

Omega 3 Fatty Acid *n-3* polyunsaturated fatty acid (PUFA)

Common Indications:

- Inflammatory conditions, including arthritis
- Cardiovascular protection
- High triglycerides
- Neuroprotection, including ADHD, depression and other neurological disturbances
- Skin conditions
- Weight loss

General Comments:

Fish oils are composed of the essential fatty acids eicosapentaenoic acid (EPA) and docosahexa enoic acid (DHA).^{1,2} EPA and DHA come from the polyunsaturated fatty acid (PUFA), alpha-linolenic acid (ALA) and are classified as omega-3 fatty acids. The human body can convert a very small amount of alpha linolenic acid into EPA & DHA but not in adequate amounts to be healthy, thus EPA & DHA are "essential" fatty acids and must be consumed in the diet or by supplement to reach healthy levels.

The classic American diet is high in Omega 6 fatty acids and very low in Omega 3 acids, leading to an average 30:1 ratio of omega 6:omega3. A healthy ratio is closer to 1:1 to 3:1. This excess in Omega 6 leads to an inflammatory chemistry that contributes to risk for diabetes, diabetes, cardiovascular disease, neurological disturbances, asthma, allergies, joint pain and arthritis. Omega 3 fatty acids have an anti-inflammatory impact by suppressing inflammatory cytokines such as IL-1, IL-6 and TNFalpha.

Fish oil has been reported beneficial in improving lipid profiles and decreasing inflammation, leading to lower risk of developing cardiovascular disease and diabetes. Omega 3 fatty acids also improve immune function and neurological function.

Benefits & Mechanism of Action:

Inflammatory conditions, including arthritis

Omega-3 fatty acids help decrease inflammatory signaling and the metabolic consequences of chronic inflammation, including metabolic syndrome, cancer, heart disease, allergies/asthma, ulcerations, type 2 diabetes and insulin resistance.^{3,4,5,6,7,8,9} They also help to reduce the pain of rheumatoid arthritis in adults.^{10,11}

Cardiovascular protection

Omega-3 fatty acids help maintain/support cardiovascular health. They help to reduce blood pressure to within normal limits and reduce atherosclerosis.^{12,13,14,15,16,17}

High triglycerides

Omega-3 fatty acids help to reduce serum triglycerides/triacylglycerols.^{18,19,20}

Neuroprotection, including ADHD, depression and other neurological disturbances

Omega-3 fatty acids help support the development of the brain, eyes and nerves in children and adolescents.^{21,22,23,24} They have neuroprotective properties and help support neurological function, including cognition, depression and those with ADHD.^{25,26,27,28,29,30}

Skin conditions

Omega-3 fatty acids help improves skin conditions like eczema/psoriasis.

Weight loss

Helps improve weight loss through inhibition of key enzymes responsible for lipid synthesis, such as fatty acid synthase and stearoyl-CoA desaturase-1, enhancement of lipid oxidation and thermogenesis, and prevention of free fatty acids from entering adipocytes for lipogenesis. PUFAs also exert suppressive effects on several key factors involved in adipocyte differentiation and fat storage.^{31,32}

Dose: 1,000 to 2,000 mg daily.

- 3 to 4 grams of EPA + DHA are recommended for treatment of cardiovascular rissues
- Up to 8 gm may be used in aggressive therapies such as cancer or cognitive improvement.

Patients should purchase quality fish oil supplements that are treated/filtered for heavy metal contaminants, such as mercury and lead as well as dioxins and PCB's

Symptoms of Depletion:

Deficiency is primarily due to a lack of dietary intake and the fact that omega-3 has been almost totally removed from most processed foods. Symptoms of omega-3 fatty acid deficiency include a wide variety of imbalances related to organ, endocrine, and immune function, leading to insulin resistance, obesity, inflammation, type 2 diabetes, cardiovascular disease and cancer.

Conditions that leave a patient with an increased need for omega 3 fatty acids include:

• Diets high in omega-6 fatty acids may lead to imbalances in body's natural omega-6:omega-3 fatty acid profile • Diets high in trans-fatty acids also deplete omega-3 fatty acids from the body, leading to fatty acid imbalances.

Food and supplements that may decrease omega-3 fatty acids include:

• Olestra - a non-fat, calorie-free cooking oil that inhibits absorption of fat-soluble nutrients

Cautions & Side Effects: There is no known toxicity when using fish oil (omega-3 fatty acids) as a dietary supplement.³³

Medication interactions

Medications with increased effects while taking omega-3 fatty acids include:

Anticoagulant medications

Medications that can decrease the amount of omega-3 fatty acids include:

- Mineral oil
- Orlistat and the OTC product, Alii
- The bile acid sequestrants colestipol and cholestyramine

Although some of the fish that contain omega-3 fatty acids also contain low levels of mercury, the Food and Drug Administration has reported that consuming several servings of fish each week poses no risk to healthy people and conveys many health benefits. Women who are pregnant or planning to become pregnant should avoid Atlantic mackerel, shark, swordfish, and tilefish, and should limit consumption of white albacore tuna to under 6 oz. per week.

