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## **Supplementation of evening primrose oil- benefits and limitations. Results of the latest studies**

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## **Abstract**

### **Introduction**

One of the most frequently used herbal drugs in the pharmaceutical industry is *Oenothera biennis*, traditionally called evening primrose. Oil extracted from seeds of a plant is a rich source of unsaturated fatty acids- omega 6 essential fatty acids (EFAs). Healing properties of evening primrose oil (EPO) have been used for ages in order to alleviate symptoms of various medical conditions. Nowadays, studies and clinical trials are conducted with the aim of verifying its effectiveness.

### **The aim of the study**

Summarize current knowledge on the effectiveness of evening primrose oil in treatments of various diseases.

### **Material and methods**

The search of the Pubmed database was carried out using keywords, in order to find the latest publications.

### **Summary**

Despite limitations, research shows that supplements containing evening primrose oil (EPO) demonstrate promising results in treatments of various medical conditions, including menopause, premenstrual syndrome, skin problems or multiple sclerosis. However, more well-designed clinical trials are needed to evaluate long-term effectiveness.

**Keywords:** supplements; evening primrose oil (EPO); herbal medicine

## **Introduction**

Healing properties of various herbs have been known for ages. At first the use of them was discovered through trial and error methods and handed down from generation to generation. Nowadays, along with the development of science, clinical trials and studies are conducted in order to prove their effectiveness.

Despite the significant medical advancement in the field of pharmacology, relying on herbal medicinal products as a source of healthcare is widespread. Moreover, the use of plants as products of treatment is a relevant component of the cultural heritage of various communities.

According to the World Health Organization (WHO), nearly 80% of the world's population is dependent on herbal products as a source of natural therapies. [1],[2]. In regard to the aging population and increasing costs for the health system, medical plants can provide economical benefits. [2]

Latterly, the currency of herbal supplements has increased. It is believed that herbal medicinal products promote a healthy lifestyle and have moderate impact on the organism. Nevertheless, the awareness of the potential adverse outcomes remains limited due to the insufficient tests and lack of suitable monitoring. [1]

Various plants have many applications in the pharmaceutical industry. One of the most frequently used is *Oenothera biennis*, traditionally called evening primrose. This herb is also known as tree primrose, sun cups, sundrops, king's cure-all, fever plant, evening star, and night willow-herb. [3] The plant is characterized by its yellow flowers, blooming in the evening.[4] Originally, it occurred naturally in North, Central and South America- now is widespread through Europe and Asia.[2][3][5][6] Natives used its stem and leaf juices as the treatment of cutaneous conditions and wounds. [3] Nowadays, the efficiency of supplements including *O.biennis* have been analyzed as agents supporting treatments of various diseases, such as multiple sclerosis, rheumatoid arthritis, diabetic neuropathy, Sjogren's syndrome, atopic eczema, psoriasis, premenstrual syndrome, mastalgia, menopause. [4][7][8] Even the impact of evening primrose on labor induction and cervical ripening was investigated, but without effective results .[9]

Currently, the pharmaceutical industry extracts oil from seeds of *O.biennis* in order to acquire evening primrose oil- EPO. An oil is a rich source of unsaturated fatty acids- omega 6 essential fatty acids (EFAs)- including linoleic and gamma-linoleic acids (GLAs). [3][4]

EPO contains 65-80% of linoleic acid, 8-14% of gamma-linoleic acid, 7-10% of palmitic acid, 6-11% of oleic acid and 1,5-3,5% of stearic acid.[2][10] GLAs are known for their anti-inflammatory activities and decreasing impact on the synthesis of prostaglandins.[3] [11][12] Scientists analyze anti-inflammatory and anti-oxidative properties of leftovers after seed harvesting, such as defatted seeds or aerial parts of evening primrose and the results seemed to be promising.[5] EPO is considered as a safe supplement- presents minor interactions with other drugs and minor adverse side effects, such as headaches, abdominal pain, indigestion, nausea, softening of stools.[3]

EPO and menopause

According to the World Health Organization (WHO), natural menopause is considered to have occurred after 12 months without menstruation due to the loss of ovarian follicular function and applies to women between ages 45 and 55 years. Along with increasing life expectancy, more than one-third of women's lives have occurred after menopause. Menopausal symptoms affect about 74% to 80% of women and disturb the quality of life. Among them the most common are hot flashes, night sweats, sleep disorders, fatigue, restlessness, lack of concentration, palpitations, joints pain, vaginal dryness, dyspareunia and urinary symptoms.[4][13] Multiple clinical trials have been conducted concerning menopausal conditions and using of evening primrose oil.

