Effects of Soy Isoflavones and Evening Primrose Oil on Female Aging and Diseases

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Abstract. Functional dietary factors play a crucial role in influencing the process of aging and the development of various diseases, especially in women. Among the plethora of dietary components studied, soy isoflavones and evening primrose oil (EPO) have emerged as intriguing subjects due to their potential effects on female aging and the management of female-specific diseases. Soy isoflavones, phytoestrogens abundant in soybeans, have been studied for their potential role in mitigating age-related hormonal changes and associated health problems in women. Evening primrose oil, abundant in gamma-linolenic acid (GLA), has been researched for its potential benefits in addressing a range of women's health issues.This study aims to provide a comprehensive overview of the current understanding of the effects of soy isoflavones and evening primrose oil on female aging and female-specific diseases. By synthesizing findings from clinical trials, epidemiological studies, and mechanistic investigations, this paper endeavors to elucidate the significance of these dietary elements in enhancing women's health throughout their lives.

Keywords: Soy isoflavones; Evening primrose oil; Female health.

1. Introduction

The study of the influence of dietary factors on women's aging and health has received considerable attention these years as researchers explore the intricate relationship between diet and various aspects of women's well-being. Aging is associated with physiological changes, hormonal fluctuations, and an increased risk of chronic disease, making it imperative to explore dietary interventions that may mitigate these effects. Among the numerous dietary components that have been studied, soy isoflavones and EPO have emerged as promising candidates for their potential role in promoting women's health and managing female-specific diseases. Soy isoflavones, such as genistein and daidzein, are plant-derived compounds with structural similarity to estrogen, leading to investigations of their estrogenic effects and potential benefits for women's health [1]. Similarly, EPO, derived from seeds of the evening primrose plant, this plant contains GLA, an omega-6 fatty acid with anti-inflammatory and hormonal regulatory attributes [2]. Both soy isoflavones and evening primrose oil have been studied for their potential effects on menopausal symptoms, bone health, breast pain, and other women's health conditions. The aim of this study is to provide a synthesis of the current evidence on the role of soy isoflavones and EPO on female aging and female-specific diseases, with a focus on elucidating their mechanisms of action and potential clinical implications.

2. Female Aging and Related Diseases

A number of factors, including genomic instability, epigenetic modifications, impaired proteostasis, disrupted nutrient sensing, cellular senescence, altered intercellular communication, and telomere attrition, contribute to the onset of aging. Aging is a progressive, age-related physiological deterioration associated with increased susceptibility to cellular death or dysfunction [3]. Telomeres, located at the chromosome ends, consist of non-coding sequences essential for preserving genomic integrity by shielding chromosome ends from damage and fusion. With each cell division, telomeres undergo attrition, leading to cellular aging, disease, and death. Telomerase, a ribonucleoprotein enzyme with DNA polymerase activity, uses an RNA template to elongate telomeric repeats at

chromosome ends, thereby preventing chromosome attrition [4]. Telomerase is prominently active in stem cells; increased telomerase activity may retard chromosomal erosion.

Female aging is a complex physiological process involving gradual changes in multiple systems and organs. As women age, they experience several physiological and biochemical changes, including changes in hormone levels, decreased bone density, and changes in skin elasticity and muscle structure. These changes lead to a few age-related health issues, such as menopausal syndrome, osteoporosis, cardiovascular diseases, mastalgia, and polycystic ovary syndrome. Female aging is a multifaceted process that is closely associated with various health problems.

Menopause, characterized by a cessation of menstruation for at least 12 consecutive months due to a gradual decline in ovarian estrogen production, typically commences in the late 30s. By the mid-50s, most women undergo near-complete depletion of estrogen secretion. Projections suggest that the demographic of peri- and post-menopausal women, at risk of associated health issues, is anticipated to reach 1.2 billion worldwide by the year 2030 [5].

