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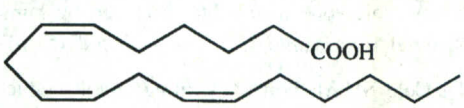
Evening Primrose Oil

DESCRIPTION

Evening primrose oil (EPO) is derived from the seeds of the evening primrose plant also known as *Oenthera biennis*. The evening primrose is native to North America, where it is regarded as a weed. This biennial plant is thought to be a complex of several closely related species belonging to the *Onagraceae* family.

EPO is a rich source of the long-chain fatty acid gamma-linolenic acid (GLA). The health benefits of EPO are attributed to GLA. GLA is an unusual constituent of living matter and is found in very few plants. These include, in addition to evening primrose, black currant, borage and hemp. GLA content in EPO ranges from approximately 7 to 14%. Typical EPO supplements contain about 9% GLA.

GLA is an all cis n-6 long-chain polyunsaturated fatty acid. It is comprised of 18 carbon atoms and three double bonds. GLA is also known as GLA; 18: 3n-6 and gamolenic acid, and chemically it is known as 6, 9, 12-octadecatrienoic acid; (Z, Z, Z)-6, 9, 12-octadecatrienoic acid, and cis-6, cis-9, cis-12-octadecatrienoic acid. GLA is present in EPO in the form of triglycerides. One such triglyceride in EPO contains two linoleic acid residues and one of GLA. This triglyceride, called di-linoleoyl-mono-gamma-linenyl-glycerol (DLMG), makes up about 18 to 19% of the triglycerides in EPO. GLA is concentrated in the sn-3 position in the triglycerides. GLA is represented by the following chemical structure:



GLA (gamma-linolenic acid)

EPO is approved in the United Kingdom as a pharmaceutical treatment for atopic dermatitis and mastalgia.

ACTIONS AND PHARMACOLOGY

ACTIONS

EPO may have anti-inflammatory and antithrombotic activities.

MECHANISM OF ACTION

The possible anti-inflammatory and anti-aggregatory actions of EPO may be accounted for by examining the role of GLA in eicosanoid biochemistry. GLA is metabolized to the 20-carbon polyunsaturated fatty acid dihomo-gamma-linolenic acid (DGLA; 20: 3n-6), which is a precursor to the 1-series prostaglandins, such as prostaglandin E_1 (PGE_1). The action of PGE_1 on inflammatory cells (e.g., polymorphonuclear leukocytes or PMNs) is mostly inhibitory. PGE_1 increases intracellular cyclic AMP (cAMP). This increase reduces the release of lysosomal enzymes, PMN chemotaxis and the margination and adherence of PMNs in the blood vessels. PGE_1 is also thought to inhibit lymphocyte function.

PGE_1, in addition to its role in suppressing the inflammatory process, inhibits platelet aggregation and has vasodilatory activity.

GLA, via its metabolite DGLA, has an inhibitory effect on leukotriene (LT) synthesis. Leukotriene B_4 (LTB_4) is an inflammatory mediator. DGLA is metabolized to 15-hydroxyl DGLA, which blocks the conversion of arachidonic acid to LTs, such as LTB_4.

In summary, GLA may suppress inflammation through its metabolism to DGLA, which, in turn, can competitively inhibit the pro-inflammatory 2-series prostaglandins and 4-series leukotrienes. The incorporation of GLA and its metabolites in cell membranes may also play a role in the possible anti-inflammatory, antithrombotic, anti-atherogenic and antiproliferative actions of EPO.

PHARMACOKINETICS

GLA-laden triglycerides in EPO are absorbed from the small intestine aided by bile salts. During this process, there is some deacylation of the fatty acids of the triglycerides. Reacylation takes place within the mucosal cells of the small intestine, and the GLA-laden triglycerides enter into the lymphatics in the form of chylomicrons. GLA-laden chylomicrons are transported from the lymphatics into the blood where GLA is carried in lipid particles to the various tissues of the body.

