This scientific information is intended for healthcare professionals.

Scientific dose of omega-3 for the heart (based on the GISSI study)

- EPA and DHA help maintain normal **blood pressure**[1], normal **triglyceride levels**[2] and normal function of the **heart**[3]

With a daily intake of [(1)] 3 g EPA+DHA, [(2)] 2 g EPA+DHA, [(3)] at least 250 mg EPA+DHA

Applications and recommended use

Supporting heart health
Maintaining triglyceride levels
Moderate blood pressure support

Typical indications for EPA+DHA:

- Secondary prevention of myocardial infarction
- Ventricular arrhythmia induced by oxygen deficiency
- Chronic heart failure
- Prevention atrial fibrillation after bypass-surgery
- Hypertriglyceridemia
- Hypertension

Combination with drugs

Omega-3 may be combined with a cardio-aspirin, ß-blockers, ACE-inhibitors, fibrates, sartans, diuretics and/or statins.

Interactions and precautions

The European Food Safety Authority (EFSA) considers the long-term use of **5 g EPA+DHA/day** to be safe for adults, **without increasing the risk of spontaneous bleeding or bleeding complications** (even with concomitant use of low-dose acetylsalicylic acid or anti-coagulants).[1]
Omega-3 fatty acids do **not** have a **clinically relevant effect on LDL cholesterol levels**. At daily doses of 2-6 g EPA+DHA may induce a small increase in LDL-cholesterol concentrations of about 3%, which does not have an adverse effect on cardiovascular disease risk.[1]
Omega-3 fatty acids do **not** have a **clinically relevant effect on blood sugar control** (no changes in HbA1c, possibly small increases of 2-6 mg/dl in fasting glucose).[2-4]

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Scientific information

The cardiovascular health benefits of EPA and DHA vary from modulations in endothelial functions (through prostaglandin homeostasis, relaxation of the blood vessel wall, induction of less atherogenic LDL particles and improved plaque stability) to antiarrhythmic effects (shifts in the voltage potential of cardiac muscle cells, reduced risk of ventricular fibrillation in response to oxygen deficiency, increased heart rate variability, better cardiac muscle adaptation capacity).[5-7]

According to the advice of the **European Society of Cardiology** cardiac patients preferably use **~1 g EPA+DHA per day** after a recent **heart attack** as well as in cases of **chronic heart failure**.[8]
The cardiac patients (n = 11323) who were eligible to participate to the Italian GISSI Prevenzione study had, at the earliest 3 months before, suffered a heart attack. For 3.5 years they used ~1 g EPA+DHA (EPA/DHA ratio = 1.2/1) per day on top of their conventional treatments (blood thinner, blood pressure-lowering drug, cholesterol-lowering medicine). Thanks to the omega-3 supplementation their risk of sudden death was reduced with 45%.[9-12]
In the placebo-controlled GISSI-HF study patients with chronic heart failure (irrespective of the left ventricular ejection fraction)
(n = 3494) used ~1 g EPA+DHA/dag (EPA/DHA ratio = 1.2/1) per day. The researchers came to the final conclusion that thanks to the omega-3 supplementation per 1000 patients 18 lives were saved and 17 hospitalizations due to cardiovascular problems were prevented.[13]

Patients who needed to undergo **bypass-surgery** (n=79) used ~2 g EPA+DHA/day (EPA/DHA ratio = 1.2/1) in a placebo-controlled trial setting from 5 days before surgery until discharge from the hospital. Thanks to the omega-3 supplementation patients had a shorter hospital stay (p = 0,017) and a 54.4% reduced risk of experiencing postoperative atrial fibrillation (p = 0,013).[14]

In hyperlipidemic patients (n = 16511) with a mean triglyceride level of 216 mg/dl supplementation with 3.25 g EPA+DHA per day on average induced a reduction in **triglyceride levels** of 40 mg/dl.[15] A severely elevated triglyceride level (> 500 mg/dl) can be lowered by 45% with a dose of 3-4 g EPA+DHA/day.[16]

