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# **Evening Primrose Oil**

Scientific Name(s): Oenothera biennis L.

Common Name(s): Common evening primrose, Evening primrose

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Overview Family Dosage Pregnancy Interactions Side effects

### Clinical Overview

#### Use

Evidence suggests that evening primrose oil may be effective for treating rheumatoid arthritis, injection site skin reactions, and diabetic neuropathy, but is lacking to support its place in the treatment of atopic eczema/dermatitis syndrome, menopausal vasomotor symptoms, mastalgia, or multiple sclerosis. In combination with vitamin D, evening primrose oil has improved glycemic and lipid profiles in women with gestational diabetes.

### **Dosing**

Evening primrose oil has been administered orally in clinical trials at doses between 1 and 8 g/day in adults and 2 and 4 g/day in children. The typical content of gamma-linolenic acid (GLA) in the oil is 8% to 10%.

#### **Contraindications**

No contraindications have been identified.

## **Pregnancy/Lactation**

Information regarding safety and efficacy in pregnancy and lactation is lacking. A case report exists of transient petechiae in a newborn following oral and intravaginal use of evening primrose oil for cervical ripening for a week prior to the infant's birth. Both linoleic and GLA are normally present in breast milk, and it is reasonable to assume that evening primrose oil may be taken while breast-feeding.

#### Interactions

See Drug Interactions section.

### **Adverse Reactions**

Evening primrose oil was previously suspected to lower the seizure threshold in schizophrenic patients; however, this is now disputed.

## **Toxicology**

No toxicity, carcinogenicity, or teratogenicity has been reported.

## **Scientific Family**

• Onagraceae

## **Botany**

The evening primrose is a large, delicate wildflower native to North America with blooms usually lasting only 1 evening, but it is not a true primrose. Primrose is a yellow-flowered annual or biennial and can grow from 1 to 3 m in height. The fruit is a dry pod approximately 5 cm long that contains many small seeds.1, 2, 3

## Chemistry

Seeds from O. biennis contain 14% of a fixed oil known as evening primrose oil that can contain 50% to 70% *cis*-linoleic acid and 7% to 10% *cis*-GLA. Wild varieties of O. biennis contain highly variable amounts of linoleic acid and GLA; however, extensive crossbreeding has produced a commercial variety that consistently yields oil with 72% *cis*-linoleic acid and 9% GLA.2, 3 Also found are *cis*-6,9,12-octadecatrienoic acid; small amounts of oleic, palmitic, and stearic acids; steroids; campesterol; and beta-sitosterol. Mucilage and tannin in the plant parts have been analyzed.2

## **Uses and Pharmacology**

Essential fatty acids are important as cellular structural elements and as precursors of prostaglandins. Essential fatty acids are the biologically active parts of polyunsaturated fats that cannot be manufactured by the body and must be provided by the diet in relatively large amounts.(2) Recommended intake of linoleic acid and alpha-linolenic acid are 12 g and 1.1 g, respectively, for women 19 to 30 years of age.(4)

In theory, the GLA provided by evening primrose oil can be converted directly to the prostaglandin precursor di-homogamma-linolenic acid and might be beneficial to individuals unable to metabolize *cis*-linoleic acid to GLA or those with low dietary intake of *cis*-linoleic acid. However, this relationship was not proven in a pharmacokinetic study in healthy participants.(5)

## Atopic dermatitis/Dermatologic disorders

#### Clinical data

Atopic eczema/dermatitis syndrome has been recommended by an international task force to encompass all forms of eczema, including atopic dermatitis.(67) A number of reviews and randomized clinical trials show a lack of support for the use of evening primrose oil for atopic dermatitis.(6, 7, 8, 9) Many of the trials are of poor quality and have apparent issues of bias.(9, 10, 11) In 2013, a Cochrane review evaluated 19 placebo-controlled, randomized clinical trials conducted in adults and children that assessed evening primrose oil for the treatment of signs and symptoms of eczema. Meta-analyses conducted with 7 studies using participant-reported improvements (n = 176) and 8 using physician-assessed improvements (n = 289) support previous reports of the lack of effectiveness of evening primrose oil.(67)

While an older review suggested promising results(12) the most comprehensive meta-analysis to date did not establish efficacy.(10) Clinical studies continue to be conducted, with a gradual time-dependent improvement suggested.(13)

### Cardiovascular disease

There is no recent evidence to support older studies(38, 39, 40) suggesting that evening primrose oil reduced platelet aggregation. An observational study suggests serum linoleic acid may protect against ischemic stroke.(41) Despite limited older trials in humans and numerous studies using rats and rabbits, there are no recent randomized, controlled trials demonstrating a beneficial effect of evening primrose oil on cholesterol levels or serum lipids. A more recent randomized, controlled trial found no effect on endothelial function or vascular tone with evening primrose oil supplementation.(42)

