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EPA (EICOSAPENTAENOIC ACID)

Also Known As:

Acide Eicosapentaénoïque, Acide Éthyle-Eicosapentaénoïque, Acide Gras Essentiel, Acide Gras d'Huile de Poisson, Acide Gras N-3, Acide Gras Omega, Acide Gras Oméga 3, Acide Gras Polyinsaturé, Acide Gras W3, Acido Eicosapentaenoico, EPA, E-EPA, Eicosapentanoic Acid, Essential Fatty Acid, Ethyl Eicosapentaenoic Acid, Ethyl-Eicosapentaenoic Acid, Ethyl-EPA, Fish Oil Fatty Acid, N-3 Fatty Acid, Omega Fatty Acid, Omega 3, Oméga 3, Omega 3 Fatty Acids, Omega-3, Omega-3 Fatty Acids, Polyunsaturated Fatty Acid, PUFA, W-3 Fatty Acid.
CAUTION: See separate listings for Cod Liver Oil, DHA (Docosahexaenoic Acid), Fish Oil, and Krill Oil.

Scientific Name:

Eicosapentaenoic acid.

People Use This For:

Orally, eicosapentaenoic acid (EPA) is used for cystic fibrosis, intrauterine growth retardation, treating depression, pregnancy-induced hypertension in high-risk pregnancies, age-related macular degeneration (AMD), coronary artery disease, schizophrenia, personality disorder, Alzheimer's disease, and diabetes.
In combination, EPA is used with docosahexaenoic acid (DHA) in fish oil preparations for a variety of conditions, including preventing and reversing heart disease, decreasing ectopic ventricular beats, asthma, cancer, dysmenorrhea, menopause, hay fever, lung diseases, lupus erythematosus, lupus nephritis, and IgA nephropathy. They are also used in combination for migraine headache prophylaxis in adolescents, atopic dermatitis, Behcet's syndrome, hyperlipidemia, hypertension, psoriasis, Raynaud's syndrome, rheumatoid arthritis, Crohn's disease, and ulcerative colitis. EPA is also used in combination with RNA and L-arginine in the perioperative period to reduce infections, improve wound healing, and shorten recovery time.

Safety:

LIKELY SAFE ...when used orally or intravenously, and appropriately (1004, 1016, 7819, 15497).
POSSIBLY UNSAFE ...when used orally in high doses. Doses greater than 3 grams daily might decrease blood coagulation and increase the risk of bleeding (1313).
PREGNANCY AND LACTATION: Insufficient reliable information available; avoid using.

Effectiveness:

POSSIBLY EFFECTIVE

Coronary artery disease. Population research suggests that increased dietary consumption of EPA is associated with a slightly decreased risk of death in patients with coronary artery disease (10322). Preliminary clinical research shows that patients with hypercholesterolemia and a history of coronary artery disease who take EPA 1800 mg daily have a reduced the risk of major coronary events by 19%; however, EPA doesn't appear to reduce sudden cardiac death (15497).

Depression. Taking eicosapentaenoic acid (EPA) orally 1 gram twice daily with standard therapy seems to improve symptoms of recurrent major depression, such as depressed mood, guilt feelings, worthlessness, and insomnia after two weeks of treatment (10872). Some research suggests that the ethyl form of EPA, ethyl-eicosapentaenoate (ethyl-EPA), might also be helpful for treating depression. It appears that 1 gram per day of ethyl-EPA may be more effective for depression than 2 or 4 grams per day (10215).

Menopausal symptoms. Clinical research shows that taking ethyl-EPA 500 mg orally, three times daily, provides modest, but significant reduction in the frequency of hot flashes compared to placebo. After 8 weeks of treatment, the mean number of hot flashes decreased by 1.58 daily in women taking ethyl-EPA. However, taking ethyl-EPA did not significantly decrease the severity of hot flashes or improve overall quality of life (16901).

Personality disorder. Taking EPA (as ethyl eicosapentaenoic acid) orally provides modest improvement in aggressive behavior and depression in women with moderately severe borderline personality disorder (10348).

Psoriasis. Taking EPA in combination with low-dose (20 mg per day) etretinate (Tegison, no longer available in the US) seems to be more effective than etretinate alone for plaque psoriasis (1000). EPA given intravenously in combination with docosahexaenoic acid (DHA) appears to improve psoriatic lesions better than omega-6-lipid emulsion (1004).

Surgery. Supplementing the diet with EPA in combination with RNA and L-arginine before surgery or in the postoperative period appears to reduce the number of perioperative infections, improves wound healing, and shortens recovery time (5531, 5532, 5533, 7819).