Food Sources:

Fish oil is found in cold-water fishes, such as halibut, mackerel, salmon, striped bass, rainbow trout, tuna, and sardines. Omega-3 fatty acids are also found in marine algae, hemp, walnuts, flaxseed oil and purslane (Portulaca oleracea).

Nutrient Interactions:

Niacin

Certain nutrients are required for proper function of delta-6 desaturase enzyme activity, which converts omega-3 fatty acids to EPA and DHA. The nutrients include niacin, pyridoxine, ascorbic acid, and zinc. Thus, a deficiency of any of these nutrients could impair the biosynthesis of EPA and DHA.

Pyridoxine

Certain nutrients are required for proper function of delta-6 desaturase enzyme activity, which converts omega-3 fatty acids to EPA and DHA. The nutrients include niacin, pyridoxine, ascorbic acid, and zinc. Thus, a deficiency of any of these nutrients could impair the biosynthesis of EPA and DHA.

Ascorbic acid

Certain nutrients are required for proper function of delta-6 desaturase enzyme activity, which converts omega-3 fatty acids to EPA and DHA. The nutrients include niacin, pyridoxine, ascorbic acid, and zinc. Thus, a deficiency of any of these nutrients could impair the biosynthesis of EPA and DHA.

Zinc

Certain nutrients are required for proper function of delta-6 desaturase enzyme activity, which converts omega-3 fatty acids to EPA and DHA. The nutrients include niacin, pyridoxine, ascorbic acid, and zinc. Thus, a deficiency of any of these nutrients could impair the biosynthesis of EPA and DHA.

References:

General Comments

- 1. Kris-Etherton PM, Taylor DS, Yu-Poth S, et al. Polyunsaturated fatty acids in the food chain in the United States. Am J Clin Nutr . 2000;71(1 Suppl):179S-188S.
- 2. Mozaffarian D, Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and the benefits. JAMA . 2006 Oct 18;296(15):1885-99. Review.

Inflammatory conditions, including arthritis

- 3. Al-Harbi MM, Islam MW, Al-Shabanah OA, Al-Gharably NM. Effect of acute administration of fish oil (omega-3 marine triglyceride) on gastric ulceration and secretion induced by various ulcerogenic and necrotizing agents in rats. Food Chem Toxicol. 1995;33(7):555-558.
- 4. Aronson WJ, Glaspy JA, Reddy ST, Reese D, Heber D, Bagga D. Modulation of omega-3/omega-6 polyunsaturated ratios with dietary fish oils in men with prostate cancer. Urology . 2001;58(2):283-288.
- 5. Belluzzi A, Boschi S, Brignola C, Munarini A, Cariani C, Miglio F. Polyunsaturated fatty acids and inflammatory bowel disease. Am J Clin Nutr . 2000;71(suppl):339S-342S.
- 6. Connolly JM, Gilhooly EM, Rose DP. Effects of reduced dietary linoleic acid intake, alone or combined with an algal source of docosahexaenoic acid, on MDA-MD-231 breast cancer cell growth and apoptosis in nude mice. Nutrition Can . 1999;35(1):44-49.
- 7. Terry P, Lichtenstein P, Feychting M, Ahlbom A, Wolk A. Fatty fish consumption and risk of prostate cancer. Lancet . 2001;357(9270):1764-1766.
- Tsai W-S, Nagawa H, Kaizaki S, Tsuruo T, Muto T. Inhibitory effects of n-3 polyunsaturated fatty acids on sigmoid colon cancer transformants. J Gastroenterol . 1998;33:206-212.

- 9. Tsujikawa T, Satoh J, Uda K, Ihara T, Okamoto T, Araki Y, et al. Clinical importance of n-3 fatty acid-rich diet and nutritional education for the maintenance of remission in Crohn's disease. J Gastroenterol . 2000;35(2):99-104.
- 10. Kremer JM. N-3 fatty acid supplements in rheumatoid arthritis. Am J Clin Nutr . 2000;(suppl 1):349S- 351S.
- 11. Proudman SM, Cleland LG, James MJ. Dietary omega-3 fats for treatment of inflammatory joint disease: efficacy and utility. Rheum Dis Clin North Am. 2008 May;34(2):469-79.

