

The Effects of Omega-3 Fatty Acids on Heart Diseases

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Abstract. Omega-3 (ω -3) is a group of multiple unsaturated fatty acids, commonly found in deep-sea fish, seal oil. In recent years, ω -3 has become a hot topic in the treatment and prevention of cardiac diseases, however, a systematic explanation of the related regulatory mechanisms is lacking. The theme of this paper is the effects of ω -3 on heart diseases, after collected the data from last five years, then made a system analysis. Finally it concluded that ω -3 can raise benign cholesterol in high-density lipoprotein (HDL) and reduce body's oxidized bad cholesterol in low-density lipoprotein (LDL).it also can participate in arachidonic acid metabolism to produce Prostaglandin-I-3 (PGI 3) to regulate vascular elasticity, platelets and thrombus quantity.in addition, it also has an important role in regulating human blood pressure, AS risk and heart rate. All of these indicators are linked to an increased chance of heart diseases, so the conclusion is that ω -3 mainly plays a role in relieving vascular obstruction and heart function.

Keywords: LDL; HDL; blood vessels; AS; heart rate.

1. Introduction

Heart diseases can take millions of lives in all parts of the world every year, but very effective prevention and treatment to them have not appeared. There are many studies that found that intaking omega-3 fatty acid (ω -3), including two fatty acids: eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is a successful approach to prevent heart diseases. And the protective effect may rise with the increase of ω -3.

Many existing studies have explained why from different perspectives. Latest studies showed that tall-dose EPA treatment is beneficial, it was a key approach to further significantly reduce cardiac disease in patients with persistent hypertriglyceridemia, and other mechanisms of action may contribute to heart protection, including reducing inflammation and platelet aggregation [1]. The atherosclerosis (AS) is also a confirmed symptom associated with major cardiac diseases and the oxidized low-density lipoprotein (LDL) contains poor cholesterol that has the AS-promoting effects while ω -3 can reduce oxidized LDL. On the other hand, high-density lipoprotein (HDL) can prevent reactive oxygen species (ROS) from oxidizing cholesterol in LDL while ω -3 can increase the amount of HDL containing benign cholesterol and thus indirectly prevent AS [2].

Therefore, it is very important to summarize the regulatory mechanism of the specific effect of ω -3 on heart diseases to make the way for further quantitative research. This paper will summarize the mechanism by which ω -3 affects heart diseases through the elaboration of the mechanism of it on human LDL, HDL, blood vessels, AS and heart rate.

2. The Effects of ω -3 on Bad Cholesterol and Triglyceride (TG) in LDL

LDL belongs to lipoprotein, which can deliver cholesterol to cells in distal organs. When LDL modified by oxidation is excessive, the cholesterol that it carries will stick to the wall of the artery, and there will be a risk of AS in humans after a period of time [3].

The EPA and DHA from ω -3 both can not only help the human body defecate neutral or acid cholesterol together but also inhibit the liver lipid's synthesis, so they can reduce the bad cholesterol and TG in LDL and blood fat, making fat not easily accumulate in the arterial wall to slow down the progress of AS. moreover, they can also avoid some heart diseases such as angina pectoris, coronary heart disease, myocardial infarction and so on.

About the effects on cholesterol, it can refer to the experiment of Sunil Chikkalakshmi Gurumallu et al. Because sesame seed oil (SSO) and Flax seed oil (FSO) are both rich in ω -3. thus they divided 54 Wistar albino rats into 9 groups; The experimental group received FSO oral medication (FSO: 43mg/kg, SSO: 292mg/kg) and SSO oral medication (FSO: 86mg/kg, SSO: 584mg/kg), at the last step of the project, they studied chemical figures including antioxidant enzyme condition and lipid profile in mice, after 28 days of process it clearly raised the antioxidant enzyme activity in rats including super oxide dismutase (SOD) and catalase (CAT) [4]. Thus, the treatment may prevented the appearance of oxidized cholesterol in LDL. Moreover, it was observed that the fat content of whole cholesterol (TG) dropped clearly, very low-density lipoprotein (VLDL), LDL, and histopathological examination confirmed the results as well (Fig. 1) [4].

About TG, except for those mentioned above, ω -3 also can reduce it through other various pathways, which are still being explored (Fig. 2) [5].

