



Review Article

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The Effect of Evening Primrose Oil (EPO) On Benign and Malignant Breast Disorders: A Mini Review



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Abstract

Benign and malignant breast disorders are among the most common disorders affecting men and especially women in the world. Benign breast disorders include mastalgia, mastitis, breast abscess, breast cyst, fibrocystic breast changes, and nipple discharge. Although benign breast disorders are very common among women, the importance of breast examinations refers to malignant disorders or breast cancer. Among the methods of prevention and treatment of breast disorders, the use of herbal medicine and herbal compounds is notable. Evening primrose (EP) is one of the effective plants with antioxidant and anticancer properties that is effective in both benign and malignant breast disorders by modulating inflammation and pain in the breast tissue. This article, for the first time, emphasizes the anti-inflammatory and pain-modifying properties of evening primrose oil (EPO) and provides a brief overview of breast disorders and how EPO can manage inflammation and pain in breast tissue.

Keywords: Breast; Cancer; Evening primrose; Gamma-Linolenic acid; Lactational mastitis

Abbreviations: AA: Arachidonic acid; COX: Cyclooxygenase; EP: Evening primrose; EPO: Evening primrose oil; EFAs: Fatty acids; GLA: Gamma-linolenic acid; LT: Leukotrienes; LA: Linoleic acid; LOX: Lipoxygenase; PGE1: Prostaglandin E1

Introduction on Breast

Diseases associated with the abnormal growth of cells in the body, known as tumors and cancers, pose significant challenges in healthcare, and their prevalence and impact on global health are steadily increasing [1,2]. In the following are some of the most important breast disorders.

Breast Inflammation

Mastitis refers to inflammation of the breast. If it occurs in lactating women, it is called lactational mastitis. Clinical signs include a localized erythematous area that is warm, firm, painful, and tender to the touch. It is often unilateral. Diagnostic tests include breast milk culture, mammography, and ultrasound. Mastitis is treated with antibiotics, analgesics, and antipyretics drugs [3].

Breast Abscess

A breast abscess is a localized collection of pus in the breast during lactation caused by *Staphylococcus aureus* and *Streptococcus* species. The skin over the breast may become red and swollen, a palpable mass, and fever may be present. Drainage of the abscess may be done with ultrasound guidance or surgical incision and drainage [4].

Breast Cysts

Cysts are fluid-filled sacs in the breasts of premenopausal women between the ages of 35 and 50. They develop because of hormonal changes caused by monthly menstruation, when increased estrogen in the body stimulates breast tissue, leading to the formation of breast cysts, and are almost always benign. After

menopause, cysts are less common and do not increase the risk of breast cancer [5]. Clinical manifestations include a palpable fluid-filled mass, a round or oval movable mass, soft tissue like a grape or balloon filled with water, but sometimes a hard, clear, yellow or dark brown discharge may be released from the nipple. Cysts are diagnosed with a breast ultrasound and/or fine needle aspiration. They usually do not require treatment. Taking herbs such as Evening Primrose (EP) relieve pain by reducing inflammation in breast Cysts [6].

Breast Cancer

Cancer is the abnormal growth of cells in the body with the potential to invade or spread to other parts of the body. Possible signs and symptoms include mass, abnormal bleeding, a persistent cough, unexplained weight loss, and inflammation. Inflammation is often a sign of cancer progression [7]. The cells responsible for causing inflammation at the site of cancer are genetically stable and therefore not subject to the rapid emergence of drug resistance. Inflammation in cancer includes intrinsic and extrinsic inflammation, whereas extrinsic inflammation is driven by many factors, including bacterial and viral infections, autoimmune diseases, obesity, smoking, and excessive alcohol consumption, that promote cancer progression [8].

In contrast, intrinsic cancer inflammation is driven by cancer-initiating mutations and contributes to cancer progression by activating inflammatory cells. The result of both extrinsic and intrinsic inflammation is suppression of the immune system and cancer progression. Therefore, targeting inflammation is an important strategy in the prevention and treatment of malignant cancers such as breast cancer, as well as fibrocystic breast changes, the most common benign lesion presenting with breast pain (mastalgia) [9,10].

Mastalgia

Benign breast disorders are noncancerous disorders of the breast. The breast is composed of ductal, glandular, fibrous, and fatty tissue that changes or regresses throughout a woman's life depending on the levels of the hormone's estrogen and progesterone. Common breast imaging tests include mammography, ultrasound, and MRI, which are a standardized system for performing breast imaging examinations, interpreting findings, reporting results, providing recommendations to patients and providers, and auditing between BI-RADS 0 scores [11].