Cardiovascular protection

- 12. Andreassen AK, Hartmann A, Offstad J, Geiran O, Kvernebo K, Simonsen S. Hypertension prophylaxis with omega-3 fatty acids in heart transplant recipients. J Am Coll Cardiol. 1997;29(6):1324-1331.
- 13. Angerer P, von Schacky C. n-3 polyunsaturated fatty acids and the cardiovascular system. Curr Opin Lipidol . 2000;11(1):57-63.
- 14. Appel LJ. Nonpharmacologic therapies that reduce blood pressure: a fresh perspective. Clin Cardiol . 1999;22(Suppl. III):III1-III5.
- 15. Gerber PA, Gouni-Berthold I, Berneis K. Omega-3 fatty acids: role on metabolism and cardiovascular disease. Curr Pharm Des. 2013;[Epub ahead of print].
- 16. Von Schacky C, Angere P, Kothny W, Theisen K, Mudra H. The effect of dietary omega-3 fatty acids on coronary atherosclerosis: a randomized, double-blind, placebo-controlled trial. Ann Intern Med . 1999;130:554-562.
- 17. Yosefy C, Viskoper JR, Laszt A, Priluk R, Guita E, Varon D, et al. The effect of fish oil on hypertension, plasma lipids and hemostasis in hypertensive, obese, dyslipidemic patients with and without diabetes mellitus. Prostaglandins Leukot Essent Fatty Acids . 1999;61(2):83-87.

High triglycerides

- Conquer JA, Holub BJ. Supplementation with an algae source of docosahexaenoic acid increases (n-3) fatty acid status and alters selected risk factors for heart disease in vegetarian subjects. J Nutr . 1996;126(12):3032-3039.
- Davidson MH, Maki KC, Kalkowski J, Schaefer EJ, Torri SA, Drennan KB. Effects of docosahexaenoic acid on serum lipoproteins in patients with combined hyperlipidemia. A randomized, double-blind, placebo-controlled trial. J Am Coll Nutr . 1997;16:3:236-243.

20. 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. 2008 Sep 5. [Epub ahead of print]

Neuroprotection, including ADHD, depression and other neurological disturbances

- 21. Uauy R, Hoffman DR. Essential fat requirements of preterm infants. Am J Clin Nutr . 2000;71(1 suppl):245S-250S.
- 22. Uauy-Dagach R, Valenzuela A. Marine oils as a source of omega-3 fatty acids in the diet: how to optimize the health benefits. Prog Food Nutr Sci . 1992;16(3):199-243.
- 23. Xiang M, Alfven G, Blennow M, Trygg M, Zetterstrom R. Long-chain polyunsaturated fatty acids in human milk and brain growth during early infancy. Acta Paediatr . 2000;89(2):142-147.
- 24. Cunnane SC, Francescutti V, Brenna JT, Crawford MA. Breast-fed infants achieve a higher rate of brain and whole body docosahexaenoate accumulation than formula-fed infants not consuming dietary docosahexaenoate. Lipids . 2000;35(1):105-111.
- 25. Arnold LE, Kleykamp D, Votolato N, Gibson RA, Horrocks L. Potential link between dietary intake of fatty acid and behavior: pilot exploration of serum lipids in attention-deficit hyperactivity disorder. J Child Adolesc Psychopharmacol . 1994;4(3):171-182.
- 26. Baumgaertel A. Alternative and controversial treatments for attentiondeficit/hyperactivity disorder. Pediatr Clin of North Am . 1999;46(5):977-992.
- Burgess J, Stevens L, Zhang W, Peck L. Long-chain polyunsaturated fatty acids in children with attention- deficit hyperactivity disorder. Am J Clin Nutr . 2000; 71(suppl):327S-330S.
- 28. Carter JR, Schwartz CE, Yang H, et al. Fish oil and neurovascular reactivity to mental stress in humans. AM J Physiol Regul Integr Comp Phsiol. 2013;304(7):R523-30.
- 29. Hibbeln JR. Fish consumption and major depression. Lancet . 1998;351(9110):1213.
- Stoll AL, Severus WE, Freeman MP, et al. Omega 3 fatty acids in bipolar disorder: a preliminary double- blind placebo-controlled trial. Arch Gen Psychiatry . 1999:56(5):407-412.

Weight loss

- 31. Li JJ, Huang CJ, Xie D. Anti-obesity effects of conjugated linoleic acid, docosahexaenoic acid, and eicosapentaenoic acid. Mol Nutr Food Res. 2008 Jun;52(6):631-45. Review.
- 32. Spencer M, Finlin BS, Unai R, et al. Omega-3 fatty acids reduce adipose tissue

macrophages in human subjects with insulin resistance. Diabetes. 2013;[Epub ahead of print].

Cautions & Side Effects

33. Villani AM, Crotty M, Cleland LG, et al. Fish oil administration in older adults: is there potential for adverse events? A systematic review of the literature. BMC Geriatr. 2013;13:41.