### Diabetic neuropathy

A review of 3 randomized, controlled trials suggested evening primrose oil might improve symptoms of diabetic neuropathy. Dosages in these trials ranged from 360 to 480 mg GLA daily. Few adverse effects were noted in these trials, and there was no increase in blood glucose levels.(43, 44)

As a component of medical nutrition therapy for patients with type 2 diabetes, the American Diabetes Association Standards of Care (2014) recommends higher quality dietary fat intake, as an alternative to decreased fat intake, by replacing saturated and/or trans fats with mono- and poly-unsaturated fatty acids in the diet. This Mediterranean-style approach to eating may improve glycemic control and cardiovascular disease risk factors (moderate-quality evidence). (69)

### Dyslexia/Brain development

Current interest in the use of evening primrose oil for enhancing intellectual performance in children is yet to be validated by rigorous research. Studies conducted in children with dyslexia suggest improved reading, spelling, and behavior(45, 46) while a Cochrane systematic review and a long-term study (39 months) showed no long-term benefit in infants fed formula supplemented with long-chain polyunsaturated fatty acids.(47, 48) An open study found benefit with the use of a fish oil and evening primrose oil combination in children with dyslexia.(49)

## **Eye conditions**

Study results disagree as to the effect of evening primrose oil on dry eye syndrome(37, 50, 51) and there is concern regarding high intake of linoleic and linolenic acid and the risk of cataract development.(52, 53)

#### Gestational diabetes mellitus

A prospective, double-blind, randomized placebo-controlled trial in 60 Iranian women with gestational diabetes mellitus investigated the effect of vitamin  $D_3$  (1,000 units) plus evening primrose oil (1,000 mg) on insulin resistance and lipid parameters. When compared to changes seen with placebo, supplementation with vitamin D and evening primrose oil for 6 weeks produced significant improvements in vitamin D levels (-0.1 vs + 6.9 ng/mL, P < 0.001); fasting plasma glucose (-3.6 vs + 1.5 mg/dL, P = 0.04); serum insulin concentrations (-2 vs + 4.6 microunits/mL, P = 0.004); homeostasis model of assessment-insulin resistance (HOMA-IR; -0.5 vs + 1.1, P = 0.003); HOMA-beta-cell function (-7.7 vs + 17.4, P = 0.007); triacylglycerol (-20 vs + 34.3 mg/dL, P < 0.001); very low-density lipoprotein (-4 vs + 6.9 mg/dL, P < 0.001), low-density lipoprotein (-18 vs + 1.8 mg/dL, P = 0.001), and total cholesterol (-22.1 vs + 5.3 mg/dL, P < 0.001); as well as the ratio of total to high-density lipoprotein (HDL) cholesterol (-0.3 vs + 0.3 mg/dL, P < 0.001). Changes in mean weight (P = 0.75), body mass index (P = 0.52), and HDL-cholesterol (P = 0.13) were not found to be significantly different between groups. Quantitative Insulin Check Index (P = 0.007) was found to be significantly different between groups.

## Hyperpigmentation

Topical application of saponified evening primrose oil reduced ultraviolet B-induced hyperpigmentation, while a decrease

in melanin production has been demonstrated in vivo with the saponified oil.(54)

#### **Inflammation**

Local injection-site reactions after subcutaneous injections of 5-azacitidine and bortezomib have been reduced with topical application of evening primrose oil.(55, 66) Additionally, the time to complete resolution of bortezomib-induced skin reactions was shortened (median, 4 days).(66)

### **Mastalgia**

#### Clinical data

There is little evidence to support the efficacy of evening primrose oil in treatment of mastalgia, with most trials finding no advantage over placebo. (14, 15, 16, 17) Although 23% taking evening primrose oil experienced a complete response in a small randomized, comparator trial (n = 135) after 6 months of therapy, this response was statistically significantly less than the group receiving the study drug Centchroman, a novel nonsteroidal selective anti-estrogen oral contraceptive, which showed an 86% response (P < 0.05).(65) A meta-analysis of clinical trials found no evidence of effect in pain relief, with a mean pain score difference of -2.78 (95% confidence interval, -7.97 to 2.4).(18)

