



The effect of primrose on cardiovascular and physical health of women: A review and meta-analysis

El efecto de la primula sobre la salud física y cardiovascular de las mujeres: una revisión y un metanálisis

Khatereh Rostami, Community Based Psychiatric Care Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, <https://orcid.org/0000-0003-0433-2267>, Email: khaterehrostami61@yahoo.com
Najimeh Beygi, Department of Critical Care Nursing, Fasa University of Medical Sciences, Fasa, Iran, <https://orcid.org/0000-0002-7446-2035>, Email: Najimehbeygi1166@gmail.com
Fateme Kafami Ladani, PHD in Nursing, Nursing Care Research Center, Iran University of Medical Sciences, Tehran, Iran, <https://orcid.org/0000-0003-2054-6839>, Email: Nazi_kafame@yahoo.com
Roya Dokoohaki, Assistant professor, Department of Nursing, School of Nursing and Midwifery, Shiraz University of Medical Sciences, Shiraz, Iran, <https://orcid.org/0000-0002-6613-0647>, Email: dokoohakir@sums.ac.ir
Masumeh Ghazanfarpour, Reproductive Health, Family and Population Research Center, Kerman University of Medical Sciences, Kerman, Iran, <https://orcid.org/0000-0003-4639-3711>, Email: Masumeh.ghazanfarpour@yahoo.com
Soudabeh Behzadi, Assistant Professor, Department of Nursing, Arsanjan Branch, Islamic Azad University, Arsanjan, Iran, <https://orcid.org/0000-0003-3898-0545>, Email: So.Behzadi@iau.ac.ir
Rafat Rezapour-Nasrabad, Department of Psychiatric Nursing and Management, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran, <https://orcid.org/0000-0002-7157-586X>, Email: Rezapour.r@sbm.ac.ir
Fereshteh Derayati, Department of Nursing and Midwifery, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran & Department of Cell and Developmental Biology, Roudehen Branch, Islamic Azad University, Roudehen, Iran, <https://orcid.org/0009-0006-1092-7266>, Email: fereshtederayati@yahoo.com
*Corresponding Author: Fereshteh Derayati, Department of Nursing and Midwifery, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran & Department of Cell and Developmental Biology, Roudehen Branch, Islamic Azad University, Roudehen, Iran, <https://orcid.org/0009-0006-1092-7266>, Email: fereshtederayati@yahoo.com
Received: 11/20/2022 Accepted: 02/19/2023 Published: 03/12/2024 DOI: <http://doi.org/10.5281/zenodo.10903548>

Abstract

Introduction & Background: Cardiovascular disease is on the agenda worldwide due to its many costs. This study aims to investigate the effects of evening primrose oil on women's mental health.

Methods: The search strategy of electronic databases included PubMed, Cochrane Library, Web of Science and Scopus. Original clinical trials from January 1, 2023 published in English were searched by two independent investigators in two stages.

Results: Administration of vitamin D and EPO improves blood sugar and lipid profile in women with gestational diabetes. The level of LDL showed a statistically significant decrease in evening primrose compared to the control group in prediabetes postmenopausal women. However, the levels of FBS, HDL, TG and cholesterol did not change statistically. The use of vaginal EPO significantly improved the Bishop score in pregnant women and cervical dilatation before hysteroscopy. Evening

primrose oil significantly reduced menopausal symptoms such as psychological symptoms and hot flashes. Sexual function and postpartum pain were significantly improved in patients receiving EPO. The effect of EPO and vitamin E in relieving breast pain was the same. The results of meta-analysis showed that evening primrose oil can significantly reduce the severity of periodic mastalgia compared to the control (-0.3 to -0.53: CI 95%) is -0.92, which is statistically significant has ($p=0.01$).

Conclusion: EPO can be recommended as a safe and effective drug to improve cardiac function by controlling cholesterol and menopause symptoms, sexual function and postpartum complications, breast pain. Also, EPO improves blood sugar and lipid profile in women with gestational diabetes.

Keywords: Evening primrose, psychological, physical, women, obstetrics, gynecological.

