to contain substantial amounts of lead, as well as other toxic elements, such as arsenic, mercury and cadmium. A second-generation "bone meal" product called microcrystalline hydroxyapatite, or MCHA, is being marketed as a calcium supplement and is claimed to be free of contaminants.

Bone meal is also used as a high-phosphorus fertilizer and in some pet foods.

ACTIONS AND PHARMACOLOGY

MECHANISM OF ACTION

See Calcium and Phosphorus.

PHARMACOKINETICS

See Calcium and Phosphorus.

Hydroxyapatite is apparently well-absorbed from the gastrointestinal tract.

INDICATIONS AND USAGE

Bone meal is still sold as a "natural" source of calcium. Its use should be avoided owing to potential toxic-metal contamination.

RESEARCH SUMMARY

The use of bone meal as a calcium and phosphorus source is no longer recommended. Several researchers have reported that many bone meal preparations are contaminated with toxic metals. In one study, bone meal samples were contaminated with significant amounts of lead, arsenic, mercury and other metals. Dolomite and calcium carbonate supplements labeled "oyster shell" or "natural source" have also been found to be contaminated with these metals.

One researcher has advised that "physicians must consider the possibility of unrecognized self-poisoning from the consumption of such substances, especially in the context of unexplained neurologic, gastrointestinal, cutaneous and hematologic disorders."

The feeding of meat and bone meal to cattle, contaminated with bovine spongiform encephalopathy (BSE) tissue, led to an epidemic of BSE in the British cattle population in the 1990s.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Bone meal is contraindicated in those with hypercalcemia. Conditions that cause hypercalcemia include hyperparathyroidism, hypervitaminosis D, some granulomatous diseases, sarcoidosis and cancer. Bone meal is also contraindicated in those with calcium pyrophosphate dihydrate (CPPD) deposition disease.

PRECAUTIONS

Bone meal is no longer recommended as a calcium and/or phosphorus supplement because of possible presence of toxic substances, such as lead. Children are especially sensitive to the effects of lead. Children, pregnant women and nursing mothers should absolutely avoid bone meal supplements.

ADVERSE REACTIONS

See Calcium. Prolonged use of bone meal contaminated with toxic elements, such as lead, may cause the typical toxic effects of these substances. Lead may produce abdominal pain, anemia and central nervous system damage.

OVERDOSAGE

There are no known reports of overdosage of bone meal.

DOSAGE AND ADMINISTRATION

No recommended dose. Second-generation "bone meal" supplements known as microcrystalline hydroxyapatite, or MCHA, are available as calcium supplements and are claimed to be free of contaminants.

LITERATURE

Boulos FM, von Smolinski A. Alert to users of calcium supplements as antihypertensive agents due to trace mineral contaminants. *Am J Hypterten.* 1988; 1(3 Pt 3):137S-142S.

Bourquin BP, Evans DR, Cornett JR, et al. Lead content of 70 brands of dietary calcium supplements. *Am J Public Health.* 1993; 83:1155-1160.

Groschup MH. [Bovine spongiform encephalopathy in ruminants and the new variant of Creutzfeldt-Jakob disease in humans.] [Article in German.] *DTW Dtsch Tierarzl Wochenschr.* 1999; 106:329-331.

Roberts HJ. Potential toxicity due to dolomite and bone meal. *South Med J.* 1983; 76:556-559.

Whiting SJ. Safety of some calcium supplements questioned. *Nutr Rev.* 1994; 52:95-97.

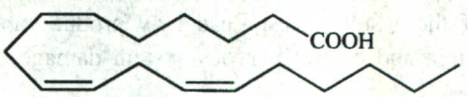
Borage Oil

DESCRIPTION

Borage oil is derived from the seeds of the borage plant (*Borago officinalis*), a member of the Boraginaceae family. Borage oil, also known as starflower oil and borage seed oil, is a rich source of the long-chain polyunsaturated fatty acid gamma-linolenic acid (GLA). The possible health benefits of borage oil are attributed to GLA. GLA is an unusual constituent of living matter and is found in very few plants. These include, in addition to borage, evening primrose, blackcurrant and hemp. The amount of GLA in borage oil, as the percentage of total fatty acid content, ranges from about 20% to 27%. Typical borage oil supplements contain approximately 24% 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. 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 borage oil in the form of triglycerides. GLA is concentrated in the sn-2 position in the triglycerides. GLA has the following chemical structure:



GLA (gamma-linolenic acid)

ACTIONS AND PHARMACOLOGY

ACTIONS

Borage oil may have anti-inflammatory and antithrombotic activities.

MECHANISM OF ACTION

The possible anti-inflammatory and anti-aggregatory actions of borage oil 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, inhibits 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 borage oil.

