

## Omega-3 fatty acids, fish oil, alpha-linolenic acid

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*While some complementary and alternative techniques have been studied scientifically, high-quality data regarding safety, effectiveness, and mechanism of action are limited or controversial for most therapies. Whenever possible, it is recommended that practitioners be licensed by a recognized professional organization that adheres to clearly published standards. In addition, before starting a new technique or engaging a practitioner, it is recommended that patients speak with their primary healthcare provider(s). Potential benefits, risks (including financial costs), and alternatives should be carefully considered. The below monograph is designed to provide historical background and an overview of clinically-oriented research, and neither advocates for or against the use of a particular therapy.*

### Related Terms:

- $\alpha$ -linolenic acid (ALA, C18:3n-3), alpha-linolenic acid, cod liver oil, coldwater fish, docosahexaenoic acid (DHA, C22:6n-3), eicosapentaenoic acid (EPA, C20:5n-3), fish oil fatty acids, fish body oil, fish extract, fish liver oil, halibut oil, long chain polyunsaturated fatty acids, mackerel oil, marine oil, menhaden oil, n-3 fatty acids, n-3 polyunsaturated fatty acids, omega fatty acids, omega-3 oils, polyunsaturated fatty acids (PUFA), salmon oil, shark liver oil, w-3 fatty acids.
- **Note:** Should not be confused with omega-6 fatty acids.

### BACKGROUND

- Dietary sources of omega-3 fatty acids include fish oil and certain plant/nut oils. Fish oil contains both docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), while some nuts (English walnuts) and vegetable oils (canola, soybean, flaxseed/linseed, olive) contain alpha-linolenic acid (ALA).
- There is evidence from multiple studies supporting intake of recommended amounts of DHA and EPA in the form of dietary fish or fish oil supplements lowers triglycerides, reduces the risk of death, heart attack, dangerous abnormal heart rhythms, and strokes in people with known cardiovascular disease, slows the buildup of atherosclerotic plaques ("hardening of the arteries"), and lowers blood pressure slightly. However, high doses may have harmful effects, such as an increased risk of bleeding. Although similar benefits are proposed for alpha-linolenic acid, scientific evidence is less compelling, and beneficial effects may be less pronounced.
- Some species of fish carry a higher risk of environmental contamination, such as with methylmercury.

### SCIENTIFIC EVIDENCE

#### Uses

*These uses have been tested in humans or animals. Safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider.*

**Grade\***

<p><b>High blood pressure</b></p> <p>Multiple human trials report small reductions in blood pressure with intake of omega-3 fatty acid. DHA may have greater benefits than EPA. However, high intakes of omega-3 fatty acids per day may be necessary to obtain clinically relevant effects, and at this dose level, there is an increased risk of bleeding. Therefore, a qualified healthcare provider should be consulted prior to starting treatment with supplements.</p>	<p><b>A</b></p>
<p><b>Hypertriglyceridemia (fish oil / EPA plus DHA)</b></p> <p>There is strong scientific evidence from human trials that omega-3 fatty acids from fish or fish oil supplements (EPA + DHA) significantly reduce blood triglyceride levels. Benefits appear to be dose-dependent. Fish oil supplements also appear to cause small improvements in high-density lipoprotein ("good cholesterol"); however, increases (worsening) in low-density lipoprotein levels (LDL/"bad cholesterol") are also observed.</p> <p>It is not clear if alpha-linolenic acid significantly affects triglyceride levels, and there is conflicting evidence in this area.</p> <p>The American Heart Association has published recommendations for EPA + DHA. Because of the risk of bleeding from omega-3 fatty acids, a qualified healthcare provider should be consulted prior to starting treatment with supplements.</p> <p>There is growing evidence that reducing C-Reactive Protein (CRP) is beneficial towards favorable cardiovascular outcomes, although additional research is pending in this area. The data on fish oils and CRP levels is mixed.</p>	<p><b>A</b></p>
<p><b>Secondary cardiovascular disease prevention (fish oil / EPA plus DHA)</b></p> <p>Several well-conducted randomized controlled trials report that in people with a history of heart attack, regular consumption of oily fish or fish oil/omega-3 supplements reduces the risk of non-fatal heart attack, fatal heart attack, sudden death, and all-cause mortality (death due to any cause). Most patients in these studies were also using conventional heart drugs, suggesting that the benefits of fish oils may add to the effects of other therapies.</p>	<p><b>A</b></p>
<p><b>Primary cardiovascular disease prevention (fish intake)</b></p> <p>Several large studies of populations ("epidemiologic" studies) report a significantly lower rate of death from heart disease in men and women who regularly eat fish. Other epidemiologic research reports no such benefits. It is not clear if reported benefits only occur in certain groups of people, such as those at risk of developing heart disease. Overall, the evidence suggests benefits of regular consumption of fish oil. However, well-designed randomized controlled trials which classify people by their risk of developing heart disease are necessary before a firm conclusion can be drawn.</p>	<p><b>B</b></p>