Introducción y antecedentes. Las enfermedades cardiovasculares están en la agenda mundial debido a sus múltiples costos. Este estudio tiene como objetivo investigar los efectos del aceite de onagra en la salud mental de las mujeres.

Métodos. La estrategia de búsqueda en bases de datos electrónicas incluyó PubMed, Cochrane Library, Web of Science y Scopus. Dos investigadores independientes buscaron en dos etapas los ensayos clínicos originales del 1 de enero de 2023 publicados en inglés.

Resultados. La administración de vitamina D y EPO mejora el azúcar en sangre y el perfil de lípidos en mujeres con diabetes gestacional. El nivel de LDL mostró una disminución estadísticamente significativa en onagra en comparación con el grupo de control en mujeres posmenopáusicas con prediabetes. Sin embargo, los niveles de FBS, HDL, TG y colesterol no cambiaron estadísticamente. El uso de EPO vaginal mejoró significativamente la puntuación de Bishop en mujeres embarazadas y la dilatación cervical antes de la histeroscopia. El aceite de onagra redujo significativamente los síntomas de la menopausia, como los síntomas psicológicos y los sofocos. La función sexual y el dolor posparto mejoraron significativamente en las pacientes que recibieron EPO. El efecto de la EPO y la vitamina E para aliviar el dolor de mama fue el mismo. Los resultados del metanálisis mostraron que el aceite de onagra puede reducir significativamente la gravedad de la mastalgia periódica en comparación con el control (-0,3 a -0,53: IC 95%) es -0,92, lo cual es estadísticamente significativo ($p=0,01$).

Conclusión. La EPO se puede recomendar como un fármaco seguro y eficaz para mejorar la función cardíaca controlando el colesterol y los síntomas de la menopausia, la función sexual y las complicaciones posparto, dolor de mama. Además, la EPO mejora el perfil de lípidos y azúcar en sangre en mujeres con diabetes gestacional.

Palabras clave: Onagra, psicológica, física, mujer, obstetricia, ginecológica.

Today, an increasing amount of researchers is interested in the use of alternative medicine by women, especially in the reproductive age and pregnancy period^{1,2}. Despite the increase in access to effective modern medical treatments, the prevalence of side effects associated with these drugs has led to the emergence of complementary medicine-based treatments as a desirable and acceptable option in the treatment of various diseases³. Today, the use of medicinal plants Due to its low cost and fewer side effects, it has found a special place in therapeutic interventions⁴.

Evening primrose received its scientific name, *Oenothera biennis*, is one of the favorite herbal resarchers medical staff and patients. This short-lived and two-year-old plant contains large amounts of essential unsaturated fatty acids, phenolic and estrogenic compounds, the acetone extract of this plant has the highest amount of phenolic and flavonoid compounds, phenolic compounds and linear aliphatic alcohol are considered active ingredients of Maghrib⁵. This herbal contains sterols (such as betasisterol and campesterol) that modulate the effects of cytokines, nitric oxide, interferon gamma and thromboxane B2 and suppress COX-2 gene expression, and for this reason it has more anti-inflammatory activity than borage flower. Evening primrose oil is a rich of PUFA, and the gammalinoleic acid in it directly converts PUFA into prostaglandin⁶. mild side effects such as nausea and stool softening and mild headache have been reported as a result of taking evening primrose oil, which of course is well tolerated^{7,8}.

Evening primrose has no serious complications during pregnancy and breastfeeding⁵.

Regarding the effects of evening primrose, various researches have been conducted in the field of medical sciences, based on some researches of evening primrose oil in the treatment of depression, inflammation, fluid retention, fatigue, mood disorders, skin eczema, allergies, rheumatoid arthritis, heart and sweat diseases, cirrhosis, multiple sclerosis, high blood pressure, problems of the urinary system, nervous system, Vascular health, glands and name have had a positive effect⁹. Sexual function¹⁰, menopause¹¹⁻¹³, and mastalgia¹⁴, cervical dilatation¹⁵, has been effective. postpartum pain¹⁶, have been done. However, so far, a review study that has comprehensively examined the effects of evening primrose oil on cardiovascular diseases, obstetrics, and women's mental health has not been found in the literature review. Therefore, we decided to review the effects of evening primrose oil in various fields of women health with this review.

