrial fibrillation even though most of the RCTs have failed to establish the cardioprotective nature of omega-3 PUFAs in respect to atrial fibrillation prevention. EPA plus DHA improves endothelial function and systemic arterial compliance and can account for the reductions in blood pressure when taking fish oil (Sherratt & Mason, 2018; Preston Mason, 2019; Weinberg et al., 2021).

7. Alter Prostaglandin Synthesis

PGI3 derived from omega-3 fatty acid metabolite of arachidonic acid, stimulates vasodilation and enhances vascular compliance. Thus, preventing and curing cardiovascular diseases, including atherosclerosis, controlling vascular sclerosis and blockage is the significant characteristic of this feature. Like PGI2, PGI3 promotes vascular compliance by binding to the prostacyclin receptor and activating adenylate cyclase with subsequent generation of cAMP, and protein kinase A. In addition, PGI3 is used to treat cardiac diseases more so coronary arteries diseases because it prevents the formation of blood clots (Lyu, 2023).

Recommended Dosage of Omega-3 fatty Acid

Guidelines regarding omega 3 fatty acids (Table 4) were issued by well-known nutritional and cardiovascular health organizations.

2022 AHA/ACC/HFSA Heart Failure Management Guideline: Heart failure patients (NYHA class II-IV) have a reduction in cardiovascular hospitalizations and mortality with the supplementation of omega-3 fatty acids (V, A). Before, omega-3 fatty acids have not been recommended to treat heart disease. Thus, current data suggest that EPA may be an effective treatment in purified concentrations and doses in patients with ASCVD Research on how to use omega 3 fatty acids in treatment for heterogeneous heart diseases (arrhythmias, cardiomyopathy, hypertension, sudden cardiac arrest etc. (Heidenreich et al., 2022; Li et al., 2022).

Market Value According to GOED (2022), the market value of the EPA and DHA omega-3 products during the previous year was approximately $1.53 billion in 2021, an increase of 5.5% when compared to 2020 levels. The international Omega-3 market can potentially hit 115,031 metric tons with a CAGR of 2.1% (Global EPA and DHA Omega-3 Products Market Report 2022 2020-2021 Data and Projections to 2024, 2022). The GOED states that omega-3 fatty acids can also be present in processed food, finished pharmaceuticals, specialty foods, processed foods, baby foods, and dietary supplements. The EPA and DHA omega-3 finished product market was estimated to be worth $47 billion in the year 2021, with annual growth rates of 3.2% expected for 2023 for EPA and DHA omega-3 finished product market in Asia, Africa, and the Middle East (Karageorgou et al., 2023).

Conclusion

Finally, this consonance between the first, large scale trials involving omega 3 fatty acids, and the subsequent RCTs, suggest an initial cardiac benefit to omega 3 fatty acids whereas the latter are less enthusiastic about the usefulness of omega 3 fatty acids for the prevention of CVD. One possible source of this phenomenon may be the great development of the cardiovascular service during the last decades. This may also explain why omega-3 fatty acid supplementation has failed to demonstrate significant benefits in recent populations who are on chronic statin therapy, antihypertensive agents, state-of-the-art revascularization procedures and consuming improved diets including fish consumption. These developments raised the difficulty of disentangling the role of omega-3s in contemporary prevention of cardiovascular diseases. More detailed investigation is needed to assess their place within today's pharmacological therapies and nutritional advice for CVD prevention

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