<p><b>Protection from cyclosporine toxicity in organ transplant patients</b></p> <p>There are multiple studies of heart transplant and kidney transplant patients taking cyclosporine (Neoral®), who were administered fish oil supplements. The majority of trials report improvements in kidney function, and less high blood pressure compared to patients not taking fish oil. Although several recent studies report no benefits on kidney function, the weight of scientific evidence favors the beneficial effects of fish oil.</p>	<u>B</u>
<p><b>Rheumatoid arthritis (fish oil)</b></p> <p>Multiple randomized controlled trials report improvements in morning stiffness and joint tenderness with the regular intake of fish oil supplements for up to three months. Benefits have been reported as additive with anti-inflammatory medications such as NSAIDs (like ibuprofen or aspirin). However, because of weaknesses in study designs and reporting, better research is necessary before a strong favorable recommendation can be made. Effects beyond three months of treatment have not been well evaluated.</p>	<u>B</u>
<p><b>Angina pectoris</b></p> <p>Preliminary studies report reductions in angina associated with fish oil intake. Better research is necessary before a firm conclusion can be drawn.</p>	<u>C</u>
<p><b>Asthma</b></p> <p>Several studies in this area do not provide enough reliable evidence to form a clear conclusion, with some studies reporting no effects, and others finding benefits. Because most studies have been small without clear descriptions of design or results, the results cannot be considered conclusive.</p>	<u>C</u>
<p><b>Atherosclerosis</b></p> <p>Some research reports that regular intake of fish or fish oil supplements reduces the risk of developing atherosclerotic plaques in the arteries of the heart, while other research reports no effects. Additional evidence is necessary before a firm conclusion can be drawn in this area.</p>	<u>C</u>
<p><b>Bipolar disorder</b></p> <p>Several studies in this area do not provide enough reliable evidence to form a clear conclusion.</p>	<u>C</u>