The search strategy was to screen electronic databases including PubMed, Cochrane Library, Web of Science and Scopus. Original clinical trials from 1, 2023 January published in English were searched by two independent researchers in two stages. The used keywords were (obstetrics OR midwifery OR gynecology OR pregnancy OR breastfeeding OR postpartum blue OR postpartum depression OR hot flashes OR menopause OR cardiovascular) AND (Evening primrose).

Data were analyzed using Comprehensive Meta-Analysis software. Finally, the heterogeneity index between studies was determined by I^2 and Q Cochran test. Significance level was considered to be less than 0.05¹⁷. Random or fixed effect model was used to report data based on heterogeneity level.

Evening primrose oil on menopause symptoms

In first study, there was a reduction in the psychological score in both groups. However, Prominent alleviation in the evening primrose oil than control group (mean difference: -3.44; $P < 0.01$)¹⁸. In second study, the number of hot flashes decreased significantly and quality of life improved significantly in both groups during eight weeks ($P < 0.05$). the percentage of improvement in black cohosh was significantly superior to EPO group¹⁹.

Evening primrose on Glycemia, Lipid Profiles and Cardiovascular status

In first study, Absalan et al, LDL level showed a statistically significant reduce in evening primrose group than in pre-diabetic postmenopausal women. However, FBS, HDL, TG and cholesterol level didn't change statistically significant²⁰. In second study, compared with the placebo, combination vitamin D plus EPO changes significantly in fasting plasma glucose ($P=0.04$), serum insulin concentrations ($P=0.004$), homeostasis model of assessment (HOMA) insulin resistance ($P=0.003$), HOMA-B cell function ($P=0.007$) and the quantitative insulin sensitivity check index ($P=0.007$) TH placebo group. In addition, vitamin D and EPO supplementation resulted in significant reductions in serum TAG ($P<0.001$), VLDL ($P<0.001$), TC ($P<0.001$), LDL concentrations ($-P=0.001$) and TC/HDL ($P<0.001$) After 6 weeks of intervention²¹.

Evening Primrose oil on cervical dilation

In first study, researcher showed that two softgels of evening primrose four to six 4-6 hours before hysteroscopy had beneficial effect on cervical dilation. Ease of cervical dilatation was seen in all women receive intravaginal evening primrose oil 4 to 6 hours before diagnostic hysteroscopy²².

In the second study, compared with the control group, vaginal application of EPO improved significantly bishop score in pregnancy women¹⁵.

Evening Primrose oil on postpartum blues

In Nikoomazhab et al., study, duration of postpartum blues in women receive a daily dose of 1 gr of evening primrose oil was significantly less than the placebo group ($p=0.004$)⁹.

Evening primrose on sexual function

Torkan et al., compared to the control group, the sexual function score improved significantly in EPO group. Orgasm ($P = 0.04$) and sexual satisfaction ($P=0.001$) dimensions improved significantly in evening primrose oil than in the control group²³.