The natural aging process in menopausal women induces changes in skin characteristics, this is the most obvious feature. The expression of estrogen receptors within the dermal cellular compartment implies alterations in dermal cell metabolism due to decreased estrogen levels during menopause, thereby affecting collagen and glycosaminoglycan turnover. Reduced collagen synthesis correlates with decreased skin elasticity, while decreased glycosaminoglycans lead to compromised hydration and turgidity. Therefore, all these changes are fundamental manifestations of skin aging [6]. Aging in women can also lead to a variety of diseases. Soy isoflavones and evening primrose oil have been extensively studied for their role in preventing female aging and managing women's health issues. Supplementation with soy isoflavones and evening primrose oil may provide comprehensive health benefits for women, helping to prevent female aging and manage women's health issues, including skin aging, osteoporosis, and premenstrual syndrome.

3. Function and Mechanism of Soy Isoflavones and EPO

The impact of dietary functional ingredients on anti-aging and preventing diseases in women may be positive as they help fight free radical damage and slow down the cellular aging process. Soy isoflavones and evening primrose are the two major dietary functional components which can help women improve the aging and female diseases.

3.1. Soy Isoflavones

Isoflavones are phytochemicals found predominantly in numerous plants and seeds, with a wide distribution across different species within the Leguminosae family. Soy isoflavones consist primarily of three main isoflavones: daidzein, genistein, and to a lesser extent glycitein (isoflavone aglycones). The predominant natural form of isoflavones is as glycoside conjugates [7]. Soy isoflavones have been shown to have a variety of biological activities, including anti-inflammatory and antioxidant qualities as well as promise for preventing osteoporosis and coronary heart disease.

3.1.1 Antioxidant

Soy products and soy proteins represent significant sources of isoflavones, which possess both phytoestrogenic and antioxidant properties, potentially contributing to their cardioprotective effects. Additionally, research demonstrates that isoflavones actively scavenge free radicals, with the most active isoflavones in soy products, genistein and daidzein, demonstrating ROS quenching activity. It has been shown that genistein and daidzein protect DNA from oxidative damage and inhibit the synthesis of 8-hydroxy-2′-deoxyguanosine in cells. Furthermore, by boosting the activity of antioxidant scavenging enzymes and strengthening the antioxidant defense system, isoflavones may help to indirectly reduce oxidative damage in cells [8].

The existing literature provides evidence that increasing soy product intake significantly increases levels of glutathione, superoxide dismutase, total antioxidant capacity, and total radical trapping antioxidant parameter, while decreasing levels of malondialdehyde [9].

3.1.2 Anti-Aging

Skin deprived of estrogen, as observed in the postmenopausal women, shows a reduction in collagen, elastin, fibroblast activity and vascularity. In addition, increased cellular degradation results in, atrophy, wrinkling, dryness, and reduced resistance to oxidative stress, all of which contribute to the appearance of aging skin [10]. Having a greater attraction to ERβ, which is abundant in the cardiovascular tissues, skin and bone, soy isoflavones differ from the α-subtype, which is mainly found in reproductive and breast tissues. Documented effects of soy isoflavones include protection of skin tissue from lipid peroxidation, stimulation of fibroblast proliferation, and attenuation of collagen degradation. Isoflavones, beyond their estrogenic attributes, have been documented to exhibit scavenging capabilities and to ameliorate DNA damage. The structural resemblance of isoflavones to 17β-estradiol elucidates their potential in anti-aging interventions via interaction with estrogen receptors [11]. Irrespective of the stage of women's hormone fluctuations, premenopausal, perimenopausal, or postmenopausal, soy isoflavones act as a collective force.

According to Rizzo's research [12], the study's subjects' facial wrinkles, skin pigmentation intensity, and skin hydration were all significantly reduced in postmenopausal women who took a standardized multicomponent soy protein isolate with added isoflavones. Fitzpatrick skin types I, II, and III corresponded to the skin types of these women. In this study, calorie-matched casein without added isoflavones was contrasted with soy protein with added isoflavones (SPII). At weeks 16 and 24, they discovered that the SPII group's mean wrinkle severity had decreased by 5.9% and 7.1%, respectively. At weeks 16 ($p < 0.05$) and 24 ($p < 0.0001$), the SPII group's wrinkle severity was significantly lower than that of the casein group (Fig. 1). Furthermore, by week 24, the SPII group's mean hyperpigmentation severity had decreased by 2.4%. Additionally, at week 24, the SPII group's pigmentation intensity was considerably lower ($p < 0.05$) than the casein group's (Fig. 2). At week 24, the soy protein intervention group demonstrated a substantial increase in skin hydration in the patients' left and right cheeks, respectively, by 39% and 68% ($p < 0.05$) relative to baseline (Fig. 3). In contrast, the casein intervention group did not show any statistically significant changes.