<p><b>Cancer prevention</b></p> <p>Several population (epidemiologic) studies report that dietary omega-3 fatty acids or fish oil may reduce the risk of developing breast, colon, or prostate cancer. Randomized controlled trials are necessary before a clear conclusion can be drawn.</p>	<p><u>C</u></p>
<p><b>Cardiac arrhythmias (abnormal heart rhythms)</b></p> <p>There is promising evidence that omega-3 fatty acids may decrease the risk of cardiac arrhythmias. This is one proposed mechanism behind the reduced number of heart attacks in people who regularly ingest fish oil or EPA + DHA. Additional research is needed in this area specifically before a firm conclusion can be reached.</p>	<p><u>C</u></p>
<p><b>Colon cancer</b></p> <p>Omega-3 fatty acids are commonly taken by cancer patients. Although preliminary studies report that growth of colon cancer cells may be reduced by taking fish oil, effects on survival or remission have not been measured adequately.</p>	<p><u>C</u></p>
<p><b>Crohn's disease</b></p> <p>It has been suggested that effects of omega-3 fatty acids on inflammation may be beneficial in patients with Crohn's disease when added to standard therapy, and several studies have been conducted in this area. Results are conflicting, and no clear conclusion can be drawn at this time.</p>	<p><u>C</u></p>
<p><b>Cystic fibrosis</b></p> <p>A small amount of research in this area does not provide enough reliable evidence to form a clear conclusion.</p>	<p><u>C</u></p>
<p><b>Dementia</b></p> <p>Well-designed clinical trials are needed before omega-3 fatty acids can be recommended for the prevention of cognitive impairment or dementia.</p>	<p><u>C</u></p>
<p><b>Depression</b></p> <p>Several studies on the use of omega 3 fatty acids in depression, including positive results in postpartum depression, do not provide enough reliable evidence to form a clear conclusion or replace standard treatments. However, based on one recent study, omega-3 fatty acids may have therapeutic benefits in childhood depression. Promising initial evidence requires confirmation with larger, well-designed trials.</p>	<p><u>C</u></p>

<p><b>Dysmenorrhea (painful menstruation)</b></p> <p>There is preliminary evidence suggesting possible benefits of fish oil/omega-3 fatty acids in patients with dysmenorrhea. Additional research is necessary before a firm conclusion can be reached.</p>	<p><u>C</u></p>
<p><b>Eczema</b></p> <p>Several studies of EPA for eczema do not provide enough reliable evidence to form a clear conclusion.</p>	<p><u>C</u></p>
<p><b>IgA nephropathy</b></p> <p>There are conflicting results from several trials in this area.</p>	<p><u>C</u></p>
<p><b>Infant eye / brain development</b></p> <p>Well-designed research is necessary before a clear conclusion can be reached.</p>	<p><u>C</u></p>
<p><b>Lupus erythematosus</b></p> <p>There is not enough reliable evidence to form a clear conclusion in this area.</p>	<p><u>C</u></p>
<p><b>Nephrotic syndrome</b></p> <p>There is not enough reliable evidence to form a clear conclusion in this area.</p>	<p><u>C</u></p>
<p><b>Preeclampsia</b></p> <p>Several studies of fish oil do not provide enough reliable evidence to form a clear conclusion in this area.</p>	<p><u>C</u></p>
<p><b>Prevention of graft failure after heart bypass surgery</b></p> <p>There is limited study of the use of fish oils in patients after undergoing coronary artery bypass grafting (CABG). Additional evidence is necessary before a firm conclusion can be drawn in this area.</p>	<p><u>C</u></p>
<p><b>Prevention of restenosis after coronary angioplasty (PTCA)</b></p> <p>Several randomized controlled trials have evaluated whether omega-3 fatty acid intake reduces blockage of arteries in the heart following balloon angioplasty (percutaneous transluminal coronary angioplasty/PTCA). The evidence in this area</p>	<p><u>C</u></p>