In patients with hypertension supplementation with at least 3.3 g EPA+DHA per day (n = 1356) was able to reduce systolic and diastolic **blood pressure** with 2.9 and 1.6 mm Hg, respectively.[17] The strongest effects of EPA+DHA supplementation were observed in untreated hypertensive patients: reductions of 4.51 mm Hg and 3.05 mm Hg in systolic and diastolic blood pressure, respectively.[18]

References

1. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA); Scientific Opinion related to the Tolerable Upper Intake Level of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA). EFSA Journal 2012;10(7):2815.
2. Hartweg J, Perera R, Montori V, Dinneen S, Neil HA, Farmer A. Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. Cochrane Database Syst Rev 2008; (1):CD003205.
3. Maki KC, Lawless AL, Kelley KM, Dicklin MR, Schild AL, Rains TM. Prescription omega-3-acid ethyl esters reduce fasting and postprandial triglycerides and modestly reduce pancreatic ß-cell response in subjects with primary hypertriglyceridemia. Prostaglandins Leukot Essent Fatty Acids 2011; 85(3-4):143-8.

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4. Jeppesen C, Schiller K, Schulze MB. Omega-3 and omega-6 fatty acids and type 2 diabetes. Curr Diab Rep 2013; 13(2):279-88.
5. Rupp H. Omacor (prescription omega-3-acid ethyl esters 90): From severe rhythm disorders to hypertriglyceridemia. Adv Ther 2009; 26(7):675-90.
6. Cheng JW, Santoni F. Omega-3 fatty acid: a role in the management of cardiac arrhythmias? J Altern Complement Med 2008; 14(8):965-74.
7. Lavie CJ, Milani RV, Mehra MR, Ventura HO. Omega-3 polyunsaturated fatty acids and cardiovascular diseases. J Am Coll Cardiol. 2009; 54(7):585-94.
8. Kromhout D, Yasuda S, Geleijnse JM, Shimokawa H. Fish oil and omega-3 fatty acids in cardiovascular disease: do they really work? Eur Heart J 2012; 33(4):436-43.
9. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Lancet 1999; 354(9177):447-55.
10. Marchioli R, Levantesi G, Macchia A, Maggioni AP, Marfisi RM, Silletta MG, Tavazzi L, Tognoni G, Valagussa F; GISSI-Prevenzione Investigators. Antiarrhythmic mechanisms of n-3 PUFA and the results of the GISSI-Prevenzione trial. J Membr Biol 2005; 206(2):117-28.
11. Bays H. Clinical overview of Omacor: a concentrated formulation of omega-3 polyunsaturated fatty acids. Am J Cardiol 2006; 98(4A):71i-76i.
12. Bays H. Fish oil composition of Omacor and the GISSI trial. Am J Cardiol 2007; 99(10):1483-4.
13. Gissi-HF Investigators, Tavazzi L, Maggioni AP, Marchioli R, Barlera S, Franzosi MG, Latini R, Lucci D, Nicolosi GL, Porcu M, Tognoni G. Effect of n-3 polyunsaturated fatty acids in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. Lancet 2008; 372(9645):1223-30.
14. Calò L, Bianconi L, Colivicchi F, Lamberti F, Loricchio ML, de Ruvo E, Meo A, Pandozi C, Staibano M, Santini M. N-3 Fatty acids for the prevention of atrial fibrillation after coronary artery bypass surgery: a randomized, controlled trial. J Am Coll Cardiol 2005; 45(10):1723-8.
15. Eslick GD, Howe PR, Smith C, Priest R, Bensoussan A. Benefits of fish oil supplementation in hyperlipidemia: a systematic review and meta-analysis. Int J Cardiol 2009; 136(1):4-16.
16. Lavie CJ, Milani RV, Mehra MR, Ventura HO. Omega-3 polyunsaturated fatty acids and cardiovascular diseases. J Am Coll Cardiol. 2009; 54(7):585-94.
17. Morris MC, Sacks F, Rosner B. Does fish oil lower blood pressure? A meta-analysis of controlled trials. Circulation 1993; 88(2):523-33.
18. Miller PE, Van Elswyk M, Alexander DD. Long-Chain Omega-3 Fatty Acids Eicosapentaenoic Acid and Docosahexaenoic Acid and Blood Pressure: A Meta-Analysis of Randomized Controlled Trials. Am J Hypertens. 2014 Mar 6.

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