# Supplements to help manage total cholesterol, LDL and HDL

# Omega-3 (Fish Oil)

**COMMON NAME:** Fish Oil

SCIENTIFIC NAME: Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), n-3, polyunsaturated fatty acid (PUFA)

# **NOT RECOMMENDED - EVIDENCE**

## LEVELS OF EVIDENCE

#### Recommended:

Several well-designed studies in humans have shown positive benefit. Our team is confident about its therapeutic potential.



#### Not Recommended - Fvidence:

Our team does not recommend this product because clinical trials to date suggest little or no benefit.



#### **Recommended with Caution:**

Preliminary studies suggest some benefit. Future trials are needed before we can make a stronger recommendation.



### Not Recommended - High Risk:

Our team recommends against using this product because clinical trials to date suggest substantial risk greater than the benefit.

**Evaluated Benefits**No evidence of efficacy or not indicated



#### Source

Fish oil from salmon, mackerel, herring, sardine, and anchovy

#### Indications/Population

Hypertriglyceridemia

Patients with risk factors for cardiovascular disease

#### **Mechanism of Action**

Diets rich in n-3 fatty acids have been shown to be cardioprotective; these diets decreased inflammation, platelet aggregation, cardiac arrhythmias, triglycerides, very low-density lipoprotein (VLDL), small dense LDL particles, inflammatory markers, remnant-like lipoparticle cholesterol (RLP-C), oxidized low-density lipoprotein (ox-LDL), heart rate, and blood pressure. They also improved atherosclerotic plaque stability and endothelial relaxation.

The omega-3 polyunsaturated fatty acids (PUFA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) are long-chain, highly unsaturated fatty acids that are incorporated into membrane phospholipids due to their lipophilic nature. They serve as precursors for bioactive lipid mediators, including eicosanoids, prostaglandins, leukotrienes, protectins, and resolvins. In general, EPA-derived mediators have anti-inflammatory effects.

Omega-3 PUFA have been shown to reduce triglyceride synthesis via inhibition of diacylglycerol acyltransferase, fatty acid synthase, and acetyl CoA carboxylase enzymes. Omega-3 PUFA also enhance fatty acid  $\beta$ -oxidation via a peroxisome proliferator-activated receptor.

Omega-3 fatty acids increase the conversion rate of VLDL to LDL cholesterol in the liver. Both EPA and DHA effectively lower plasma triglyceride concentrations. Only DHA increases LDL and HDL particle sizes. There are some differences in the composition of fish oil from natural cold-pressed fish, and fish oil processed to contain only EPA and DHA. Natural fish oil has other omegas, such as omega-7 (palmitoleic acid), that may also have cardiovascular benefits.

#### Side Effects

Gastrointestinal, including fish-tasting burp, GERD, and diarrhea

#### **Dosing**

A dose as low as 1 gram per day has been shown to reduce postprandial hyperlipidemia.

AHA recommendations for n-3 FA intake:

- 1. Patients without documented CHD should eat a variety of (preferably oily) fish at least twice a week. Include oils and foods rich in alpha-linolenic acid (flaxseed, walnuts, canola and soybean oils).
- 2. Patients with documented CHD should consume 1 gram EPA + DHA per day, preferably from oily fish. EPA + DHA supplements could be considered in consultation with the physician.
- 3. Patients needing triglyceride lowering should take 2–4 grams of EPA + DHA per day provided as capsules under a physician's care.





#### **Drug Interactions/Cautions**

Fish oil omega-3 supplements can raise the level of LDL cholesterol through the mechanism of action of conversion of VLDL to LDL cholesterol. Omega-3 can inhibit platelet aggregation and increase bruising or bleeding time in patients on warfarin.

#### **Notes**

Omega 3's (fish oil) have been proven effective in lowering triglyceride levels.

The European Food Safety Authority (EFSA), the American Heart Association (AHA), and the Food Standards — Australia and New Zealand (FSANZ) organization have all recognized n-3 PUFA as a preventative measure against the development of CVD, primarily by reducing risk factors for CVD, including elevated blood triglyceride levels.

The AHA released a statement in 2011 indicating that a daily dosage of 2–4 grams of n-3 PUFA, specifically EPA and DHA, confers a 25–30 % decrease in serum triglyceride levels.

The JELIS study demonstrated that adding EPA to statin therapy significantly reduced major coronary events compared with statin therapy alone in hypercholesterolemic patients.

The FDA has ruled that intakes of up to 3 grams per day of marine omega-3 fatty acids have Fish Fish oil has "Generally Recognized as Safe" (GRAS) status in the United States.

The FDA recently has approved a qualified health claim for EPA and DHA omega-3 fatty acids in dietary supplements, which may reduce the risk of heart disease.

Fish oil supplements are essentially mercury free.

The free fatty acid forms of omega-3 fatty acids are not dependent on pancreatic enzyme activity, are readily absorbed, and, therefore, have improved bioavailability and are less dependent on meal fat content.

The bioavailability of ethyl ester omega-3 fatty acids, which are found in dietary supplements, is significantly reduced if consumed with a low-fat diet. Novel formulations utilizing free fatty acids, emulsions, or reconstituted triglycerides can significantly improve the bioavailability.

#### References

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