remains inconclusive.	
<p><b>Primary cardiovascular disease prevention (<math>\alpha</math>-linolenic acid [ALA])</b></p> <p>Additional research is necessary before a conclusion can be drawn in this area.</p>	<u>C</u>
<p><b>Psoriasis</b></p> <p>Several studies in this area do not provide enough reliable evidence to form a clear conclusion.</p>	<u>C</u>
<p><b>Schizophrenia</b></p> <p>There is promising preliminary evidence from several randomized controlled trials in this area. Additional research is necessary before a firm conclusion can be reached.</p>	<u>C</u>
<p><b>Secondary cardiovascular disease prevention (<math>\alpha</math>-linolenic acid [ALA])</b></p> <p>Several randomized controlled trials have examined the effects of alpha-linolenic acid in people with a history of heart attack. Although some studies suggest benefits, others do not. Additional research is necessary before a conclusion can be drawn in this area.</p>	<u>C</u>
<p><b>Stroke prevention</b></p> <p>Several large studies of populations ("epidemiologic" studies) have examined the effects of omega-3 fatty acid intake on stroke risk. Some studies suggest benefits, while others do not. Effects are likely on ischemic or thrombotic stroke risk, and very large intakes of omega-3 fatty acids ("Eskimo" amounts) may actually increase the risk of hemorrhagic (bleeding) stroke. At this time, it is unclear if there are benefits in people with or without a history of stroke, or if effects of fish oil are comparable to other treatment strategies.</p>	<u>C</u>
<p><b>Ulcerative colitis</b></p> <p>It has been suggested that effects of omega-3 fatty acids on inflammation may be beneficial in patients with ulcerative colitis when added to standard therapy, and several studies have been conducted in this area. Better research is necessary before a clear conclusion can be drawn.</p>	<u>C</u>
<p><b>Appetite / weight loss in cancer patients</b></p> <p>There is preliminary evidence that fish oil supplementation does not improve appetite or prevent weight loss in cancer patients. Further study is warranted.</p>	<u>D</u>

<p><b>Diabetes</b></p> <p>The available scientific evidence suggests that there are no significant long-term effects of fish oil in patients with diabetes. Most studies in this area are not well designed.</p>	<u><b>D</b></u>
<p><b>Hypercholesterolemia</b></p> <p>Although fish oil is able to reduce triglycerides, beneficial effects on blood cholesterol levels have not been demonstrated. Fish oil supplements appear to cause small improvements in high-density lipoprotein ("good cholesterol"); however, increases (worsening) in low-density lipoprotein levels ("bad cholesterol") are also observed. Fish oil does not appear to affect C-reactive protein (CRP) levels.</p>	<u><b>D</b></u>
<p><b>Transplant rejection prevention (kidney and heart)</b></p> <p>There are multiple studies of heart transplant and kidney transplant patients taking cyclosporine (Neoral®), who were administered fish oil supplements. The majority of trials report improvements in kidney function (glomerular filtration rate, serum creatinine), and less hypertension (high blood pressure) compared to patients not taking fish oil. However, several recent studies report no benefits on kidney function, and no changes have been found in rates of rejection or graft survival.</p>	<u><b>D</b></u>
<p><i>*Key to grades: A: Strong scientific evidence for this use; B: Good scientific evidence for this use; C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work); F: Strong scientific evidence against this use (it likely does not work).</i></p>	

## TRADITION/THEORY

The below uses are based on tradition, scientific theories, or limited research. They often have not been thoroughly tested in humans, and safety and effectiveness have not always been proven. Some of these conditions are potentially serious, and should be evaluated by a qualified healthcare provider. There may be other proposed uses that are not listed below.

- Acute myocardial infarction (heart attack), acute respiratory distress syndrome (ARDS), age related macular degeneration, aggressive behavior, agoraphobia, AIDS, allergies, Alzheimer's disease, anticoagulation, antiphospholipid syndrome, attention deficit hyperactivity disorder (ADHD), anthracycline-induced cardiac toxicity, bacterial infections, psychological disorders (borderline personality disorder), breast cysts, breast tenderness, chronic fatigue syndrome (postviral fatigue syndrome), chronic obstructive pulmonary disease, cirrhosis, common cold, congestive heart failure, critical illness, deficiency (omega-3 fatty acid), dermatomyositis, diabetic nephropathy, diabetic neuropathy, dyslexia, dyspraxia, endocrine disorders (glycogen storage diseases), exercise performance enhancement, fibromyalgia, gallstones, gingivitis, glaucoma, glomerulonephritis, gout, hay fever, headache, hepatorenal syndrome, hypoxia, ichthyosis (skin disorder), immunosuppression, inflammatory conditions (Behcet's syndrome), joint problems (cartilage repair), kidney disease prevention, kidney stones, leprosy, leukemia,