GLA is metabolized to the 20-carbon polyunsaturated fatty acid dihomo-gamma-linoleic acid (DGLA), which is converted to prostaglandin E_1 (PGE_1). It may also be metabolized to eicosapentaenoic acid (EPA). GLA and DGLA are normally not found as free fatty acids in cells. They occur mainly in cell membranes as components of phospholipids, neutral lipids and cholesterol esters. PGE_1 is metabolized to smaller prostaglandin remnants, which are primarily polar dicarboxylic acids, most of which are excreted in the urine.

INDICATIONS AND USAGE

EPO appears to be effective in some cases of rheumatoid arthritis and may be indicated in some other inflammatory disorders, such as Sjogren's syndrome and ulcerative colitis. Possible other indications include diabetic neuropathy, osteoporosis, acute respiratory distress syndrome (ARDS),

hypertension and elevated serum lipids. EPO has been used with some preliminary success in some cancers, principally cerebral gliomas. It has not proved useful for tardive dyskinesia, premenstrual syndrome or menopausal flushing. It may be indicated in some cases for atopic dermatitis, particularly to help with itching, as well as for uremic skin conditions in hemodialysis patients. It should probably not be used in efforts to enhance immunity as it may be immunosuppressive.

RESEARCH SUMMARY

See GLA.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to an EPO-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid EPO supplements. Those with a history of partial complex seizure disorders, such as temporal lobe epilepsy, should avoid using EPO. Likewise, those with other types of seizure disorders and schizophrenics who are being treated with certain neuroleptic drugs, such as aliphatic phenothiazines (e.g., chlorpromazine), which may lower seizure threshold, should avoid using EPO. Because of possible antithrombotic activity of EPO, those with hemophilia or other hemorrhagic diatheses and those taking warfarin should exercise caution in the use of this supplement.

EPO supplementation should be halted before any surgical procedure. Because of its possible inhibition of lymphocyte function, those with immune deficiency disorders, such as AIDS, should exercise caution in the use of EPO.

ADVERSE REACTIONS

EPO may cause gastrointestinal symptoms like nausea, vomiting, flatulence, diarrhea and bloating. Headaches have also been reported in those taking EPO. It may precipitate symptoms of undiagnosed complex partial seizures and should be used, if at all, with extreme caution in those with a history of seizure disorder or those taking drugs that lower the seizure threshold, such as aliphatic phenothiazines.

INTERACTIONS

DRUGS

Use of EPO in schizophrenics who are being treated with certain neuroleptic agents which lower seizure threshold e.g., aliphatic phenothiazines, such as chlorpromazine, may cause partial complex seizures (e.g., temporal lobe epilepsy), as well as other types of seizures. Interactions may occur between EPO and warfarin, aspirin and NSAIDs. Such interactions, if they were to occur, might be manifested by nosebleeds, increased susceptibility to bruising and hematuria. If these symptoms occur, EPO intake should be stopped.

NUTRITIONAL SUPPLEMENTS

Interactions may occur if EPO is used with supplements that have antithrombotic activity, such as fish oils. This may be manifested by nosebleeds and increased susceptibility to bruising.

HERBS

Interactions may occur if EPO is used with such herbs as garlic (*Allium sativa*) and ginkgo (*Ginkgo biloba*). Such interactions may be manifested by nosebleeds and easy bruising.

OVERDOSAGE

There are no reports of overdosage with EPO.

DOSAGE AND ADMINISTRATION

EPO is available in capsules and also in topical preparations for cosmetic use. A capsule of EPO typically contains about 9% GLA. Doses used for the management of rheumatoid arthritis range from about 360 milligrams to 2.8 grams daily in divided doses (expressed as GLA). For management of atopic dermatitis, doses of 320 to 480 milligrams daily are used in divided doses (expressed as GLA). Doses of up to 2 grams daily (expressed as GLA) have been used by those with hypertriglyceridemia. EPO supplements should contain an antioxidant, such as vitamin E, to protect the unsaturated fatty acids against oxidation.

LITERATURE

See GLA monograph for additional literature.

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Fisetin

DESCRIPTION

Fisetin is a member of the flavonol subclass of flavonoids. Related members of the subclass include kaempferol, myricetin and quercetin. Fisetin is found in fruits, including strawberries, persimmons, kiwi fruit, peaches, grapes, apples