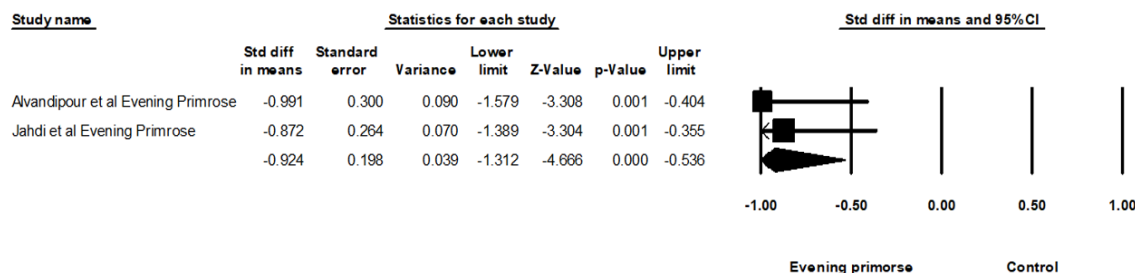
Evening Primrose on Pain

In first trials, the severity of postpartum pain had a significant decrease after treatment with evening primrose in multiparous women¹⁶. In the second trial by Pruthi et al.,²⁴ Evening primrose and vitamin E had a similar effect in the treatment of mastalgia. In the third study by Masoumi et al., Evening primrose more than vitamin E caused a decrease in the treatment of premenstrual syndrome symptoms⁸. In fourth trial by Jaafarnejad et al., All three drugs of flaxseed, evening primrose oil, and vitamin E reduced the duration of mastalgia, but this decrease was significant in the flaxseed group²⁵. In fifth trial by Seraji et al.²⁶ Evening primrose was not more effectiveness than vitamin E. In contrast to above studies, in Ghazanfor study, vitamin E oil was more effectiveness than Evening promise in treatment of mastalgia is similar high was statistically significant (p value < 0.05)²⁷.

Meta-analysis

The results of our meta-analysis showed that the standardized mean difference between the two groups of evening primrose oil and control (-1.3 to -0.53: CI 95%) is -0.92, which is statistically significant. ($P=0.01$)^{28,29}, and indicates that evening primrose oil can significantly reduce the severity of periodical mastalgia in comparison with control (Figure 1).

Figure 1. comparison of Evening primrose v.s control on mastalgia. The horizontal lines denote the 95% CI, ■ point estimate (size of the square corresponds to its weight); ♦, cbined overall effect of treatment.



Effect of EPO and Vitamin E was same in relief pain of breast. The results of meta-analysis showed that evening primrose oil can significantly reduce the severity of periodical mastalgia in comparison with control (-1.3 to -0.53; CI 95%) is -0.92, which is statistically significant. ($p=0.01$). Combination of vitamin D and evening primrose oil can improved Glycemia and Lipid Profiles in Women with Gestational Diabetes²¹, Using of evening primrose reduces LDL levels in pre-diabetic postmenopausal women, which can reduce the risk of cardiovascular diseases²².

black cohosh is more effective than primrose oil) in reduction of severity of hot flashes and improvement of the quality of life²³. Evening primrose oil was effective in reducing the severity of postpartum pain in multiparous²⁴. There was a reduction in the psychological score in both groups. However, prominent alleviation in the evening primrose oil group. Longer trials are necessary to make more reliable decisions about the use of evening primrose oil and its safety in clinical practice²⁵. A single dose of g EPO (1000 m) palced in the posterior vaginal fornix at 41 weeks gestation and improved Bishop score and reduced parturition time in post-term pregnancies²⁶. vaginal application of EPO can increase cervical dilation and bishop score²⁷, The sexual function score improved significantly in EPO group compared to the control group²⁸. the severity of postpartum pain had a significant decrease after tremet with evening primrose in Multiparous Women²⁹. The results of analyzing showed that effect of Evening primrose. and Vitamin E was same in relief pain of breas³⁰. Pervious meta-analysis with three trials showed that showed that effect of Evening primrose. and Vitamin E was same in relief pain of breas³¹.

In relation to the mechanism of vitamin e in reducing breast pain, it can be said that vitamin e is one of the common treatments for mastalgia, the main properties of which are related to antioxidant effects, and it caused to prevents the oxidation of unsaturated fatty acids and reduces saturated fatty acids. It also is effective for non-