malaria, male infertility, mastalgia (breast pain), memory enhancement, menopausal symptoms, menstrual cramps, methotrexate toxicity, multiple sclerosis, myopathy, nephritis (autoimmune), neuropathy, night vision enhancement, obesity, osteoarthritis, osteoporosis, otitis media (ear infection), panic disorder, peripheral vascular disease, pregnancy nutritional supplement, premature birth prevention, premenstrual syndrome, prostate cancer prevention, protection from isotretinoin drug toxicity, Raynaud's phenomenon, Refsum's syndrome, retinitis pigmentosa, Reye's syndrome, seizure disorder, Sjogren's syndrome, suicide prevention, systemic lupus erythematosus, tardive dyskinesia, tennis elbow, ulcerative colitis, urolithiasis (bladder stones), vision enhancement, weight loss.

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## DOSING

*The below doses are based on scientific research, publications, traditional use, or expert opinion. Many herbs and supplements have not been thoroughly tested, and safety and effectiveness may not be proven. Brands may be made differently, with variable ingredients, even within the same brand. The below doses may not apply to all products. You should read product labels, and discuss doses with a qualified healthcare provider before starting therapy.*

### Adults (18 years and older):

- **Average dietary intake of omega-3/omega-6 fatty acids:** Average Americans consume approximately 1.6 grams of omega-3 fatty acids each day, of which about 1.4 grams (~90%) comes from  $\alpha$ -linolenic acid, and only 0.1-0.2 grams (~10%) from EPA and DHA. In Western diets, people consume roughly 10 times more omega-6 fatty acids than omega-3 fatty acids. These large amounts of omega-6 fatty acids come from the common use of vegetable oils containing linoleic acid (for example: corn oil, evening primrose oil, pumpkin oil, safflower oil, sesame oil, soybean oil, sunflower oil, walnut oil, wheatgerm oil). Because omega-6 and omega-3 fatty acids compete with each other to be converted to active metabolites in the body, benefits can be reached either by decreasing intake of omega-6 fatty acids, or by increasing omega-3 fatty acids.
- **Recommended daily intake of omega-3 fatty acids (healthy adults):** For healthy adults with no history of heart disease, the American Heart Association recommends eating fish at least two times per week. In particular, fatty fish are recommended, such as anchovies, bluefish, carp, catfish, halibut, herring, lake trout, mackerel, pompano, salmon, striped sea bass, tuna (albacore), and whitefish. It is also recommended to consume plant-derived sources of  $\alpha$ -linolenic acid, such as tofu/soybeans, walnuts, flaxseed oil, and canola oil. The World Health Organization and governmental health agencies of several countries recommend consuming 0.3-0.5 grams of daily EPA + DHA and 0.8-1.1 grams of daily  $\alpha$ -linolenic acid. A doctor and pharmacist should be consulted for dosing for other conditions.

### Children (younger than 18 years):

- Omega-3 fatty acids are used in some infant formulas, although effective doses are not clearly established. Ingestion of fresh fish should be limited in young children due to the presence of potentially harmful environmental contaminants. Fish oil capsules should not be used in children except under the direction of a physician.

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## SAFETY

*The U.S. Food and Drug Administration does not strictly regulate herbs and supplements. There is no guarantee of strength, purity or safety of products, and effects may vary. You should always read product labels. If you have a*



*medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy. Consult a healthcare provider immediately if you experience side effects.*

## **Allergies**

- People with allergy or hypersensitivity to fish should avoid fish oil or omega-3 fatty acid products derived from fish. Skin rash has been reported rarely. People with allergy or hypersensitivity to nuts should avoid alpha linolenic acid or omega-3 fatty acid products that are derived from the types of nuts to which they react.