Mastalgia is defined as breast pain that may be cyclical or noncyclical. It is the most common breast complaint in women. Approximately 60 to 70 percent of women experience some degree of mastalgia, often accompanied by breast nodulation [12]. Because of its importance in the initiation of breast malignancies, we will first review the types of mastalgia before discussing its treatment [13].

Classification of Mastalgia

- Cyclical mastalgia: Breast pain 1 to 2 weeks before menstruation, diffuse and bilateral, with some radiating to the upper arm and armpit, and may vary in severity from bilateral to unilateral. The pain is related to hormonal sensitivity and resolves with the onset of menstruation [14].
- Noncyclical mastalgia, which is unrelated to the menstrual cycle and can persist until menopause; it is usually unilateral and localized and occurs in the 40s or 50s, often before menopause [15]. Symptoms include burning, aching, or aching in the breast. Various causes include cysts, periductal mastitis, stretching of Cooper's ligaments, traumatic fat necrosis, Mondor's disease, diabetic mastopathy, and neoplasia [12].
- Finally, nonbreast pain can resemble mastalgia. Causes of chest wall pain include costochondritis (Tietze's disease), radicular pain such as cervical spondylitis, and herpes zoster, which can cause pain like mastalgia [16]. Gynecological symptoms such as periodic breast pain, which are often chronic in nature, are more popular with herbal and natural supplements with fewer side effects than alternative therapies used as first-line treatment for periodic breast pain, including flaxseed, Evening primrose oil (EPO), and vitamin E [17]. We will review the effects of EPO on breast cancer in the following

Evening Primrose

Conventional treatments for inflammatory diseases often include the use of nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, immunosuppressants, or biologic agents [18]. However, due to the adverse effects of these treatments on the one hand, and the limited efficacy or high cost of treatment on the other, there is a need to explore alternative treatment options. The use of herbal medicines has been a strong and ever-present option since the early stages of cancer treatment. These medicines play a valuable role in the management of inflammatory diseases [19,20].

Also, in fibrocystic breast changes, where mastalgia causes concern and fear of breast cancer and as a result, excessive use of over-the-counter painkillers as well as inappropriate intervention, excessive mammography, and undesirable, ineffective, and unnecessary self-treatment, the use of herbal and nutritional supplements is often suggested as an alternative treatment for women with moderate to severe breast pain [21]. Given that natural compounds have also been used in anti-inflammatory diseases [22]. In this study, we investigated the effects of EPO, derived from the seeds of *Oenothera biennis*, on breast cancer progression, due to its potential therapeutic effects.

Evening Primrose and Inflammation

EPO is a non-hormonal drug rich in essential fatty acids (EFAs), including linoleic acid (LA) and gamma-linolenic acid (GLA),

which are precursors of anti-inflammatory substances in the body [1]. GLA is metabolized to prostaglandin E1 (PGE1), which

is a potent anti-inflammatory mediator and leads to modulation of immune responses and reduction of inflammation (Figure 1).