POSSIBLY INEFFECTIVE

Age-related macular degeneration (AMD). Increased dietary consumption of EPA doesn't appear to prevent AMD (10324).

Allergic rhinitis (hayfever). Taking EPA orally doesn't appear to relieve hayfever symptoms, including wheezing, cough, and nasal symptoms (1036).

Asthma. Taking EPA orally doesn't seem to have any effect on asthma symptoms when given for four weeks (1023).

Cystic fibrosis. Taking EPA orally as a single agent doesn't seem to improve symptoms of cystic fibrosis (1006, 1027).

Diabetes. Taking EPA orally doesn't seem to substantially improve cholesterol or other serum lipids or decrease blood sugar or hemoglobin A1C (HbA1C) in patients with type 2 diabetes (10321).

Eclampsia. Taking EPA orally doesn't seem to improve pregnancy-induced hypertension in women with high-risk pregnancies (1027).

Hypertension. The combination of 0.48 grams EPA plus 0.12 grams gamma-linolenic acid doesn't appear to decrease slightly elevated diastolic blood pressure (85 to 94 mm Hg) (13771).

Intrauterine growth. Taking EPA orally doesn't seem to reduce the risk of intrauterine growth (1027).

INSUFFICIENT RELIABLE EVIDENCE to RATE

Alzheimer's disease. Population research suggests that higher dietary intake of EPA is not associated with a decreased risk of developing Alzheimer's disease (15041).

Attention deficit-hyperactivity disorder (ADHD). Some research shows that low plasma levels of EPA and other fatty acids are associated with ADHD in children (15496); however, it is not known if taking EPA supplements can treat or prevent ADHD.

Prostate cancer. Population research suggests that higher serum levels of EPA are associated with a lower risk of developing prostate cancer (15736).

Schizophrenia. There is inconsistent evidence about the effectiveness of EPA for schizophrenia (8720, 10347, 15039). According to one analysis of studies, EPA modestly improves the mental state in patients with schizophrenia compared to placebo. Some evidence suggests that an esterified form of EPA called ethyl-eicosapentaenoic acid might be more effective than EPA. Taking EPA doesn't appear to significantly decrease the need for conventional antipsychotics (15039).

More evidence is needed to rate EPA for these uses.

Mechanism of Action:

Eicosapentaenoic acid (EPA) is a long-chain n-3 polyunsaturated fatty acid that is found in the tissues of marine mammals and oily fish. EPA is also found in fish liver oils and in commercial fish oil products. EPA competes with arachidonic acid for inclusion in cyclooxygenase and lipoxygenase pathways (8696). This may have an anti-inflammatory effect in diseases such as psoriasis (1004).

EPA decreases blood viscosity and increases red blood cell deformability. It also decreases platelet aggregation (9930). However, EPA does not significantly affect clotting factors, fibrinogen concentrations, plasminogen activator inhibitor-1 or tissue plasminogen activator activity (10323). Pure EPA reduces serum triglyceride concentrations, increases fasting insulin and glucose concentrations, but has no effect on total and low-density lipoprotein (LDL) cholesterol in mildly hypercholesterolemic men (6143, 10322). There is some evidence that higher ratios of EPA to arachidonic acid are associated with lower ratios of total to high-density lipoprotein (HDL) cholesterol. EPA can increase HDL cholesterol by approximately 12% (10321). There is preliminary evidence that EPA decreases natural killer (NK) cell activity. Researchers think this effect might be beneficial in preventing rejection after bone marrow and organ transplantation, but further research is needed (8718).

There is evidence EPA might have an additive effect to standard treatment on symptoms associated with schizophrenia and recurrent unipolar depressive disorder, but it is unknown if EPA has any antipsychotic and antidepressant activity of its own (8720, 10872). Preliminary clinical research suggests that EPA might enhance the responsiveness of serotonin receptors in patients with schizophrenia (13762). Some evidence suggests that supplemental EPA might slow weight loss in cachectic cancer patients, possibly by inhibiting lipolysis. Other research suggests EPA does not inhibit lipolysis or lipid oxidation, suggesting a different mechanism might be responsible for this effect (8717).

Adverse Reactions:

Orally, eicosapentaenoic acid (EPA) is usually well-tolerated. Side effects reported in clinical studies include nausea; diarrhea; epigastric discomfort; skin rash; itching; nosebleed; and joint, back, and muscle pain (15497). For fish oils containing EPA and DHA, side effects can include fishy taste, belching, nosebleeds, nausea, and loose

stools (10007).

Three people with pre-existing familial adenomatous polyposis were diagnosed with malignant lesions during the course of long-term fish oil use (999); however, it is unclear if fish oil was the cause.

High doses of fish oil might also decrease blood coagulation and increase the risk of bleeding (1313).