## **Side Effects and Warnings**

- The U.S. Food and Drug Administration classifies intake of up to 3 grams per day of omega-3 fatty acids from fish as GRAS (Generally Regarded as Safe). Caution may be warranted, however, in diabetic patients due to potential (albeit unlikely) increases in blood sugar levels, patients at risk of bleeding, or in those with high levels of low-density lipoprotein (LDL). Fish meat may contain methylmercury and caution is warranted in young children and pregnant/breastfeeding women.
- Omega-3 fatty acids may increase the risk of bleeding, although there is little evidence of significant bleeding risk at lower doses. Very large intakes of fish oil/omega-3 fatty acids ("Eskimo" amounts) may increase the risk of hemorrhagic (bleeding) stroke. High doses have also been associated with nosebleed and blood in the urine. Fish oils appear to decrease platelet aggregation and prolong bleeding time, increase fibrinolysis (breaking down of blood clots), and may reduce von Willebrand factor.
- Potentially harmful contaminants such as dioxins, methylmercury, and polychlorinated biphenyls (PCBs) are found in some species of fish. Methylmercury accumulates in fish meat more than in fish oil, and fish oil supplements appear to contain almost no mercury. Therefore, safety concerns apply to eating fish but likely not to ingesting fish oil supplements. Heavy metals are most harmful in young children and pregnant/nursing women.
- Gastrointestinal upset is common with the use of fish oil supplements. Diarrhea may also occur, with potentially severe diarrhea at very high doses. There are also reports of increased burping, acid reflux/heartburn/indigestion, abdominal bloating, and abdominal pain. Fishy aftertaste is a common effect. Gastrointestinal side effects can be minimized if fish oils are taken with meals and if doses are started low and gradually increased.
- Multiple human trials report small reductions in blood pressure with intake of omega-3 fatty acids. Reductions of 2-5 mmHg have been observed, and effects appear to be dose-responsive (higher doses have greater effects). DHA may have greater effects than EPA. Caution is warranted in patients with low blood pressure or in those taking blood-pressure lowering medications.
- Although slight increases in fasting blood glucose levels have been noted in patients with type 2 ("adult onset") diabetes, the available scientific evidence suggests that there are no significant long-term effects of fish oil in patients with diabetes, including no changes in hemoglobin A<sub>1c</sub> levels. Limited reports in the 1980s of increased insulin needs in diabetic patients taking long-term fish oils may be related to other dietary changes or weight gain.
- Fish oil taken for many months may cause a deficiency of vitamin E, and therefore vitamin E is added to many commercial fish oil products. As a result, regular use of vitamin E-enriched products may lead to elevated levels of this fat-soluble vitamin. Fish liver oil contains the fat-soluble vitamins A and D, and therefore fish liver oil products (such as cod liver oil) may increase the risk of vitamin A or D toxicity.
- Increases (worsening) in low-density lipoprotein levels ("bad cholesterol") by 5-10% are

observed with intake of omega-3 fatty acids. Effects are dose-dependent.

- Mild elevations in liver function tests (alanine aminotransferase) have been reported rarely.
- Skin rashes have been reported rarely.
- There are rare reports of mania in patients with bipolar disorder or major depression. Restlessness and formication (the sensation of ants crawling on the skin) have also been reported.

### **Pregnancy and Breastfeeding**

- Potentially harmful contaminants such as dioxins, methylmercury, and polychlorinated biphenyls (PCBs) are found in some species of fish, and may be harmful in pregnant/nursing women. Methylmercury accumulates in fish meat more than in fish oil, and fish oil supplements appear to contain almost no mercury. Therefore, these safety concerns apply to eating fish but likely not to ingesting fish oil supplements. However, unrefined fish oil preparations may contain pesticides.
- It is not known if omega-3 fatty acid supplementation of women during pregnancy or breastfeeding is beneficial to infants. It has been suggested that high intake of omega-3 fatty acids during pregnancy, particularly DHA, may increase birth weight and gestational length (254). However, higher doses may not be advisable due to the potential risk of bleeding. Fatty acids are added to some infant formulas.

