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SCIENTIFIC REVIEW:
OMEGA-3 & HEART HEALTH

An overview of research, natural sources, and clinical studies

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OMEGA-3S & HEART HEALTH

Omega-3 & Cardiovascular Disease

Cardiovascular disease (CVD) is a leading cause of death and the foremost public health burden worldwide. According to WHO, 17,9 million people die each year from CVDs, an estimated 31% of all deaths worldwide. CVDs involve the heart or blood vessels (arteries and veins), including coronary heart disease (CHD), a disease of the blood vessels supplying the heart muscle. The most common risk factors for cardiovascular disorders are build-up of fat deposits on the inner walls of the vessels that supply the heart or the brain, and the most common risk factors are unhealthy diet, obesity, physical inactivity, hypertension, hyperlipidemia, diabetes, tobacco use and harmful use of alcohol.[1,2]

The marine-based omega-3 fatty acids, EPA and DHA, have been shown through many years of clinical research to greatly assist in the protection of the cardiovascular system. Large epidemiological studies have shown that people who eat a lot of fish (a rich source of EPA and DHA) have much lower rates of cardiovascular issues.[3,4] Supplementation of EPA and DHA has been shown to lower high triglycerides and blood pressure while improving the overall health of the arteries. Evidence from prospective secondary prevention studies suggests that EPA+DHA supplementation ranging from 0.5 to 1.8 g/day (either as fatty fish or supplements) significantly reduces heart health concerns.[5]

Due to a strong body of evidence, health authorities around the world (WHO, EFSA*, ISSFAL, AHA) have set dietary guidelines to increase the intake of omega-3s by including at least two servings of fish per week (particularly fatty fish) or minimum 250-500 mg/day EPA plus DHA. For patients with documented CHD, the American Heart Association (AHA) recommends 1 g of EPA and DHA (combined) per day. This may be obtained from the consumption of oily fish or omega-3 fatty acid capsules, although the decision to use the latter should be made in consultation with a physician.[6]

Omega-3 and omega-6 fatty acids

It is well-established that omega-3 and omega-6 fatty acids play important roles in human health. Due to a small conversion rate in the human body, these classes of fatty acids must be obtained from the diet predominantly. Long-chain omega-6 fatty acids include linoleic, gamma-linolenic, and arachidonic acids. Omega-3 fatty acids include long-chain alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), and the latter two can only be obtained from marine species (fish, krill, etc.).

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After consumption, both the omega-3 and omega-6 fatty acids are incorporated into cell membranes, where they not only serve as essential building blocks but also modulate membrane protein function, cellular signaling, and gene expression. Fatty acids are also precursors to mediators important for the immune system and generally, omega-6 fatty acids give rise to pro-inflammatory lipid mediators, while omega-3 fatty acids give rise to anti-inflammatory and less potent lipid mediators. Omega-3 fatty acids compete for both the space within the cell membrane and the same enzymes as the omega-6 fatty acids. The low levels of omega-3s in most Western diets have over time created an imbalance between the omega-6 to omega-3 ratio in our diet, and this is considered a contributing factor to many chronic diseases involving an inflammatory component such as for instance athero-sclerosis.[7,8]

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Clinical studies

In a recent large meta-analysis of 13 randomized controlled trials (RCTs) involving 127,477 participants, the authors found that marine omega-3 supplementation lowers the risk for most cardiovascular endpoints, even after excluding a trial testing very high-dose supplementation (REDUCE-IT). Risk reductions appeared to be linearly related to the dose of marine omega-3 supplementation. The clinical implications of this study suggest that daily marine omega-3 supplementation is effective in lowering risk of heart health conditions and that greater cardiovascular benefits may be achieved at higher doses of marine omega-3 supplementation.[9]

> Omega-3 fatty acids EPA and DHA are well known for their ability to support healthy triglyceride levels.
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High levels of triglycerides in the blood represent a well-known risk factor. The higher the levels are, the more the risk. Today, omega-3 fatty acids are used for efficient support of healthy triglyceride levels.[10] Fish oil containing omega-3 fatty acids has also been found to help a number of cardiovascular conditions through lowering blood pressure and improving the overall health of the arteries. [11, 12, 13, 14, 15, 16, 1] The many reasons to recommend omega-3s for cardiovascular health will be discussed in more detail in the next sections.

