

Evening Primrose Oil

Evening Primrose oil is a naturally rich source of omega-6 (linoleic acid), and gamma-linolenic acid (GLA). GLA is normally synthesised in the body from linoleic acid by delta-6-desaturase, and mediates an anti-inflammatory response, as it is the direct precursor to the prostaglandin E1 series. (PGE1). Evening Primrose oil also helps to maintain fluidity and permeability of delicate cell membranes, supports neurologic tissue and healthy hormone receptor activity.

Endogenous GLA formation is impaired in a number of conditions, notably atopic eczema, pre-menstrual syndrome, cyclical mastalgia and diabetes; and administration of GLA has therapeutic effects in these conditions.¹

HERBS THAT MAY ASSIST

Evening Primrose Oil
Providing gamma-linolenic acid (GLA)

CLINICAL APPLICATIONS

Key Applications:

- Atopic dermatitis (eczema)
- Female Hormonal Health
 - Premenstrual Syndrome
 - Cyclic mastalgia (breast tenderness)
 - Breast cancer and chemotherapy
- Alcoholism
- Sjogren's Syndrome

TECHNICAL INFORMATION

Essential fatty acids

Evening primrose oil delivers linoleic acid (omega-6) plus gamma-linolenic acid (GLA), the downstream metabolite that directly supports the synthesis of anti-inflammatory series 1 prostaglandins (PGE1). (See Figure 1). Omega-6 fatty acid (linoleic acid) requires conversion in the body in order to be utilised. This conversion depends on delta-6-desaturase, which is prone to interference from a variety of factors, such as nutritional deficiencies, alcohol, *trans* fats (from processed foods), smoking, pollution, stress, ageing, obesity, viral infections and other illnesses such as diabetes. This means that in the vast majority of people, the conversion is incomplete or even non-existent.

Prostaglandin PGE1 is protective by being anti-inflammatory, anti-thrombotic and anti-proliferative with a lipid lowering potential. It also enhances smooth muscle relaxation and vasodilation. Another function of GLA is as an important polyunsaturated fatty acid, as it is incorporated into cell membranes, including mitochondrial membranes, to maintain cellular integrity and fluidity.²

Unopposed omega-6 supplementation may lead to an increase in arachidonic acid production (See Figure 1). It is advised for the best anti-inflammatory result to combine evening primrose oil (GLA) supplementation with fish oils, providing EPA which favourably competes for delta-5-desaturase and so down-regulates conversion to arachidonic acid, achieving broader anti-inflammatory and anti-thrombotic effects.

By supplementing with linoleic acid, arachidonic acid (AA) increases, whereas giving GLA consistently raises the levels of DGLA but has a smaller effect on arachidonic acid. This suggests that linoleic acid may be converted to arachidonic acid, while GLA is preferentially metabolised to PGE1. The

administration of GLA, therefore, consistently raises the ratio of DGLA and its metabolites to AA and its metabolites. This is likely to have desirable effects in many people.³