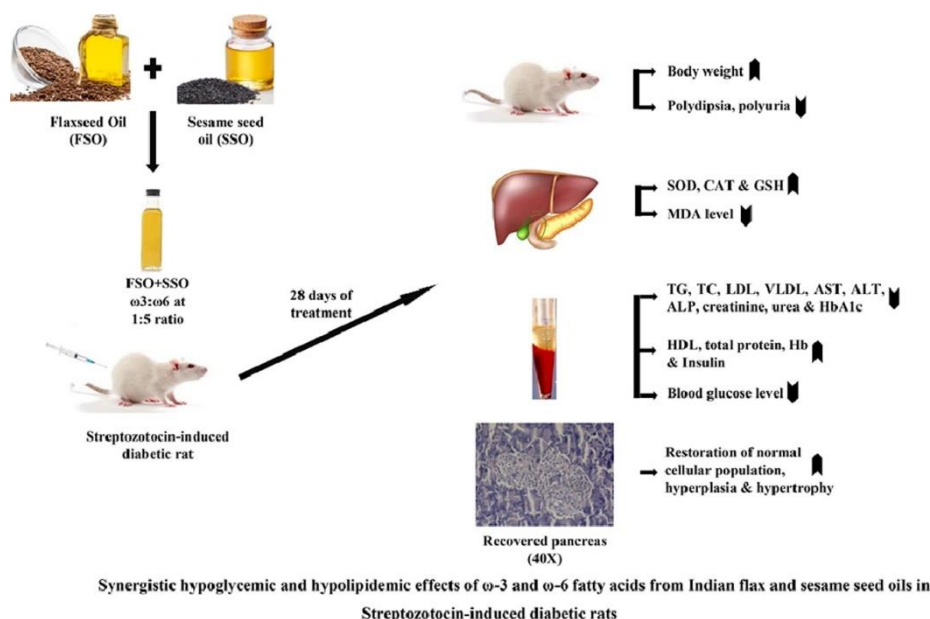


Fig 1. The significant effects of ω -3 from Indian FSO and SSO on reducing blood sugar and blood lipids of diabetic rats [4].

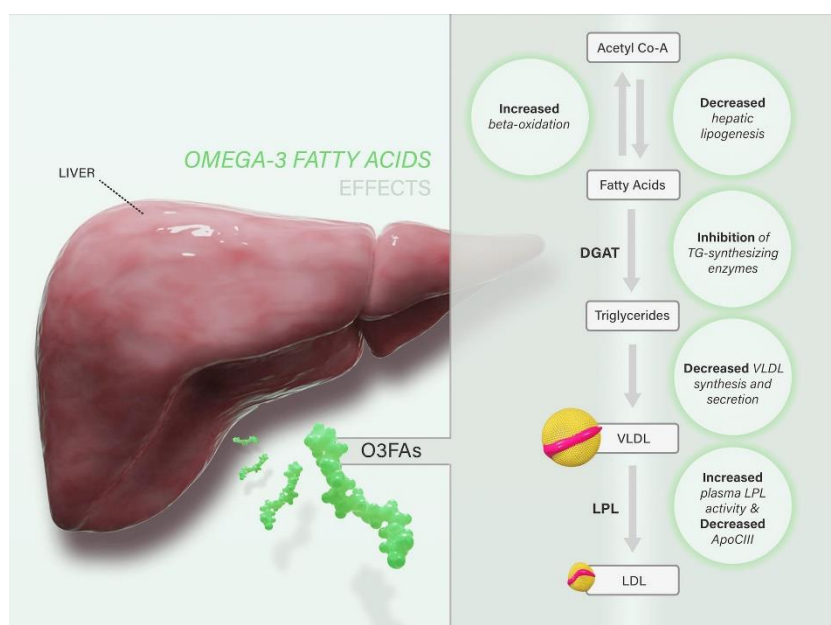


Fig 2. ω -3 reduces TG levels through several mechanisms, and ω -3 can use quantities of non-hepatic and hepatic ways to reduce the whole amount of TG. EPA and DHA also enhance the effect of lipoprotein lipase (LPL) to improve the process of lipoprotein particles' endocytosis [5].

In particular, ω -3 can inhibit acyl-coenzyme A: 1,2-diacylglycerol acyltransferase (DGAT)'s expression and improve the speed of oxidation in fatty acid, thus reducing the production of lipogenesis in the liver and VLDL [6]. Thus, it reduces the TG among them. In addition, EPA can inhibit fat's breakdown and expression of the related genes in the adipose tissue, so it can also reduce TG in human body's fat [7]. Because of this, a significant decrease was also observed in the lipid profile of triglycerides in rats in the experimental results of Sunil Chikkalakshmipura Gurumallu et al described above [4].