It has been proposed that these connections might be somewhat strengthened by evaluating the effects of isoflavones and isolated soy proteins on skin health. Future studies may adopt a multidisciplinary approach to investigate the effects of soy isoflavones on postmenopausal women, given the skin-specific features of this class of phytoestrogens.

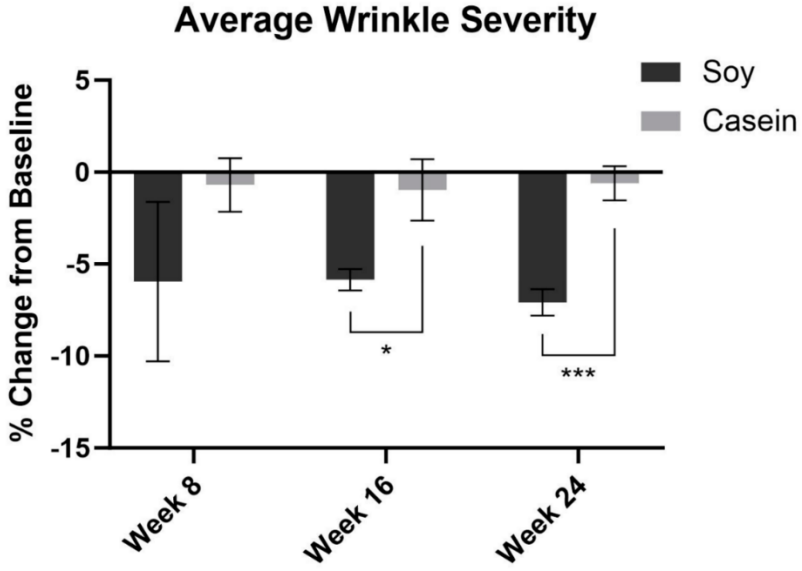

Fig. 1 Average wrinkle severity after treatment [12]

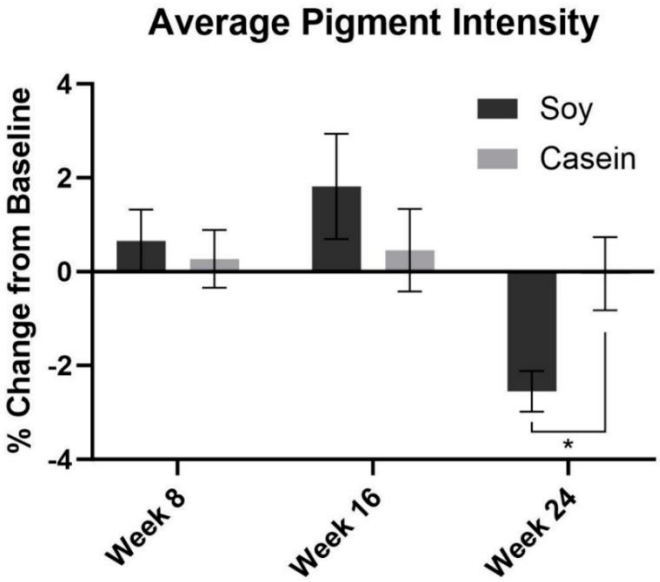

Fig. 2 Average pigment intensity after treatment [12]