saturation. The pain-relieving effects of vitamin E have been attributed to changes in prostaglandin metabolism³². The mechanism of the effect of evening primrose on reducing breast pain related to the presence of essential fatty acids in evening primrose last. So that evening primrose juice contains gammalinoleic acid, which prevents the synthesis of prostaglandins, which cause breast pain. Gammalinoleic acid is metabolized in the body after oral consumption and inhibits the metabolite of arachidonic acid and finally causes the effects It becomes anti-inflammatory³³. There are contradiction findings regarding comparison the effect evening primrose oil and Vitamin E. According to chi-square test, evening primrose oil group was significantly more effective than Vitamin E ($p < 0.05$)³⁴. In Alvandipour et al., MC Gill score in two therapeutic group (Evening Primrose Oil and vitamin E) significantly decreased in compared to placebo group ($p < 0.001$)²⁸. In contrasted two above studies, there studies did not any significant difference between evening primrose oil and Vitamin E. the first study, EPO, $p=0.18$ and EPO plus vitamin E, $P=0.16$) non significantly decreased cyclical mastalgia compared with the placebo group)^{29,30}. The Second study, showed that Gamolenic Acid (evening primrose oil) efficacy did not differ from that of placebo fatty acids, regardless of whether or not antioxidant vitamins were present³⁵. In the third study, Response rate was 70% of EPO and 56 of placebo with any significant difference between two groups³⁶. There is two possible explanation for difference among studies: high placebo effect masked beneficial effect of evening promise oil. Minor placebo effect (5-7%) observed in In Alvandipour et al.,²⁸ and Kılıç et al.³⁵, reported large placebo response rate (40-55% (for placebo)³⁶. Some studies^{30,35}. Used hydrogenated coconut oil as placebo may be beneficial in relief patient with mastalgia. Treatment responses depend on mastalgia severity and pattern of mastalgia (cyclic or noncyclic) as reported by previous studies^{37,38}.

Also, In order to resolve this contradiction, we performed a meta-analysis, our findings showed that effect of Evening primrose and Vitamin E was same in relief

pain of breast²⁶⁻³⁰. Consistent with our met analysis, A meta-analysis with eight RCTS was recently published and showed vitamin E and Evening Primrose Oil decreased equality 0.311 (CI 95%:0/888-0.266) with high heterogeneity³⁹.

Postpartum depression is the most common temporary mood disorder after childbirth, which had symptoms similar to depression, including: insomnia, low mood, tendency to cry, fatigue, irritability, and emotional instability, so that they may shed tears for several hours and suddenly calm down. pathological disorder of the hypothalamus-pituitary-adrenal axis due the rapid hormonal changes that occur in the first few days postpartum are responsible for Postpartum depression. Omega-3 fat is one of the essential fatty acids in improving the treatment of depression patients⁵. The findings of a study showed that evening primrose oil is effective during postpartum depression⁹.

Evening primrose oil with prostaglandins E1 and E2 precursors has relaxant activity on smooth muscle, which changes cervical vascular tone and consistency⁴⁰. The most important constituents of the oil are linoleic acid (6065%) and gamma linolenic acid (7-14%) Unsaturated fatty acids (PUFA) are the natural precursors of prostaglandins⁴¹. A review study by Christelle et al., was conducted with the aim of determining the effect of evening primrose oil on menopausal symptoms. It showed that evening primrose oil may reduce the severity of the general symptoms of menopause, but it is not effective in reducing the frequency and severity of vasomotor symptoms⁴². The exact mechanism of this plant on hot flashes is not known, but it may act through an estrogen agonist or antagonist, and its effects work through interaction with the estrogen receptor⁴³. Also, the effects of this plant on reducing hot flashes may be related to its properties. antioxidant and anti-inflammatory, as well as its ability to help increase alpha-tocopherol levels⁴².

The exact mechanism of medicinal plants affecting sexual function is not well known, however, based on research, herbal medicines are effective in increasing sexual function by affecting the gonads, endocrine system and brain. Herbal medicines with antioxidant effects and anti-inflammatory properties may lead to the improvement of sexual function^{44,45}, evening primrose oil improved sexual function of women in reproductive age⁴⁶, other herbal medicines with antioxidants activation improved sexual function. Rose is effective in improving sexual dysfunction, especially in people with background disorders⁴⁷. Receiving drops of rose, ginger and cinnamon in women with Depression showed a decrease in dyspareunia and an increase in orgasm and sexual desire⁴⁸. 500 mg of ginseng twice a day for 4 weeks leads to improving the quality and quantity of sexual function of postmenopausal women Phytoestrogens have various effects on sexual function. Published reports show that maritime pine bark, *T. foenum-graecum* L., and *F. vulgare* could be considered as agents to

overcome sexual dysfunctions while soy, red clover, gennistein, and flaxseed had no promising effects on these conditions⁴⁹.