In conclusion, the above experiments proved that ω -3 can prevent heart disease by preventing the oxidation of cholesterol in LDL and directly promoting the reduction of malignant cholesterol and TG to reduce the lipid blockage of blood vessels.

3. The Effects of ω -3 on HDL

HDL is a class of lipoproteins produced by the human liver and intestine. It is composed of phospholipids and 1 or 2 apoproteins. It produces effects in other lipoprotein metabolism and the transport of cholesterol from outside cells to liver. So it helps body clean up bad cholesterol from the blood and reduce fat deposition in the walls of blood vessels, thereby reducing the risk of heart disease such as coronary heart disease.

ω -3 can increase the amount of HDL containing benign cholesterol. Moreover, Cartolano Flavia De Conti et al researched ω -3's influence on HDL engineery. They selected 147 people at high risk of cardiovascular disease; every day everyone needed to eat 3g fish oil including 230 mg DHA and 370 mg EPA. Researchers got their empty blood sample at baseline period and the next 8 weeks and finally investigators assessed the fat condition and glucose condition from the plasma; from the HDL they found that the activity of its fatty acid condition, Paraonase-1 (PON1), and Apolipoprotein and cholesterol ester transfer protein (CETP) all decreased [8].

Apolipoprotein can increase the risk of coronary heart disease through many aspects. PON1 can protect the oxidation of LDL and CETP can convert HDL into LDL, so all of their reduced activity is beneficial for the prevention of cardiac disease.

This experiment also found that ω -3 increased the amount of HDL which had large size(28.7% increased) and reduced the amount of HDL which had small size(10.6% decreased) and non-esterified fatty acid (NEFA) levels (16.2% decreased) in HDL [8]. The larger particle size of HDL provides greater protection to heart, and the bigger the size and number of HDL, the lower the risk of heart diseases. On the other hand, they found that NEFA had connection with the principle of heart diseases, and higher blood NEFA levels had clear connection with raised possibility of clinical peripheral arterial disease (PAD) [9].

To make a long story short, ω -3 is well in reducing the risk of heart diseases having connection with HDL function by improving the size of HDL and modifying its lipid, antioxidant and enzyme activity.

4. The Effects of ω -3 on the Health of Blood Vessels

4.1. The Effects of ω -3 on Resilience of Blood Vessels

ω -3 can participate in arachidonic acid metabolism. Prostanoid is generated, called Prostaglandin-I-3 (PGI 3), which can release blood vessels and increase their elasticity. Therefore, ω -3 can indirectly increase vascular elasticity, and be used to prevent and treat cardiac diseases such as atherosclerosis (AS) related to vascular sclerosis and obstruction.

Because there is too little research literature on the specific regulation mechanism of PGI 3, the specific regulation of PGI 3 on vascular elasticity and other characteristics can be referred to the prostacyclin compound named Prostaglandin-I-2 (PGI 2), which has similar functions to PGI 3. PGI 2 can combine with the specific prostacyclin receptor to activate adenylate cyclase (AC).the activated AC can help adenosine triphosphate (ATP) to generate cyclic adenosine monophosphate (cAMP) by

catalyzing ATP, and then cAMP can activate cAMP-dependent protein kinase: protein kinase A (PKA) to phosphorylate its catalytic proteins, thus the process can dilate blood vessels and increase the elasticity of blood vessels (Fig. 3) [10].

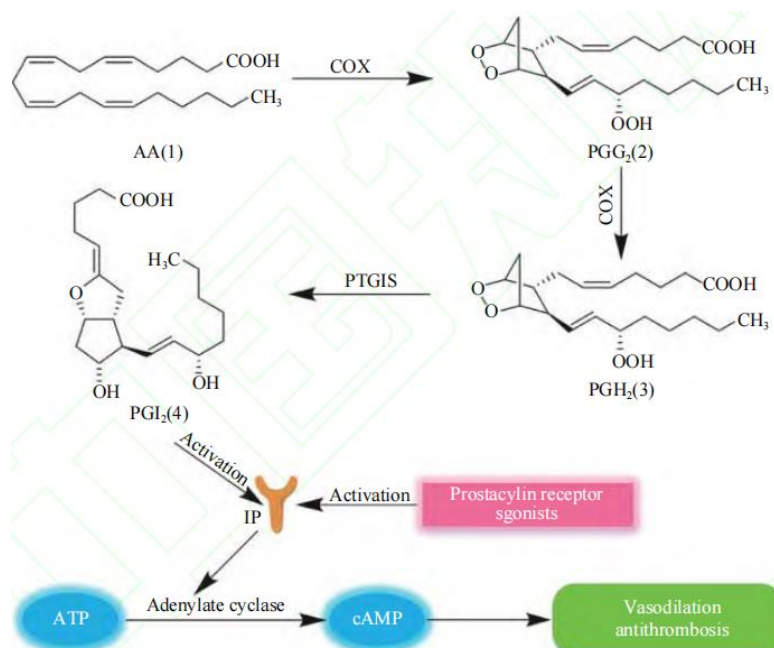


Fig 3. PGI₂ signaling pathway [11]