Coronary heart disease (CHD)

CHD, or coronary artery disease, develops when the coronary arteries (i.e., the blood vessels that supply oxygen and blood to the heart) become too narrow. CHD tends to develop when cholesterol builds up on the artery walls, creating plaques. CHD can sometimes lead to a heart attack. CHD kills 7 million+ worldwide each year (GOED). Poor diet is a leading cause of CHD burden and one of the leading risk factors related to disability-adjusted life-years. Populations consuming large amounts of marine animals and seafood, such as the Greenland Eskimos, have remarkably low rates of acute heart attack.[17]

A recent study published in Mayo Clinic Proceedings also supports that EPA and DHA consumption is associated with improved heart health and that the dosage matters. In this study, the researchers observed a greater benefit among higher-risk populations. The authors found a reduction of the risk for CHD of 16 % in those with high triglycerides and 14 % in those with high LDL cholesterol.[18]

Lower triglycerides

Omega-3 fatty acids EPA and DHA are well known for their ability to support healthy triglyceride levels. Triglycerides are a type of fat found in your blood and the fat form stored as body fat. High levels of triglycerides are linked with fatty build-up in the artery walls, which again increases the risk of cardiovascular disease. A large body of scientific evidence demonstrates that the omega-3 fatty acids EPA and DHA can lower triglycerides by about 15–30 %.[20, 21] The European Food and Safety Agency (EFSA) recommends DHA and EPA contribute to the maintenance of normal blood triglyceride levels (2 g per day).

Lower blood pressure

High blood pressure is also one of the contributing risk factors to heart attack and stroke. Systolic blood pressure (amount of pressure in your arteries during the contraction of your heart muscle) and diastolic blood pressure (amount of pressure in your arteries between beats) have both been shown to be reduced in individuals who have been given higher doses of omega-3s. Results from 70 RCTs indicates that the supplementation of low doses of EPA plus DHA (between 1 and 2 g/day) reduces systolic blood pressure, while the supplementation of > 2 g/day reduces both systolic

blood pressure and diastolic blood pressure.[22] Other studies have also shown that these omega-3 fatty acids, even in small doses, reduce blood pressure in people with elevated levels.[23, 24] Both in Europe and the USA there are regulatory approved health claims for EPA and DHA related to blood pressure. The EFSA recommendation states that 3 g DHA and EPA daily as food contributes to the maintenance of normal blood pressure. US FDA also allowed a qualified health claim for omega-3s in relation to reduction of blood pressure in 2019.

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Healthy blood vessels & reduced plaque build-up

Plaque is made up mostly of fat, cholesterol, and calcium and can accumulate in your arteries, limiting the flow of oxygen-rich blood throughout your body. The omega-3 fatty acids EPA and DHA prevent the plaques that cause your arteries to harden, as well as make arterial plaques more stable and safer in those who already have them (by reducing the risk of blood clots). Research indicates that omega-3s may also support healthy blood vessels by improving the function of the endothelial cells that line the blood vessels and reducing arterial stiffness.[25, 1, 15, 26, 27]

Reduced inflammatory response

Atherosclerosis or plaque build-up in the coronary arteries is an inflammatory disease, and it is believed that the anti-inflammatory capabilities of omega-3 is of the contributing factors to their cardio-protective effect. Omega-3 fatty acids serve as precursors to anti-inflammatory lipid mediators, to resolvins which are anti-inflammatory and inflammation resolving, and they reduce the levels of pro-inflammatory cytokines and adhesion molecules involved in plaque formation, to mention some. Research also indicates that EPA and DHA stabilize atherosclerotic plaques by decreasing the activity of immune and inflammatory cells making the plaque more vulnerable to rupture.[28] Due to our Western diets, inflammatory cells are typically rich in the n-6 fatty acid arachidonic acid, but the balance between arachidonic acid and the n-3 fatty acids EPA and DHA can be altered through oral administration of EPA and DHA.

Decreased heart rate

Arrhythmias are abnormal heart rhythms that can cause heart attacks in certain cases. Some studies have shown a link between increased intake of omega-3s and reduced heart rate and the risk of arrhythmia. [29, 30, 31]

Conclusions

Through epidemiological and clinical studies, it has been shown that the consumption of fish or fish oil can reduce multiple risk factors and support a healthy heart. The benefits of fish oil for heart health include lowering triglyceride levels, lowering blood pressure, slow down the rate that plaque builds up in arteries, reduce risk of developing an arrhythmia, and reducing inflammation. Because a diet low in seafood omega-3 fatty acids is considered a dietary risk factor and contributor to CHD, health authorities around the world recommend the intake of EPA plus DHA for heart and overall health. Fish, especially fatty fish, are the major sources of EPA and DHA. For individuals who do not eat fatty fish often, fish oil supplementation should be considered.

*EFSA recommendations:[32]

- DHA and EPA contribute to the normal function of the heart (250 mg per day)
- DHA and EPA contribute to the maintenance of normal blood pressure (3 g per day)
- DHA and EPA contribute to the maintenance of normal blood triglyceride levels (2 g per day)
- DHA contributes to maintenance of normal blood triglyceride levels (2 g per day in combination with EPA)

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