Conclusions

It seems that EPO could be recommended as a safe medication and effectiveness for obstetrics and gynecological diseases such as menopause symptoms, sexual function and postpartum complication, pain pain of breast. EPO improve glycemia and lipid profiles in women with gestational diabete, Designing the multi-center and large clinical trials on the effect of EPO on psychological and physical health women is needed for future trials.

References

1. Sepehrirad M, Toozandehjani H. Effectiveness of cognitive-behavioral group therapy training and nutritional strategies based on traditional medicine on Premenstrual Syndrome. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2015;18(177):11-9.
2. Zand Vakili F, Zare S, Rahimi K, Riahi M. The effect of evening primrose oil on changes in polycystic ovary syndrome induced by estradiol valerate in rat. *Armaghane danesh*. 2018;22(6):714-24.
3. Ernst E, editor *Herbal medicines: balancing benefits and risks. Dietary Supplements and Health: Novartis Foundation Symposium*. Wiley Online Library; 2007:
4. Ebrahimi Varzaneh F, Nahidi F, Mojab F, Pourhoseingholi MA, Panahi Z. The effect of hydro alcoholic extract of *Achillea Millefolium* capsule on duration and severity of primary dysmenorrhea pain. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2017;20(3):48-86.
5. Faghani Aghoozi M, Fayazi S, Mohammadi S, Tehranian N, Amerian M. The effects of evening primerose on clinical obstetrics of Iran: A review study. *Scientific Journal of Nursing, Midwifery and Paramedical Faculty*. 2019;5(3):15-28.
6. Shahali S, Khatami F, Abbaspour Z, Gheraghian B. The effect of vaginal evening primrose capsule on cervical ripening in nulliparous women with post-term pregnancy: A clinical trial. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2018;21(8):30-38.
7. Babazadeh R, Keramat A. Premenstrual syndrome and complementary medicine in Iran: a systematic review. *KAUMS Journal (FEYZ)*. 2011;15(2):174-187.
8. MASOUMI S, Khalili A, Delforooz A, Faradmal J, Shayan A. Comparison the effect of evening primrose oil and vitamin E on premenstrual syndrome; 2017.
9. Nikoomazhab S, Haghdoust MR, Honarmandpour A. The effect of evening primrose oil on duration of postpartum blues among primiparous women: a double-blind, randomized controlled clinical trial. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2017;20(9):64-73.
10. Solati K, Heidari-Soureshjani S, Luther T, Asadi-Samani M. Iranian