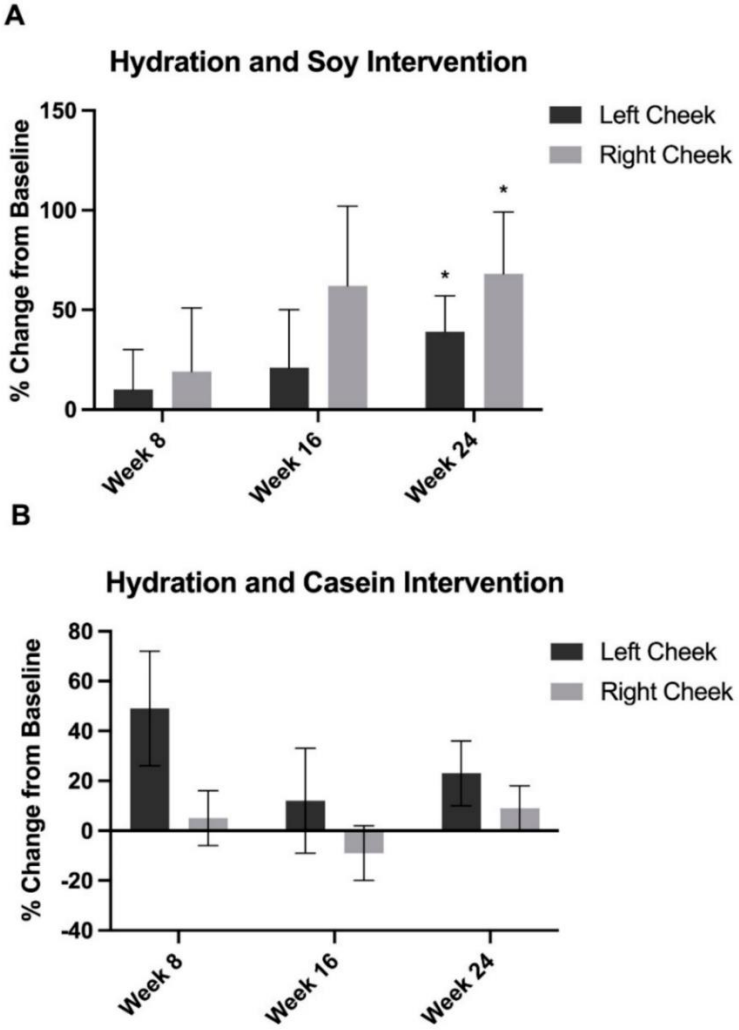

Fig. 3 skin hydration after treatment [12]

3.1.3 Osteoporosis

Osteoporosis is an orthopaedic disease characterized by progressive bone loss, which leads to a decrease in bone mass and density and changes in bone structure, thereby increasing the likelihood

of fractures. A major contributor to osteoporosis is a deficiency of certain hormones, particularly estrogen, which is particularly evident in menopausal women over the age of 50. Estrogen plays a crucial role in preventing the generation of osteoclasts, responsible for bone breakdown, while also promoting the activity of osteoblasts, responsible for bone formation [13].

Age-related bone loss is more prevalent in women than in men. According to relevant data, approximately 25-30% of older women develop serious orthopedic conditions. Whether natural or surgical, menopause leads to a rapid loss of bone mass, also known as the initial phase, followed by a phase of slow bone deterioration. This phase of accelerated bone deterioration usually occurs within the first decade after a woman stops menstruating or has her fallopian tubes surgically removed. Ovarian hormone deficiency that accompanies female menopause further increases the rate of bone turnover, creating an imbalance between resorption and formation, which accelerates bone loss [14].

Studies conducted recently have revealed that isoflavones may improve bone metabolism and increase bone mass. In order to evaluate the effect of isoflavone treatments on bone mineral density (BMD) in postmenopausal women, Ratchanon's study used a systematic review and meta-analysis. According to this meta-analysis, isoflavone treatments may be able to raise BMD at a number of skeletal locations, including the distal radius, femoral neck, and lumbar spine. Because these anatomical locations are prone to fracture in older adults with osteoporosis, they are frequently employed for BMD evaluation in clinical practice. According to BMD, this study discovered that isoflavone therapies greatly enhanced bone health in postmenopausal women. When the intervention lasted for 12 months or longer, the positive benefits were especially noticeable (Fig. 4). The best amounts of isoflavones differed depending on the skeletal site; doses greater than 400 mg/day increased BMD at every site examined. It has been discovered that genistein-containing interventions, administered at a minimum of 50 mg/day, are beneficial for enhancing bone health [15].