4.2. The Effects of ω -3 on Platelets and Thrombus in Blood Vessels

PGI₃ is also resistant to platelet aggregation in the blood vessels. Therefore, ω -3 can indirectly resist platelet aggregation by promoting the formation of PGI₃, and this regulation can be used to prevent excessive platelet aggregation from producing excess thrombosis which may block blood vessels. so PGI₃ can treat heart diseases especially coronary heart disease.

For the effect of PGI₃ on platelets and thrombus, this paper can also refer to PGI₂ which has similar function, Many studies have taken the amount of prostacyclin and the sensitivity of blood vessels to it as one of the standards that evaluate the effects on antiplatelet therapy and the treatment of cardiac diseases such as coronary heart disease are good enough or bad.

Taking the Mediterranean diet as an example, this diet pattern recommends people to consume ω -3-rich aquatic products and seafood. One of the reasons why the Mediterranean diet is believed to effectively prevent heart disease is that ω -3 can promote the production of PGI₃. Mohajeri Mahsa et al have determined the relationship between some people with angina pectoris and healthy people who adhere to the Mediterranean diet and serum prostacyclin, In total, researchers compared 100 healthy people and 100 patients with metal angina who all were referred to Adamil Imam Khomeini Hospital in 2 years from 2021 to 2022; the study used 10 filters; the results showed that patients with higher Mediterranean diet adherence had 0.34 units serum prostacyclin levels higher than those patients who had lower dependence ($p = 0.02$, Coeff = 0.34) [12]. on the other hand, Wickham Kate A et al determined the sensitivity of human blood vessels' platelets to prostacyclin in order to prove that aerobic exercise and intensive training were beneficial to reduce the risk of thrombosis related to platelets [13].

For the another effect on thrombosis, PGI₂, which has a good function to inhibit the adhesion of the vascular leukocyte to the arterial wall, can prevent the proliferation of smooth muscle cell (SMC) [14]. And it also can prevent platelet activation from forming a thrombus. by binding to receptors on blood vessels and blood cells, PGI₂ can raise the function of cAMP by activating adenylate cyclase, and then activate protein kinase A, this procedure in turn can depress platelet activation to form a thrombus and block the increase of cytosolic calcium (thus can counteract the vasoconstrictor effect) [14]. Finally, it can lead to the vasodilation and prevent thrombosis from blocking blood vessels.

In conclusion, the effects of prostaglandins synthesized by ω -3 on platelets and thrombus is important in the treatment of heart disease.

4.3. The Effects of ω -3 on Blood Pressure

ω -3 has a great effect on lowering the blood pressure of human body, and both the diastolic pressure and systolic pressure of blood vessels can be reduced.

About the specific principle of lowering blood pressure. Some clinical trials have found that ω -3 can promote the production of nitric oxide and weaken the contractile effect of noradrenaline and angiotensin on blood vessels, moreover, it can also enhance the diastolic effect of blood vessels and improve the compliance of arterial vessels, thus reducing systemic vascular resistance and blood pressure of the whole human body [15].

There has been a large prospective cohort of long studies, studying the development of cardiovascular disease in patients with normal diet containing ω -3, finally they found that high ω -3 dietary pattern was negatively associated with the risk of hypertension, in addition, other meta-analyses reviewed with the cohort also mostly showed a reduction in blood pressure in hypertensive subjects because of the ω -3 diet [16].

Reducing blood pressure and the prevention of heart disease has a very great relationship. It can prevent human from suffering from AS and then getting coronary heart disease. And it can also prevent the myocardial hypertrophy caused by long-term hypertension, later there will not be a hypertensive heart disease, heart failure, atrial fibrillation or arrhythmia, etc.

5. The Effects of ω -3 on AS

It is generally accepted that ω -3 can drop the possibility of atherosclerotic cardiovascular disease (ASCVD).