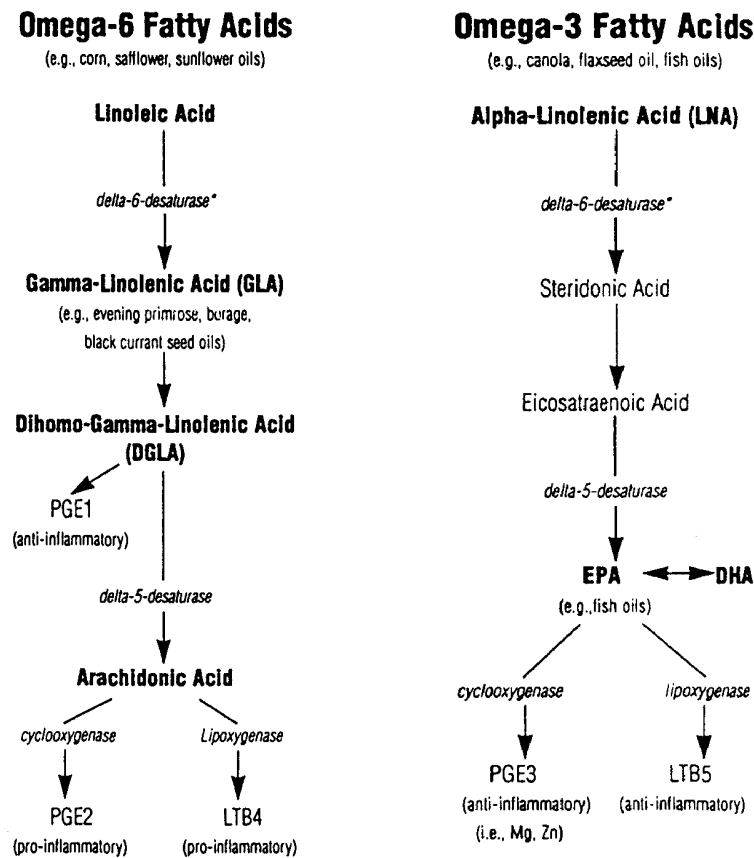


Figure 1. The omega-3 and omega-6 pathways are very similar and use the same enzymes. The results of these pathways are various families of eicosanoids. Factors thought to impair delta-6-desaturase activity include magnesium, zinc and vitamin B6 deficiency; ageing, alcohol, *trans* fatty acids; and high cholesterol levels.⁴

RESEARCH

Atopic Dermatitis (eczema)

A defect in the function of the enzyme delta-6-desaturase is thought to be a major factor in the development of atopic eczema⁵ reducing the conversion of linoleic acid to GLA. Most studies on patients with atopic eczema using GLA have found improvements in the clinical assessment of skin condition, and also a reduction in blood catecholamine concentrations, suggesting a link between stress and eczema. Atopic eczema may be an inherited abnormality of EFA metabolism.⁶

In a study on 60 patients with atopic dermatitis between 15-30 years old, 30 were treated with GLA at a dosage of 274 mg twice a day, whilst the other 30 patients were given placebo. The patients were treated for 12 weeks. Every 4 weeks they both self-assessed and were assessed by a dermatologist. The patients who received GLA showed gradual improvements in pruritus (itch), erythema (redness), vesiculation (blistering) and oozing, which were statistically significant compared with the control group. GLA was found to be effective and without side-effects for the treatment of atopic dermatitis⁷

Clinical trials have revealed varied responses to Evening Primrose oil treatment, with some finding it ineffective. It is thought that some dry atopic types of dermatitis or eczema may be more responsive to treatment. A study of 14 patients with itchy dry scaly skin gained significant improvements to their

condition, whilst also increasing serum IFN-gamma levels, and reducing serum IgE levels. These results suggest improvement through modulating the immune response.⁸

A review of studies suggests treatment doses for eczema and dermatitis of 250-500mg GLA daily (approximately 2.5-5.0 grams daily of Evening Primrose oil).⁹

FEMALE HORMONAL HEALTH

Premenstrual Syndrome (PMS)

GLA has been demonstrated to induce series-1 prostaglandins (PGE1). PGE1 appears to reduce the prolactin-induced symptoms of PMS, such as fluid retention, irritability and depression.¹⁰ This may be why supplementation with Evening Primrose oil, has been shown to benefit many women with PMS symptoms.¹¹

Studies investigating Evening Pprimrose oil, GLA and various nutrients to support essential fatty acid metabolism and their effects on PMS, demonstrate that Evening Primrose oil is a highly effective treatment for depression and irritability, breast pain and tenderness, and fluid retention associated with the premenstrual syndrome. Extra nutrients known to assist the conversion of essential fatty acids to PGE1 include magnesium, pyridoxine, zinc, niacin and ascorbic acid.¹²

Cyclic Mastalgia (breast tenderness)

As GLA is a first-line treatment for Western women with cyclical mastalgia, a study was designed using GLA from Evening Primrose oil to test its efficacy in Asian women. Thirty-four women with persistently disturbing mastalgia were supplemented with Evening Primrose oil (dose unknown). After 6 months the overall response rate was 97%. From this study, a recommendation was made that Evening Primrose oil may be recommended as a first-line specific treatment for Oriental women with disturbing cyclical mastalgia.¹³