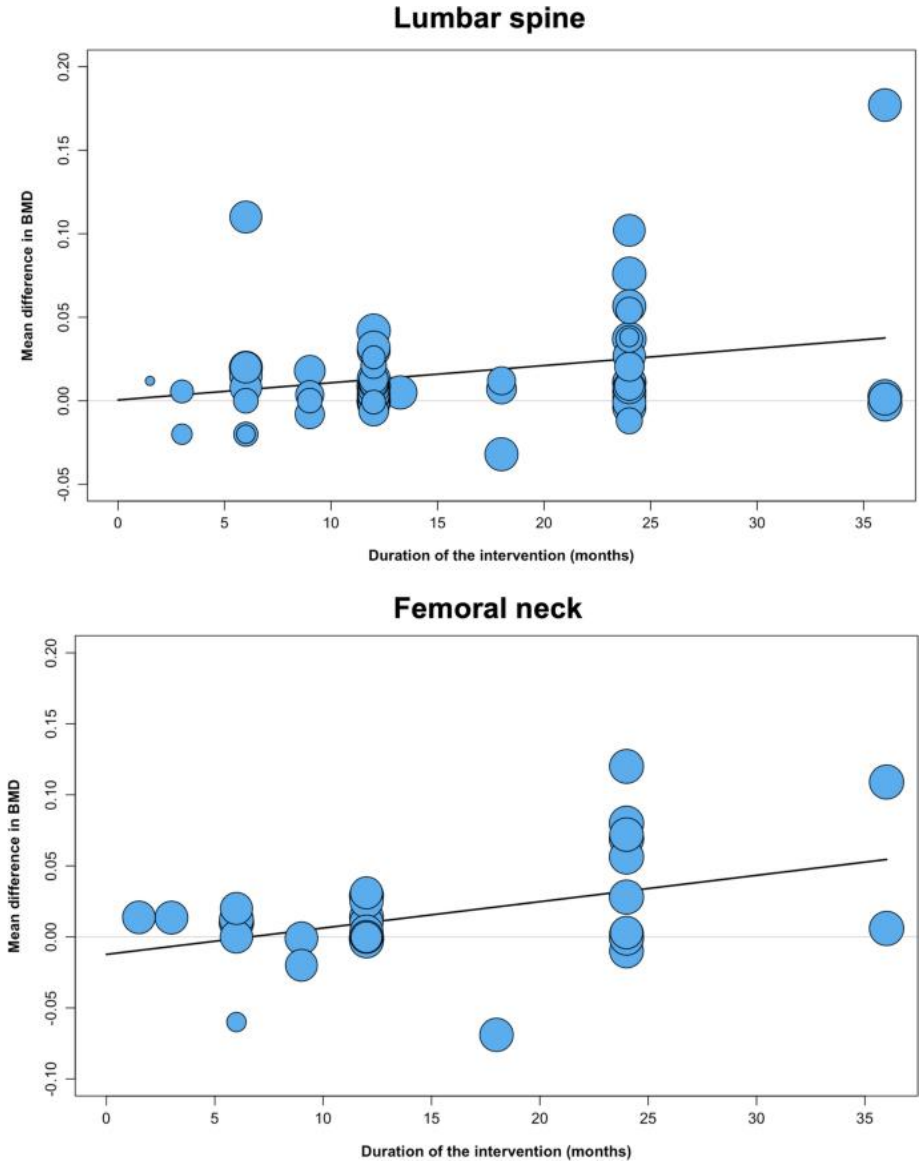

Fig. 4 Duration of the isoflavones intervention [15]

3.1.4 CVD

Although premenopausal women do not often have cardiovascular disease (CVD), there is a noticeable rise in perceived CVD risk (CVR) after menopause, especially for coronary heart disease (CHD). Hormone replacement therapy users did not appear to have a higher risk of CHD, according to an analysis of the Women's Health Initiative study. In fact, if estrogen administration is started within ten years of menopause onset, compared to non-users, there may be a reduction in CVR. The specific estrogen receptor modulation that soy isoflavones provide may be advantageous for CVR indices [16]. This has been suggested by Sathyapalan's study. SPI supplementation significantly reduced the estimated 10-year risk of coronary heart disease (27%), myocardial infarction (37%), total cardiovascular risk (24%) and cardiovascular-related death (42%), according to the Framingham equation, which computes CVR parameters [17].