The specific principle can be referred to the report produced in 2019 by Sugasini Dhavamani et al. Other else conditions being equal, they fed an atherogenic diet to rats with experimental oil and RPOO (refined palm oil) as a control, The experimental oil was rich in 10% ω -3, while RPOO lacked it. In the atherogenic diet, in contrast to the RPOO, rats fed the experimental oil showed reduced cholesterol [16]. It was a significant decrease in lipid accumulation observed in the aorta. Because the feeding of the ω -3-rich structural lipids led to the accumulation of ω -3 which were polyunsaturated long-chains, and decreased the long-chain ω -6 which were polyunsaturated in blood, liver lipids and aortic lipids [17].

In addition, the most significant influence of ω -3 on arterial stiffness and arterial wall properties in AS was also summarized by Verveniotis Alexios et al; the results showed that ω -3 could hold the development of AS; moreover, the enough ingestion of ω -3 also can regulate both human arterial stiffness and endothelial dysfunction [18].

Certainly, it will not so effectual if the content or purity of EPA and DHA are not high enough. In summary, the mechanism of action of ω -3 on heart health and arterial stiffness has been well built; however, further studies should be needed to solve some confusing results in studies and produce more effective ways for heart illness.

6. The Effects of ω -3 on Heart Rate

Arrhythmia is one of the most common heart disorders and is often the direct cause of sudden cardiac death. Coronary heart disease, myocardial infarction and so on can lead to heart ischemia and cause arrhythmia.

The evidence for this claim can be referred to the 2021 article by Anthony Ryan et al. They randomly assigned participants (70 ± 3 years) to eat 2 g/day of normal oil (number of controls = 8, 62.5% female) (1700 mg/day oleic acid) or eat fish oil being rich in ω -3 (number of experimental groups = 9, 55.6% female) [provided 560 mg/day DHA and 140 mg/day EPA] for the last 16 weeks

[19]. They finally assessed many things including ω -3 content and heart rate parameters in participants. the final ω -3 content increased in the experimental group (control groups: 6.1 ± 0.8 before start, 5.9 ± 0.6 after completion; experimental groups: 6.0 ± 0.6 before initiation, 8.3 ± 1.2 after completion) [19]. The choice of the comparison of heart rate changes was the lowest heart rate(HR) during night sleep (Fig. 4).

Although it is not founded that some very clear mechanisms of how can ω -3 directly affect heart rate, it can still indirectly prevent arrhythmias by improving myocardial infarction, coronary heart disease and other diseases as mentioned above.

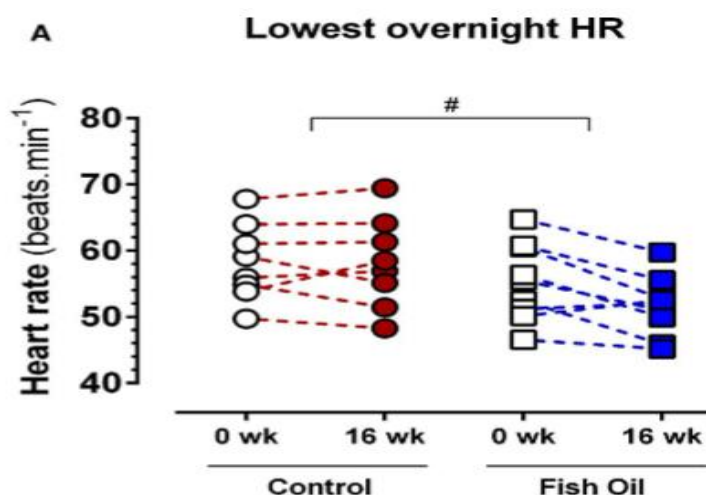


Fig 4. Lowest overnight HR [19].

7. Conclusion

ω -3 can directly play a part in the process of human defecation to reduce the oxidized cholesterol in LDL and the number of TG in human body, and it can also increase the number of HDL containing benign cholesterol and the size of the it to prevent lipid from blocking blood vessels to cause some relevant heart illness such as coronary heart disease, hypertensive heart disease and so on. ω -3 can also reduce blood vessel diastolic pressure and systolic pressure to finally reduce the whole blood pressure. Moreover, it can reduce the risk of AS and heart rate to prevent heart diseases as well through other unclear mechanisms. On the other hand, It can also indirectly reduce the risk of cardiac diseases by increasing vascular elasticity and reducing platelet aggregation and thrombus formation through the metabolite PGI₃, which can treat some heart diseases (such as cardiopulmonary bypass, hemodialysis, etc.) as a antiplatelet agent to prevent hypercoagulation.

This article has systematically summarized proven association of ω -3 and heart diseases, it can be referred to conduct quantitative aspects of the study to form a set of precise dose of ω -3 ingestion method, to make up for the current vacancy in the study data.

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