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## **INTERACTIONS**

*Most herbs and supplements have not been thoroughly tested for interactions with other herbs, supplements, drugs, or foods. The interactions listed below are based on reports in scientific publications, laboratory experiments, or traditional use. You should always read product labels. If you have a medical condition, or are taking other drugs, herbs, or supplements, you should speak with a qualified healthcare provider before starting a new therapy.*

### **Interactions with Drugs**

- In theory, omega-3 fatty acids may increase the risk of bleeding when taken with drugs that increase the risk of bleeding. Some examples include aspirin, anticoagulants ("blood thinners") such as warfarin (Coumadin®) or heparin, anti-platelet drugs such as clopidogrel (Plavix®), and non-steroidal anti-inflammatory drugs such as ibuprofen (Motrin®, Advil®) or naproxen (Naprosyn®, Aleve®).
- Based on human studies, omega-3 fatty acids may lower blood pressure and add to the effects of drugs that may also affect blood pressure.
- Fish oil supplements may lower blood sugar levels a small amount. Caution is advised when using medications that may also lower blood sugar. Patients taking drugs for diabetes by mouth or insulin should be monitored closely by a qualified healthcare provider. Medication adjustments may be necessary.
- Omega-3 fatty acids lower triglyceride levels, but can actually increase (worsen) low-density lipoprotein (LDL/"bad cholesterol") levels by a small amount. Therefore, omega-3 fatty acids may add to the triglyceride-lowering effects of agents like niacin/nicotinic acid, fibrates such as gemfibrozil (Lopid®), or resins such as cholestyramine (Questran®). However, omega-3 fatty acids may work against the LDL-lowering properties of "statin" drugs like atorvastatin (Lipitor®) and lovastatin (Mevacor®).

### **Interactions with Herbs and Dietary Supplements**

- In theory, omega-3 fatty acids may increase the risk of bleeding when taken with herbs and supplements that are believed to increase the risk of bleeding. Multiple cases of bleeding have been reported with the use of *Ginkgo biloba*, and fewer cases with garlic and saw palmetto. Numerous other agents may theoretically increase the risk of bleeding, although this has not been proven in most cases.
- Based on human studies, omega-3 fatty acids may lower blood pressure, and theoretically may add to the effects of agents that may also affect blood pressure.
- Fish oil supplements may lower blood sugar levels a small amount. Caution is advised when using herbs or supplements that may also lower blood sugar. Blood glucose levels may require monitoring, and doses may need adjustment.
- Omega-3 fatty acids lower triglyceride levels, but can actually increase (worsen) low-density lipoprotein (LDL/"bad cholesterol") levels by a small amount. Therefore, omega-3 fatty acids may add to the triglyceride-lowering effects of agents like niacin/nicotinic acid, but may work against the potential LDL-lowering properties of agents like barley, garlic, guggul, psyllium, soy, or sweet almond.
- Fish oil taken for many months may cause a deficiency of vitamin E, and therefore vitamin E is added to many commercial fish oil products. As a result, regular use of vitamin E-enriched products may lead to elevated levels of this fat-soluble vitamin. Fish liver oil contains the fat-soluble vitamins A and D, and therefore fish liver oil products (such as cod liver oil) may increase the risk of vitamin A or D toxicity. Since fat-soluble vitamins can build up in the body and cause toxicity, patients taking multiple vitamins regularly or in high doses should discuss this risk with their healthcare practitioners.

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#### AUTHOR INFORMATION

- This information is based on a systematic review of scientific literature edited and peer-reviewed by contributors to the Natural Standard Research Collaboration ([www.naturalstandard.com](http://www.naturalstandard.com)).

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#### REFERENCES

*Natural Standard developed the above evidence-based information based on a thorough systematic review of the available scientific articles. For comprehensive information about alternative and complementary therapies on the professional level, go to [www.naturalstandard.com](http://www.naturalstandard.com). Selected references are listed below.*

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