- medicinal plants effective on sexual disorders: A systematic review. *International journal of pharmaceutical sciences and research*. 2017;8(6):2415-20.
11. Saeidi R, Tafazoli M, Gholami M, MAZLOM R. New treatment for nipple soreness in breastfeeding mothers: A clinical trial study; 2015.
 12. Bozorgi M, Memariani Z, Mobli M, Salehi S, Surmaghi MH, Shams-Ardekani MR, Rahimi R. Five *Pistacia* species (*P. vera*, *P. atlantica*, *P. terebinthus*, *P. khinjuk*, and *P. lentiscus*): a review of their traditional uses, phytochemistry, and pharmacology. *The Scientific World Journal*; 2013.
 13. Mahdavi R, Heshmati J, Namazi N. Effects of black seeds (*Nigella sativa*) on male infertility: A systematic review. *Journal of Herbal Medicine*. 2015;5(3):133-9.
 14. AYDIN İ, BALTACI D, TRKYILMAZ S, NC MJDMJ. Comparison of *Vitex Agnus Castus* with Meloxicam and Placebo in Treatment of Patients with Cyclical Mastalgia. 2012;14(1): 26-34.
 15. Azad A, Pourtaheri M, Darsareh F, Heidari S, Mehrnough V. Evening primrose oil for cervical ripening prior to labor induction in post-term pregnancies: A randomized controlled trial. *European Journal of Integrative Medicine*. 2022;51(1):102-123.
 16. Amin M, Zogami SE, Rakhshandeh H, Esmaeily H, Mirtimouri M. The Effect of Evening Primrose (*Oenothera biennis*) Oil Capsule on Postpartum Pain in Multiparous Women: A Triple-Blind Randomized Clinical Trial. *Journal of Midwifery & Reproductive Health*. 2022;10(4):15-26.
 17. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in medicine*. 2002;21(11):1539-1358.
 18. Sharif SN, Darsareh F. Impact of evening primrose oil consumption on psychological symptoms of postmenopausal women: a randomized double-blinded placebo-controlled clinical trial. *Menopause*. 2020;27(2):194-8.
 19. Mehrpooya M, Rabiee S, Larki-Harchegani A, Fallahian AM, Moradi A, Ataei S, Javad MT. A comparative study on the effect of "black cohosh" and "evening primrose oil" on menopausal hot flashes. *Journal of education and health promotion*. 2018;7(1):36-49.
 20. Absalan A, Lotfipour SM, Lori Poor M, Karimi Fard M, Ahmadinia H. The effect of Evening primrose on blood sugar and lipid profile of prediabetic postmenopausal women: Randomized clinical trial. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2021;24(10):71-79.
 21. Jamilian M, Karamali M, Taghizadeh M, Sharifi N, Jafari Z, Memarzadeh MR, et al. Vitamin D and evening primrose oil administration improve glycemia and lipid profiles in women with gestational diabetes. *Lipids*. 2016;51(1):349-356.
 22. Aquino P, Fernandez H, Garcia M, Barrientos M, Apepe E, Pichay R. Determining the ease of cervical dilation in patients given evening primrose oil (Eveprim®) intravaginally before hysteroscopy in postmenopausal and nulliparous, premenopausal women ages 37-77 years old: A pilot study. *Journal of Minimally Invasive Gynecology*. 2011;18(6):S126-S127.
 23. Torkan S, Shahali S, Rastad H. Effects of evening primrose oil capsules on the sexual function of reproductive-aged women: A randomized clinical trial study. *Sexologies*. 2022;31(4):461-467.
 24. Pruthi S, Wahner-Roedler DL, Torkelson CJ, Cha SS, Thicke LS, Hazelton JH, Bauer BAJAMR. Vitamin E and evening primrose oil for management of cyclical mastalgia: a randomized pilot study. 2010;15(1):59-68.
 25. Jaafarnejad F, Adibmoghaddam E, Emami SA, Saki A. Compare the effect of flaxseed, evening primrose oil and Vitamin E on duration of periodic breast pain. *Journal of education and health promotion*. 2017;6(1):85-98.
 26. Seraji A, Salehi A, Momeni H, Kerami A, Naeimi N. The effects of evening primrose and vitex agnus on pain scale of the women with cyclic mastalgia a clinical trial. *Complementary Medicine Journal*. 2014;3(4):639-653.
 27. Ghazanfor R, Qureshi U, Adil RG, Malik S, Tariq M, Khan JS. Comparative study of effectiveness of vitamin E and evening primrose oil for pain relief in moderate cyclical mastalgia. *The Professional Medical Journal*. 2019;26(8):1328-1332.
 28. Alvandipour M, Tayebi P, ALIZADEH NR, Khodabakhshi H. Comparison between effect of evening primrose oil and vitamin E in treatment of cyclic mastalgia; 2011.
 29. Jahdi F, Tolouei R, Samani LN, Hashemian M, Haghani H, Mojab F, Memarzadeh M. Effect of evening primrose oil and vitamin b6 on pain control of cyclic mastalgia associated with fibrocystic breast changes: a triple-blind randomized controlled trial. *Shiraz E-Medical Journal*. 2019;20(5):19-28.
 30. Pruthi S, Wahner-Roedler DL, Torkelson CJ, Cha SS, Thicke LS, Hazelton JH, Bauer BA. Vitamin E and evening primrose oil for management of cyclical mastalgia: a randomized pilot study. *Alternative Medicine Review*. 2010;15(1):59-67.
 31. Irani M, Sheidaei S, Ghazanfarpour M, Nosrati SF. Comparative evaluation of evening primrose oil and vitamin E on the severity of cyclic Mastalgia: A Systematic Review and Meta-Analysis. *Iranian Journal of Obstetrics, Gynecology and Infertility*. 2020;23(3):91-98.
 32. Parsay S, Olfati F, Nahidi S. Therapeutic effects of vitamin E on cyclic mastalgia. *The breast journal*. 2009;15(5):510-514.
 33. Horrobin D. The role of essential fatty acids and prostaglandins in the premenstrual syndrome. *The Journal of reproductive medicine*. 1983;28(7):465-468.
 34. Fathizadeh N, Takfallah L, Ehsanpour S, Namnabati M, Askari S. Effects of evening primrose oil and vitamin E on the severity of periodical breast pain. *Iranian Journal of Nursing and Midwifery Research*. 2009;13(3):31-40.
 35. Goyal A, Mansel RE. A randomized multicenter study of gamolenic acid (Efamast) with and without antioxidant vitamins and minerals in the management of mastalgia. *The Breast journal*. 2005;11(1):41-47.
 36. Kılıç MÖ, Sen M, İçen D. The comparison of evening primrose oil, fructus agni casti, and reassurance in the treatment of mastalgia. *Int J Surg Med*. 2016;2(2):83-91.
 37. Pye J, Mansel R, Hughes L. Clinical experience of drug treatments for mastalgia. *The Lancet*. 1985;326(8451):373-387.
 38. Holland PA, Gateley CA. Drug therapy of mastalgia. *Drugs*. 1994;48(5):709-716.
 39. Irani M, Sheidaei S, Ghazanfarpour M, Nosrati SF, JIJoO, Gynecology, Infertility. Comparative evaluation of evening primrose oil and vitamin E on the severity of cyclic Mastalgia: A Systematic Review and Meta-Analysis. 2020;23(3):91-8.
 40. Mahboubi M. Evening primrose (*Oenothera biennis*) oil in management of female ailments. *Journal of menopausal medicine*. 2019;25(2):74-82.
 41. Masoumi SZ, Kazemi F, Refaee M, Ahmadi M, Sourinezhad H, Hamoun M. Effect of Evening Primrose Vaginal Capsule on Cer-