3.2. EPO

Known by most as the evening primrose, Oenothera biennis is native to many parts of the world. Its name comes from its yellow flowers, which bloom mostly during dusk. Made from O. biennis seeds, evening primrose oil, or "EPO", is a valuable fixed oil. The known chemical composition of EPO includes up to 25% oil in O. biennis seeds. Since the body is unable to synthesize them, linoleic acid (60–80%) and GLA (8–14%), the two primary omega-6 fatty acids that make up EPO, are both

regarded as essential fatty acids. Premenstrual syndrome (PMS), mastalgia, diabetic neuropathy, coronary heart disease, gastrointestinal disorders, and endometriosis are just a few of the conditions for which extensive clinical trials have examined the effectiveness of EPO [18]. In the treatment of feminine illnesses, EPO plays a vital role in the lives of women.

3.2.1 Managing Premenstrual Syndrome

Women who experience a variety of physical, mental, and behavioral symptoms throughout their menstrual cycle are referred to as having PMS. Anxiety, exhaustion, depression, and headaches are typical symptoms. Suicidal thoughts and insomnia are among the more severe symptoms of premenstrual dysphoric disorder (PMDD). Approximately 85% of women who are menstruation encounter these symptoms. During the luteal phase of the menstrual cycle, PMS is marked by over 150 clinical symptoms, such as cyclical mastalgia, backache, headache, sadness, irritability, and irritable bowel syndrome. Reduced prostaglandin E1 levels from an essential fatty acid shortage cause an increase in prolactin sensitivity, which is raised during ovulation and then again throughout the luteal phase [19].

It has been demonstrated that linoleic acid increases prostaglandin production and reduces PMS symptoms. In this randomized, double-blind, placebo-controlled, parallel design study, the therapeutic effect of 180 mg/d of GLA was compared with placebo during three luteal phases in 28 women with PMS. In the placebo group, participants were given edible oil that was devoid of GLA. Over the course of three cycles, blood samples were taken, and in both groups, the length and intensity of symptoms were evaluated. During the luteal and follicular phases, there were notable drops in the plasma phospholipid levels of stearic acid, oleic acid, dihomo-γ-linolenic acid, palmitic acid, and GLA. The most common symptom of PMS in women was irritable bowel syndrome, which was followed by face rashes, tiredness, cravings, and breast swelling. After treatment, the GLA group had greater plasma phospholipid levels of GLA and dihomo-γ-linolenic acid than the placebo group. In addition, compared to the placebo group, the GLA group had a significant reduction ($P < 0.05$) in irritability as well as the intensity and duration of physical, psychological, and social PMS symptoms [20].

In a randomized, placebo-controlled trial, the effectiveness of evening primrose oil was evaluated in eighty women who had received a PMS diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria. Participants were randomized to receive 1.5 g of evening primrose oil daily or a placebo for a duration of three months. After the intervention, consuming evening primrose oil considerably reduced the intensity of PMS symptoms when compared to the baseline; however, taking a placebo did not appear to have any effect on PMS scores. Specifically, after taking evening primrose oil for three months, the group that received the oil saw a decrease in symptom severity scores from 53.2 ± 14.31 to 33.62 ± 16.94, compared to 53.38 ± 13.93 and 50.27 ± 16.94 for the placebo group (Fig. 5). Between the evening primrose oil and placebo groups, there was a statistically significant difference ($P < 0.001$) in the severity levels of PMS symptoms after three months of intervention [21]. These clinical data demonstrate the safety and efficacy of evening primrose oil in the treatment of menstrual PMS symptoms.