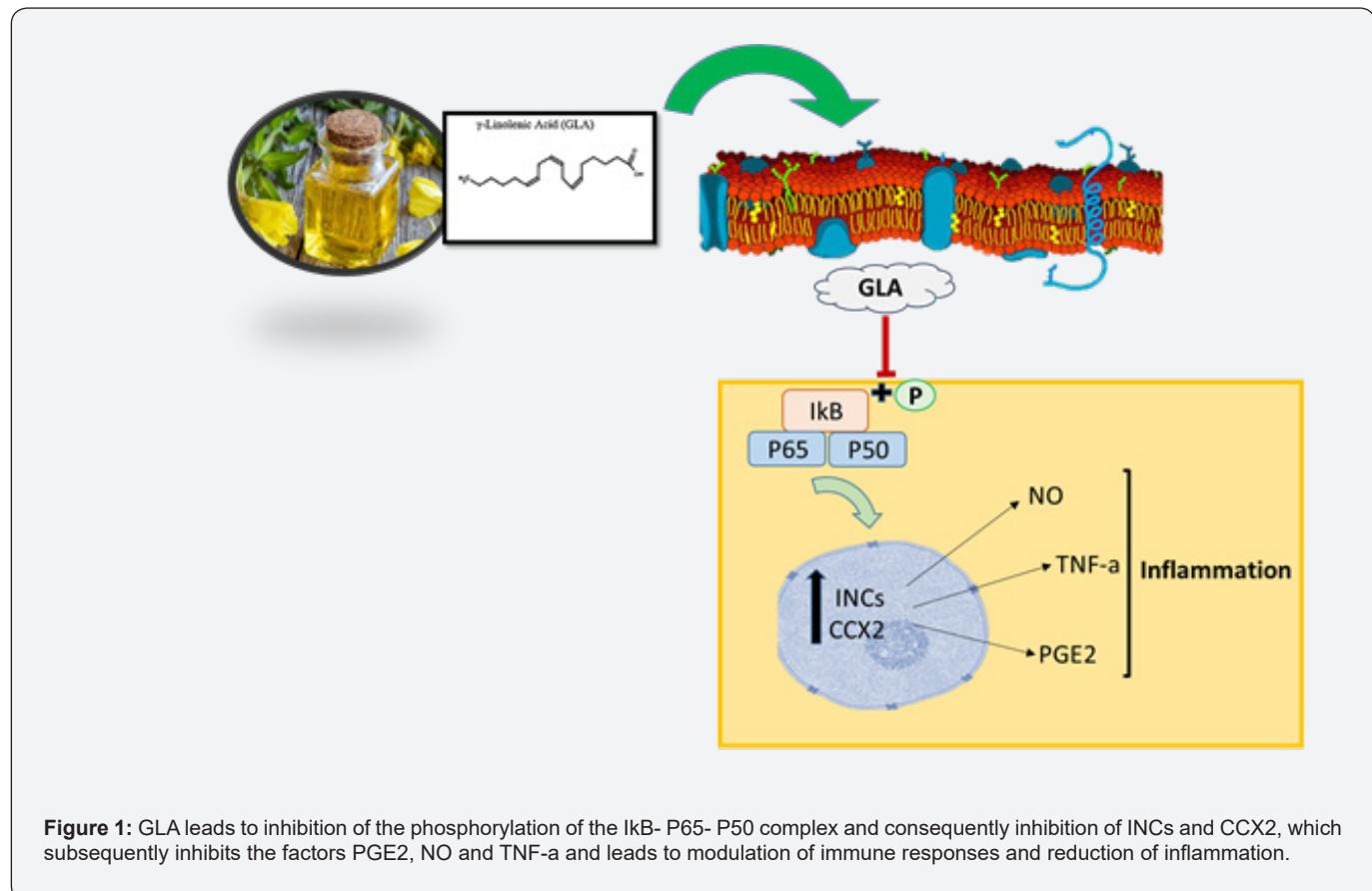


Figure 1: GLA leads to inhibition of the phosphorylation of the IkB- P65- P50 complex and consequently inhibition of INCs and CCX2, which subsequently inhibits the factors PGE2, NO and TNF- α and leads to modulation of immune responses and reduction of inflammation.

In addition, EPO contains other bioactive compounds such as flavonoids and phenolics, which have antioxidant and anti-inflammatory properties [23]. Among the polyphenols and flavonoids identified in EPO in previous studies were gallic acid, caffeic acid, epicatechin, coumaric acid, ferulic acid, rutin, and rosmarinic acid [24]. It has also been shown that EPO components exert anti-inflammatory activity by inhibiting lipoxygenase (LOX) and cyclooxygenase (COX), two pro-inflammatory enzymes that synthesize vasoconstrictors (e.g., leukotrienes (LT), prostaglandins (PG)) from arachidonic acid (AA) [25].

Evening Primrose and Mastalgia

GLA is 7% to 14%, which prevents the synthesis of PG that potentially causes breast pain [26]. A study by Elvandipour et al. [27] in Iran on mastalgia showed that taking EPO 2 grams per day, and vitamin E 400 units per day, after 6 months of intervention led to a reduction in periodic mastalgia. Also, according to the study by Mirghafurvand et al. [28] the average duration of breast pain is reduced with the consumption of EPO. Therefore, it can be analyzed that due to the reduction in plasma levels of essential EFAs such as GLA and precursors of the PGE1 class in women with periodic breast pain, supplements containing GLA such as EPO

can be used in the treatment of breast pain [16].

However, the results of the Salehi et al. [29] on study showed that the effect of EPO on periodic mastalgia was less compared to vitamin E. In this study, they consumed EPO capsules (three 322 mg capsules daily) and in the control group, one 400IU vitamin E capsule daily for two months. Due to the shorter duration of treatment, it is possible that EPO requires a longer treatment period than vitamin E to be effective. Kataria et al. [30] In their review, Ney concluded that injections of an LHRH analog (Goserelin) were more effective in treating mastalgia than vitamins, diuretics, EPO, and obsolete gamolenic acid.

Conclusion

Based on the results of this review, EPO reduces the duration of breast pain. This herbal remedy, which is the richest source of omega-3 essential EFAs, contains phytoestrogens, lignans, and antioxidants, has few side effects, and leads to a reduced risk of breast cancer. The most important mechanism of action of EPO is through GLA, which plays a role in both modulating inflammation and thus controlling malignant breast cancer, and in reducing pain in benign breast lesions.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conflict(s) of Interest

None, the authors declare no competing interests.

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Ethical Statements

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Author Contributions

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