### Menopause-associated vasomotor symptoms/premenstrual syndrome

#### Clinical data

A number of reviews and randomized clinical trials found no evidence of benefit with evening primrose oil use for menopausal vasomotor symptoms or premenstrual syndrome. (19, 20, 21, 22, 23, 24, 25) In 2004, the North American Menopause Society did not support the use of evening primrose oil for menopausal vasomotor symptoms given the lack of efficacy data, but this has not been recently reviewed. (26) The Society of Obstetricians and Gynaecologists of Canada's revised clinical practice guidelines (2021) on managing menopausal vasomotor symptoms do not recommend evening primrose oil based on a lack of evidence to support clinical benefit. (71) A 2013 randomized, double-blind, placebo-controlled trial in 56 menopausal treatment-naïve Iranian women (with at least 4 hot flashes a day) documented significant changes from baseline for hot flash severity, but not in their frequency or duration, in those randomized to receive 1,000 mg/day evening primrose oil extract for 6 weeks. Additionally, 3 Hot Flash Related Daily Interference Scale subscores improved significantly: social activity, relations with others, and sexuality. Mild self-limiting nausea was reported in 2 women in the intervention group. (68) The North American Menopause Society position statement for nonhormonal management of menopause-associated vasomotor symptoms (2015) notes that evening primrose oil is ineffective for hot flashes based on the single trial identified (Level II). (72)

## Multiple sclerosis

#### Clinical data

Despite a seemingly valid theoretical basis for the use of evening primrose oil in multiple sclerosis, there is a lack of evidence to substantiate its use.(27) A review of 3 trials suggested an effect with a slower progression of disability and improved relapse (severity and duration) scores, but a randomized, controlled trial, not included in the review, showed no effect.(28, 29, 30, 31, 32) No new trials have been published since the 1980s.

## Myalgic encephalomyelitis (chronic fatigue syndrome)

A theoretical model has been proposed for a place in therapy for evening primrose oil in this condition. Clinical trials are lacking.(56)

#### Rheumatoid arthritis

#### Clinical data

A Cochrane review of randomized trials comparing evening primrose oil with placebo suggests some benefit in using evening primrose oil for rheumatoid arthritis, despite the relative poor quality of the individual studies. A trend toward reduction of morning stiffness and joint tenderness, as well as pain relief, has been shown. The authors found the evidence to be sufficient to warrant further larger trials to provide conclusive results and define optimal dosage and duration of therapy.(34) These findings are supported by other reviews, especially with regard to effective duration of therapy.(35, 36) A more recent randomized, double-blind, placebo-controlled study enrolling 90 patients with primary Sjögren syndrome found no statistically significant in patient fatigue with a higher dosage after 6 months of therapy.(37)

#### **Urolithiasis**

An exploratory study found an increase in urinary citrate excretion following 1,000 mg/day of evening primrose oil.(57)

## **Dosing**

Evening primrose oil has been administered orally in clinical trials at doses between 6 and 8 g/day in adults and 2 and 4 g/day in children. Wide-ranging doses of 0.27 g to 6.48 g GLA per day have been used in clinical studies in mastalgia.24 The typical content of GLA in the oil is 8% to 10%.2

Evening primrose oil 1 g/day in combination with vitamin  $D_3$  (1,000 units/day) has been used to improve glycemic and lipid profiles in women with gestational diabetes.70

## **Pregnancy / Lactation**

Information regarding safety and efficacy in pregnancy and lactation is lacking. Both linoleic and GLA are normally present in breast milk, and it is reasonable to assume that evening primrose oil may be taken while breast-feeding. A case report exists of transient petechiae in a newborn following oral and intravaginal use of evening primrose oil for cervical ripening for a week prior to the infant's birth. In vitro and in vivo animal studies suggest inhibition of platelet function in the newborn may have been caused by exposure to evening primrose oil.58

According to state-wide surveys in California, Texas, and North Carolina, evening primrose oil was one of the most common herbs used by certified or licensed midwives for labor induction.73

## **Interactions**

Lithium: Evening primrose may decrease the serum concentration of lithium. Monitor therapy. (59)

Lopinavir: Evening primrose may increase the serum concentration of lopinavir. Monitor therapy. (60)

1 Evening Primrose Oil drug interactions (more detail)

## **Adverse Reactions**

Two clinical studies conducted in the 1980s among individuals with schizophrenia led to a concern that evening primrose oil might lower the seizure threshold. However, other factors may account for the observed seizures: the few participants who developed seizures were taking concomitant medicines (phenothiazines) known to lower the seizure threshold, and

also a link has been described between schizophrenia and epilepsy. There are no further reports of seizures related to evening primrose oil, which may actually have a protective effect.63

A case report of lipoid pneumonia secondary to long-term evening primrose oil use exists.64

There is no recent evidence to support older studies suggesting that evening primrose oil reduced platelet aggregation.38, 39, 40

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## **Toxicology**

Animal toxicological studies and extensive use of evening primrose oil over many years revealed no data of concern. As a nutritional supplement, the maximum label-recommended daily dose of evening primrose oil is approximately 4 g, containing 300 to 360 mg of GLA.2

## References

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### **Further information**

Always consult your healthcare provider to ensure the information displayed on this page applies to your personal circumstances.

Medical Disclaimer

#### **DRUG STATUS**

**Availability** 

**OTC** Over the counter

**CSA Schedule\*** 

N/A Not a controlled drug

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