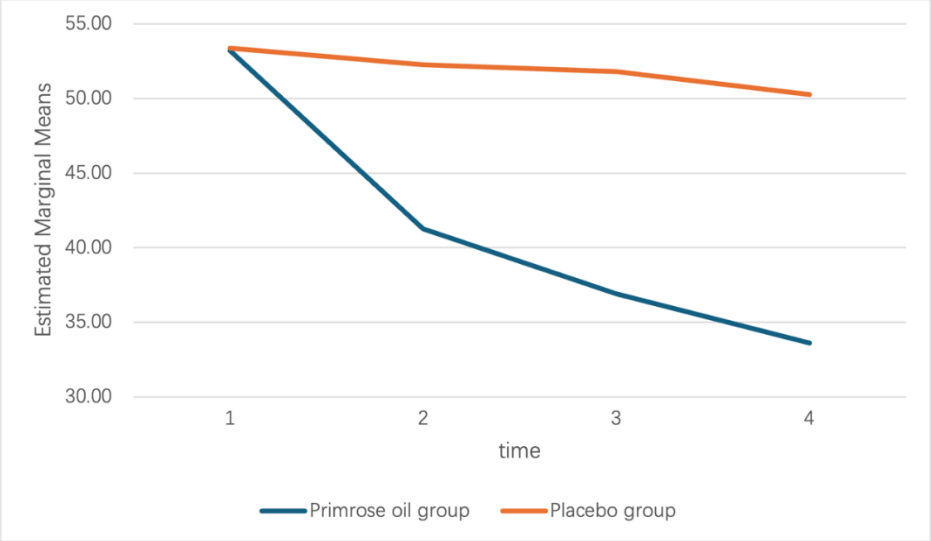

Fig. 5 PMS symptom severity scores [21]

3.2.2 Preventing Mastalgia

At some point in their life, 70% of women report having breast pain. Mastalgia, or breast discomfort, is a prevalent and upsetting ailment that affects women who are fertile. Non-cyclic breast pain is unrelated to the menstrual cycle, but cyclic breast pain is linked to hormonal oscillations during the menstrual cycle [22]. Breast tissue becomes sensitive to sex hormones when deficient in γ-linolenic acid or its derivatives, which can lead to the development of breast pain.

Despite the availability of various therapeutic approaches, EPO remains the preferred choice for many patients due to its lower recurrence rate and fewer side effects compared to hormone therapy. EPO may lessen the aforementioned symptoms by influencing prostaglandin metabolism. Furthermore, it is widely known that mastalgia is caused by a GLA shortage; as a high source of GLA, EPO may help treat this illness. Four studies out of five clinical trials with different durations of oral EPO capsule administration showed noteworthy improvements. In contrast, a research including 135 individuals discovered that oral EPO had no discernible impact on mastalgia. Overall, it appears that EPO supplementation might be useful in the management of mastalgia [23].

3.2.3 Preventing PCOS

Polycystic ovary syndrome (PCOS), which affects 5% to 15% of women, is a condition that is primarily caused by ovarian hyperandrogenism in women who are older. It can cause a variety of symptoms, including acne, hirsutism, and obesity. PCOS is frequently linked to a number of complications, such as increased body mass index, decreased HDL and elevated LDL levels. These complications raise the risk of type 2 diabetes mellitus and coronary heart disease in those who have PCOS. It has been demonstrated that vitamin D administration raises vitamin D levels and lipoprotein concentrations in PCOS patients. Furthermore, EPO influences the production of immune cells and eicosanoids in a direct and indirect manner. When vitamin D and EPO were given together as oral capsules to 60 patients over the course of a 12-week period, there were notable changes in the parameters evaluated, indicating that EPO might be useful in the management of PCOS [24].

4. Conclusion

Overall, the impact of dietary factors, particularly soy isoflavones and EPO, on female aging and female-specific diseases are complex and multifaceted. In this review, we have explored the potential role of soy isoflavones and EPO in mitigating age-related hormonal changes, alleviating menopausal symptoms, promoting bone health, and managing women's health conditions.

Research suggests that soy isoflavones, with their structural similarity to estrogen, may offer therapeutic benefits for women experiencing menopausal symptoms and age-related hormonal

changes. Similarly, evening primrose oil, rich in GLA, has shown promise in the management of several women's health concerns, including PMS, menopausal symptoms, and breast pain.

However, it is important to acknowledge the limitations and gaps in current research on soy isoflavones and evening primrose oil. Conflicting results, methodological variations, and the need for further mechanistic investigations hinder the full understanding of the efficacy, safety, and optimal dosages of these dietary factors for women's health.

Moving forward, future research efforts should focus on addressing these knowledge gaps to better elucidate the mechanisms of action and clinical implications of soy isoflavones and evening primrose oil for female aging and female-specific diseases. By integrating findings from well-designed clinical trials, epidemiologic studies, and mechanistic investigations, people can improve the understanding of the potential benefits and risks associated with incorporating these dietary factors into women's health management strategies.

In conclusion, while soy isoflavones and evening primrose oil hold promise as dietary interventions for women's health, further researches are needed to fully realize their potential and optimize their use in promoting healthy aging and managing women's health conditions.

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