Farzaneh *et al.* assessed 56 women applying 500mg EPO capsule or placebo in a randomized, double blind, placebo-controlled trial. Frequency, severity and duration of hot flashes were elaborated with Hot Flash Related Daily Interference Scale (HFR-DIS)- within 6 weeks severity percent decreased. [7][14] Mehrpooya *et al.* got to similar results regarding severity of hot flashes in their clinical research- measurements with the aid of the Menopause-Specific Quality of Life (MENQOL) questionnaire verified the reducing effect of EPO.[15] Another study by Kazemi *et al.* reveals that EPO mitigates the frequency and severity of night sweats.[13]

There are also publications suggesting positive impact of EPO on the psychological symptoms of menopause- depressed mood, irritability, anxiety and mental exhaustion. [4][16]

#### EPO and premenstrual syndrome

Premenstrual syndrome (PMS) is a condition, which is related to psychological and physical aspects of women's life. Roughly 150 unspecific symptoms are reported by menstruating women, including mood swings, anxiety, breast tenderness, abdominal bloatings or headache [17]. Due to the multiplicity of symptoms, finding the proper treatment is a struggle. Several randomized placebo-controlled clinical trials were performed in order to evidence the alleviative properties of medical herbs, including evening primrose. [7][17] Early meta-analysis showed ineffectiveness of EPO in relation to the treatment of premenstrual syndrome. Limitations of these studies arise from lack of sufficient sample sizes in clinical trials.[7][18] Nevertheless, in subsequent clinical trials the efficacy and safety of evening primrose oil was observed. In randomized double-blind placebo controlled parallel design patients received edible oil with or without  $\gamma$ -linolenic acid. The severity and duration of PMS improved in the  $\gamma$ -linolenic acid group compared to the placebo group. Similar results were observed in another placebo randomized control trial- after three months of

receiving 1,5g of EPO daily, PMS severity score reduced.[7] Given above information, more studies on larger clinical control groups should be conducted.

#### EPO and labor induction

Meta-analyses published in 2021, were aimed at investigating the effect of evening primrose oil on labor induction and cervical ripening. Studies concentrated on differences between EPO and placebo groups in terms of Bishop score, cesarean section and duration of stages of labor. Due to the high heterogeneity of the studies and their outcomes, the effectiveness of EPO on this subject requires further investigation. [9][19][20]

#### EPO and skin condition

Linoleic acid (LA) and  $\gamma$ -linolenic acid (GLA), components of evening primrose oil, are part of the ceramides of the epidermal lipid layer of the skin. Due to its quality, EPO supports processes of keratinization, hydration and acts anti-inflammatory.[21] The beneficial effect of this compound was observed during acne vulgaris treatment with isotretinoin. Despite its positive effect on skin condition, treatment with isotretinoin presents a wide range of side effects, such as leukopenia, erythropenia, decreased hematocrit, increased transaminase activity, increased cholesterol, LDL-cholesterol and triacylglycerols, teratogenicity, osteoarthritis, weight gain, dry skin, erythema, hair loss and cheilosis. Clinical trials demonstrated that combination of isotretinoin with EPO contributes to increased skin hydration and has an impact on lipid profile and levels on transaminases.[21][22]

Results of studies show that oral intake of EPO is not effective treatment of symptoms of atopic eczema- outcomes in clinical trials were similar in placebo and EPO groups.[23]

However, Korean researchers propose to use limited EPO as the adjuvant therapy in treatment of atopic dermatitis and regard it as low-risk medicine. [24][25]

#### EPO and multiple sclerosis

A study by Majdinasab *et al.* revealed that EPO had no impact on preventing the progression of multiple sclerosis (MS). However, the use of EPO had an effect on several aspects of quality of life of MS patients: increase of cognitive function, vitality and overall satisfaction with life. In comparison to the placebo group, in the experimental group, taking 1g oral capsule of EPO for 3 months in addition to the standard treatment, decrease of pain and fatigue was observed.[2]

## EPO and fertility

Nowadays, decreased fertility rate has become a serious global problem and is caused by many factors, including medical condition or lifestyle. Preconception dietary supplementation is now an increasingly common approach among women trying to conceive. Study by Chee Wai Ku *et al.* has shown that time to pregnancy (TTP) was shortened in groups with folic acid and iodine supplements intake than in non-users groups. In comparison to these results, EPO users were associated with longer TTP. Given the small proportion of EPO users in this study, the impact of EPO on fecundability should be taking under further investigation.[26]

## Summary

Herbal supplements on the basis of evening primrose oil have been put to use in various treatments for ages. Nowadays, along with the development of science, clinical trials and studies are conducted in order to prove their effective therapeutic potential. Despite limitations, EPO supplements seem to have a positive influence on alleviating symptoms of diverse medical conditions, such as menopause, premenstrual syndrome, skin problems or multiple sclerosis. Although EPO is considered as the safe medical product, further research on potential adverse effects needs to be conducted. Due to the lack of long-term follow-up of patients and small sizes of studies, well-designed clinical trials should verify effectiveness and define dosing standards of EPO.

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