There is preliminary evidence that the EPA in fish oil decreases natural killer (NK) cell activity. Due to this effect, there is concern that increased intake of EPA might have some adverse immunologic effects and possibly increase the risk for viral infections and some cancers (8718).

Interactions with Herbs & Supplements:

ANTICOAGULANT/ANTIPLATELET HERBS AND SUPPLEMENTS: Concomitant use of herbs that have constituents that might affect platelet aggregation could theoretically increase the risk of bleeding in some people (9930). These herbs include angelica, clove, danshen, garlic, ginger, ginkgo, Panax ginseng, red clover, turmeric, and others.

HERBS AND SUPPLEMENTS WITH HYPOTENSIVE EFFECTS: EPA is thought to have hypotensive effects. Theoretically, combining EPA with other herbs or supplements with hypotensive effects might increase the risk of hypotension. Some of these herbs and supplements include andrographis, casein peptides, cat's claw, coenzyme Q-10, fish oil, L-arginine, lycium, stinging nettle, theanine, and others.

Interactions with Drugs:

ANTICOAGULANT/ANTIPLATELET DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Possible • Level of Evidence = B

Theoretically, concomitant use of EPA with anticoagulant or antiplatelet drugs, including aspirin, can increase the risk of bleeding (9930).

ANTIHYPERTENSIVE DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Probable • Level of Evidence = B

Fish oils containing EPA can lower blood pressure and might have additive effects in patients treated with antihypertensives (1001, 1020, 1030, 1033); use with caution.

Interactions with Foods:

None known.

Interactions with Lab Tests:

INSULIN: EPA can increase fasting insulin concentrations and test results in mildly hypercholesterolemic patients (6143).

INTERNATIONAL NORMALIZED RATIO (INR), PROTHROMBIN TIME (PT): High doses of greater than 3 grams per day might decrease blood coagulation, increase INR and PT, and increase the risk of bleeding (1313).

LOW-DENSITY LIPOPROTEIN (LDL) CHOLESTEROL: EPA might reduce serum LDL concentrations and test results in patients with hypercholesterolemia (15497).

PULMONARY FUNCTION TESTS: EPA might cause a decline in pulmonary function tests in aspirin-sensitive individuals (11869).

TRIGLYCERIDES: EPA can reduce serum triglyceride concentrations and test results in patients with hypercholesterolemia (6143).

Interactions with Diseases or Conditions:

ASPIRIN-SENSITIVITY: Fish oils and other omega-3 fatty acids can lower pulmonary function tests in some aspirin-sensitive patients (11869).
HYPERTENSION: Fish oils including EPA can lower blood pressure and might have additive effects in patients with high blood pressure who are treated with antihypertensives (1001, 1020, 1030, 1033).

Dosage/Administration:

ORAL: Eicosapentaenoic acid (EPA) is usually administered with DHA (docosahexaenoic acid) as fish oil. A wide range of doses has been used. A typical dose is 5 grams of fish oil containing 169-563 mg of EPA and 72-312 mg of DHA.
For depression, 1 gram EPA twice daily has been used (10872).
For schizophrenia, 1-3 grams daily in divided doses of EPA or ethyl eicosapentaenoic acid has been used for 12-16 weeks (8720, 15039).
For borderline personality disorder, 1 gram of EPA daily (as ethyl eicosapentaenoic acid) has been used for up to 8 weeks (10348).
For menopausal symptoms, ethyl-EPA 500 mg three times daily has been used for up to 8 weeks (16901).
For plaque psoriasis, EPA ethyl ester 1800 mg daily has been used (1000).
Many fatty acid preparations such as EPA also contain small amounts of vitamin E as an antioxidant to prevent spoilage.
INTRAVENOUS: For plaque psoriasis, EPA 4.2 grams and docosahexaenoic acid (DHA) 4.2 grams per day has been used (1004).

Editor's Comments:

Avoid confusion with DHA (docosahexaenoic acid) and fish oils, which contain EPA and DHA. Most available data involving EPA are from research and clinical experience with fish oil products containing variable combinations of EPA and DHA. For more information, see the separate listing for Fish Oils.
Researchers are investigating oils containing stearidonic acid (SDA) from genetically modified plants as an alternative source of omega-3 fatty acids. SDA is metabolized to EPA and DHA in animals. However, further research is needed on the effects and safety of SDA in humans.

This monograph was last reviewed on 08/11/2011 and last updated on 08/11/2011. Monographs are reviewed and/or updated multiple times per month and at least once per year. If you have comments or suggestions on something that should be reviewed or included, please tell the editors. For details about our evidence-based approach, see our Editorial Principles and Process.

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