vix Preparation and Duration of First Stage of Labor in Nulliparous Women Referred to Fatemeh Hospital in Hamadan, Iran: A Single-blind Randomized Controlled Trial. *Current Drug Research Reviews Formerly: Current Drug Abuse Reviews*. 2022;14(3):247-53.

42. Christelle K, Zulkifli MM, Noor NM, Draman N. The Effects of Evening-Primrose Oil on Menopausal Symptoms: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Current Women's Health Reviews*. 2020;16(4):265-76.
43. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in medicine*. 2002;21(11):1539-58.
44. Walker HK, Hall WD, Hurst JW. *Clinical methods: the history, physical, and laboratory examinations*; 1990.
45. Aradmehr M, Senobari M. Effect of Medicinal plant of roses on sexual dysfunction of female and male subjects: A systematic review of clinical trials; 2020.
46. Shabaniyan S, Ebrahimbabaei M, Safavi P, Lotfizadeh M. Comparing the effect of rose drop, ginger, and cinnamon on sexual function in depressed women with sexual dysfunction. *Pharmacognosy Research*. 2018;10(3):55-69.
47. Najaf Najafi M, Ghazanfarpour M. Effect of phytoestrogens on sexual function in menopausal women: a systematic review and meta-analysis. *Climacteric*. 2018;21(5):437-45.
48. Mehni SA, Tork Zahrani S, Taheri Sarvtin M, Mojab FA, Mirzaei MA, Vazirnasab H. Therapeutic effects of buniunium persicum boiss (Black Zira) on candida albicans vaginitis. *Biom Pharmacol J*. 2015;8(2):1103-1109.
49. Modoodi M, Jalilvand F, Zare S, Ataei M, Esmaelzadeh Saeieh S, Mirzaei M. Investigating the prevalence of menopausal complications and its related factors in women referred to Shahrud Health Centers in 2014. *Revista Latinoamericana de Hipertension*. This link is disabled, 2020;15(2):144-149.