Breast Cancer and Chemotherapy

GLA possesses a number of potential anti-tumour properties including modulation of steroid receptor structure and function. The effect of dietary GLA on the growth, oestrogen receptor (ER) expression and the fatty acid profile of ER positive breast cancer outcomes have been investigated. In an animal model, experimental diets were administered to animals with ER positive tumours. Four groups compared: 1) a control diet, 2) control diet plus GLA supplement, 3) control diet plus tamoxifen, and 4) control diet plus GLA plus tamoxifen. Groups 3 and 4 displayed significantly slower tumour growth, with trend for slower growth in 2 compared to control Group 1, and ER expression was significantly reduced in all groups compared to the control group, with Group 4 (combined therapy) displaying markedly lower ER expression than with either therapy alone. This model of ER positive breast cancer has demonstrated significantly lower tumour ER expression in those groups receiving GLA, an effect which appears to be additive to the reduced ER expression resulting from tamoxifen alone, suggesting that Evening Primrose oil may be a useful support to tamoxifen therapy for breast cancer¹⁴.

ALCOHOLISM

Alcohol has a dual action on PGE1 formation. By enhancing synthesis of PGE1 from DGLA it can produce a temporary rise in PGE1.^{15, 16} At the same time, though, it blocks the formation of DGLA by inhibiting delta-6-desaturase.¹⁷ Alcohol may therefore produce a transient elevation of PGE1 followed by a long-term deficiency. Withdrawal from alcohol may produce a catastrophic fall in PGE1 because of the low levels of DGLA and the removal of the effect of alcohol in stimulating conversion of that DGLA. The fatty liver produced by chronic alcohol consumption in animals can be prevented by daily injections of PGE1¹⁸ and the withdrawal symptoms in alcohol-addicted mice can be prevented by treatment of the animals with either PGE1 or Evening Primrose oil.¹⁹ There is preliminary evidence in humans that hangovers, withdrawal symptoms and the craving for alcohol may all be controlled by the administration of GLA.²⁰ There is evidence that PGE1 may be a key determinant of mood and that people may drink alcohol in order to maintain an appropriate PGE1 level in the brain.²¹ If this is correct, then raising PGE1

levels by nutritional means should produce a long-term reduction in the craving for alcohol and be a major contribution to rehabilitation of alcoholics.

SJOGREN'S SYNDROME

This is a chronic autoimmune inflammatory disorder, characterised by excessive dryness of the eyes, mouth and other mucous membranes. It is often associated with other inflammatory conditions, such as rheumatoid arthritis or lupus (SLE). Dryness of the eyes may severely damage the cornea, and a lack of tears can cause permanent eye damage.

In a randomised, double blind, controlled, clinical trial involving 40 patients, the effects of oral omega-6 supplementation on the level of PGE1 in tears and the signs and symptoms of ocular discomfort in patients with Sjogren's syndrome was investigated. They were divided into two groups and were administered either 112 mg omega-6, providing 15mg GLA, twice daily; or with placebo, and were treated for 1 month. Tear PGE1 levels were significantly increased in the omega-6 group, correlating to a statistically significant reduction of symptom score. Also the corneal stain showed a significant improvement, demonstrating protection to the cornea within one month of supplementation. The authors concluded that omega-6 administration increases anti-inflammatory PGE1 levels in tears of patients with Sjogren's Syndrome and improves ocular surface signs and symptoms of ocular discomfort.²²

DOSAGE

As an indication, anti-inflammatory effects have been found at doses of 2.8 grams GLA daily over 6-12 months in rheumatoid arthritis patients. (approximately 28.0 grams Evening Primrose Oil daily)²³

CONTRAINDICATION²⁴

- **Phenothiazides:** several case reports suggest EPO may reduce seizure threshold and reduce drug effectiveness in patients with schizophrenia treated with phenothiazides
- **Epilepsy.** (See note above)

CAUTIONS

As Evening Primrose has an anti-thrombotic effect, we recommend the following cautions:

- **Oral Anticoagulants.**
- **Antiplatelet drugs:** concomitant use with EPO may theoretically increase bleeding time, however enhanced antiinflammatory effects are possible making this a beneficial interaction.
- **Surgery:** suspend high doses 1 week prior to major surgery

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