PHARMACOKINETICS

GLA-laden triglycerides in borage oil are absorbed from the small intestine aided by bile salts. During this process, there is some deacylation of the fatty acid residues 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-linolenic 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 in cells as free fatty acids. They occur mainly in cell membranes as components of phopholipids, 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

Borage oil 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 osteoporosis, diabetic neuropathy, acute respiratory distress syndrome (ARDS), hypertension and elevated serum lipids. Borage oil 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 Gamma-Linolenic Acid (GLA).

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Known hypersensitivity to a borage oil-containing product.

PRECAUTIONS

Pregnant women and nursing mothers should avoid using borage oil supplements. Those with a history of partial complex seizure disorders, such as temporal lobe epilepsy, should avoid using borage oil. 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 borage oil. Because of possible antithrombotic activity of borage oil, those with hemophilia or other hemorrhagic diatheses and those taking warfarin should exercise caution in the use of this supplement. Borage oil 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 borage oil.

Pyrrolizidine alkaloids, such as amabiline, lycopsamine and thesinine, are found in various parts of the borage plant. The unsaturated pyrrolizidine alkaloids, such as amabiline, are potentially hepatotoxic and carcinogenic. Amabiline has not been detected in borage oil supplements down to five parts per million. However, chronic consumption of borage oil containing levels of amabiline of one part per million may prove harmful. Those who use borage oil chronically should only use products that are certified free of unsaturated pyrrolizidine alkaloids.

ADVERSE REACTIONS

Borage oil may cause such gastrointestinal symptoms as nausea, vomiting, flatulence, diarrhea and bloating. Similar to evening primrose oil, borage oil 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 disorders or those taking drugs that lower the seizure threshold, such as aliphatic phenothiazines (e.g., chlorpromazine).

INTERACTIONS

DRUGS

Use of borage oil in schizophrenics who are being treated with certain neuroleptic agents that lower seizure threshold — e.g. aliphatic phenothiazines, such as chlorpromazine — may cause partial complex seizures and possibly other types of seizures. Interactions may occur between borage oil and anticoagulants, such as warfarin, as well as antiplatelet drugs, such as aspirin and NSAIDs. Such interactions may enhance the effects of the anticoagulants and antiplatelet drugs. Manifestations of such interactions, if they were to occur, include nosebleeds, hematuria and increased susceptibility to bruising. Borage oil intake should be stopped if these symptoms occur.

NUTRITIONAL SUPPLEMENTS

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

OVERDOSAGE

There are no reports of overdosage with borage oil.

DOSAGE AND ADMINISTRATION

Borage oil is available in capsules and bottles. Capsules of borage oil typically contain about 24% 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 (expressed as GLA) are used, taken daily in divided doses. Doses up to 2 grams daily (expressed as GLA) have been used by those with hypertriglyceridemia. For long-term use, borage oil should be certified free of unsaturated pyrrolizidine alkaloids. Borage oil supplements should contain an antioxidant, such as vitamin E, to protect the unsaturated fatty acids against oxidation.

LITERATURE

For additional literature, see Gamma-Linolenic Acid (GLA) and Evening Primrose Oil monographs.

Huang Y-S, Mills DE, eds. *Gamma-Linolenic Acid: Metabolism and its Roles in Nutrition.* Champaign, IL: American Oil Chemists Society Press; 1996.

Boron

DESCRIPTION

Boron, the fifth chemical element, is a dietary trace mineral found primarily in plant foods. It is essential for plant growth. Recently it has been shown to be essential in an animal species (zebra fish), and evidence is mounting that boron is probably essential for humans, as well. The first edition of *The Merck Manual* (1899) credits boric acid, the most common form of boron, with being a useful treatment for amenorrhea, dysmenorrhea, epilepsy and elevated uric acid. Boric acid has, in fact, proved to be ineffective for all of those disorders, but recent research lends some preliminary support for the use of boron for the promotion of bone and joint health. There is less evidence that it may be helpful in enhancing mental cognition.

ACTIONS AND PHARMACOLOGY

ACTIONS

Boron may have estrogen-mimetic and anti-osteoporotic activity. It may also participate in regulating the respiratory burst of neutrophils.

MECHANISM OF ACTION

The biochemical mechanism of boron is not yet known. Currently, two hypotheses have been advanced for the biochemical function of boron in animals, including humans. The first is that boron plays a role in cell-membrane functions that influence response to hormone action, trans-membrane signaling and trans-membrane movement of regulatory ions. Boron has been shown, in animal models, to influence the transport of extracellular calcium and the release of intracellular calcium in platelets activated by thrombin. It also influences redox actions involved in cellular membrane transport in plants.