Original Article

Comparison of the Effect of Fennel and Evening Primrose Oil on Menopausal Problems and Hormonal Levels: A Randomized Controlled Trial

Abstract

Background: Using natural oral supplements is one of the methods of complementary medicine that has been widely welcomed in the last decade Since studies have reported contradictory results for effectiveness of herbal medicines during menopause and no other more effective herbal medicine has been suggested yet, the researchers of this study decided to compare the fennel and Evening Primrose Oil (EPO) and their effect on menopause problems and sex hormones. **Materials and Methods:** The present study was a triple-blinded, controlled clinical trial with 125 participants randomly assigned to. An intervention group received fennel, another intervention group received evening primrose oil, and the placebo group received placebo twice daily for 8 weeks. Pre-intervention and post-intervention results were obtained using hormonal assay and the Menopause Rating Scale (MRS). **Results:** In this study, the mean follicle-stimulating hormone (FSH) and estradiol levels changed significantly in the fennel and EPO groups compared to placebo ($p < 0.001$). The difference in the mean FSH score between the fennel group and EPO group was not significant ($p = 0.304$), but the difference in the mean estradiol level between these groups was significant ($p = 0.043$). Moreover, there was a significant difference in the mean MRS score between the intervention groups before the intervention ($p < 0.05$). However, the difference in the mean MRS score between the fennel and EPO groups was not significant after the intervention ($p = 0.322$). **Conclusions:** Consumption of fennel and EPO can significantly change FSH, estradiol, and psychological menopausal symptoms in postmenopausal women.

Keywords: *Evening primrose oil, fennel oil, hormones, menopause*

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Introduction

Menopause is a natural, important, and emotionally effective point in a woman's life, and it occurs on average between the ages of 48 and 52.[1] Following the decrease in ovarian function and estrogen during menopause, numerous symptoms occur, including vasomotor instability, genital atrophy, painful intercourse, itching, urinary incontinence, mood disorders, and cardiovascular and osteoporosis symptoms.[2] The severity of these symptoms varies at different stages of menopause and with differences in the personality of women. Hormonal treatment,[3] supplement therapy,[4] and psychotherapy[5] are some of the methods suggested to decrease problems during menopause. Hormone therapy is not recommended to everyone due to the increased risk of cancer, stroke, heart attack, and thromboembolism; therefore, only 20% of postmenopausal women use hormone therapy.[3] Using natural oral supplements is one of the complementary therapies that has been widely welcomed in the last decade and can be suggested as an alternative treatment. There have been many studies on the effectiveness of supplement therapy in reducing menopausal symptoms,[6-8] but the data are still limited and non-conclusive. The efficacy of a few supplements such as black cohosh in reducing menopause problems has been demonstrated in previous studies.[9] However, some herbal supplements such as fennel (Foeniculum vulgare) and Evening Primrose Oil (EPO) are still being studied, and scientists have not reached a consensus on them.[10,11]

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Fennel, a type of herb of the apiaceae family, is regarded as a phytoestrogen; 3 classes of phytoestrogens (isoflavones, coumestans, and lignans) are found at high concentrations in fennel.[12] Phytoestrogens bind ER (α and β) and act as an antagonist or agonist of estrogen.

During menopause, when estrogen levels are low in the woman body, phytoestrogens exert their estrogenic effects more strongly.[13] The use of fennel in the diet has been approved by the FDA since 1965, and in 1970, fennel was included in the list of fruits and vegetables without any restrictions on consumption.[14] The main ingredient of EPO is Gamolenic acid; this fatty acid authorizes the synthesis of anti-inflammatory substances such as 15-hydroxy-eicosatrienoic acid and prostaglandin E. Prostaglandins function as central neurotransmitters and influence the hypothalamic pituitary axis,[15] and EPO is thought to help counter menopausal hormonal changes by increasing the production of prostaglandins.[16]

There is a theory that herbal therapy, such as hormone therapy, can affect sex hormones such as estradiol, and ultimately, reduce the severity of menopausal symptoms.[17] Evaluation of menopause symptoms after herbal therapy using a questionnaire is one method for the determination of herbal effectiveness. The menopause rating scale (MRS)[18] can be utilized to monitor the progress of menopausal symptoms.[7] Even though some studies have been performed on the effectiveness of fennel[10] and EPO[11] on menopause symptoms, hormonal changes have not been measured during the use of herbs in menopausal women by researchers so far due to its high laboratory costs. The studies of hormonal changes show the controversy over the effectiveness of herbal medicines during menopause. Moreover, contradictory results have been reported for the effectiveness of herbal medicines during menopause and no other more effective herbal medicine has been suggested yet. Thus, the researchers of this study decided to compare these two herbal medicines (Fennel and Evening primrose oil) and determine their effect on menopause symptoms and sex hormones.

Materials and Methods

The present study was a triple-blinded randomized controlled trial (IRCT20160404027207N2). Menopausal women of 45-60 years of age, who were married, their menses had ceased for at least 1 year, had no specific disease, did not take any medication, had no sensitivity to honey, had no addiction, were not using sedation techniques, and referred to health clinics affiliated to Shiraz University of Medical Sciences, Iran, from May-2020 to November-2020, were included in this study. Women who did not take the medication for more than 6 consecutive days or started taking another drug, were diagnosis with psychotic disorders, or started a special diet were excluded from the study. Individuals who met the inclusion criteria and were willing to participate in the research were included in the researcher's list after signing a written consent form. The participants were assured that their information would be kept confidential and that they could leave the study at any stage of the research if they wished or did not need further treatment. In the simple random sequences step, a table of random numbers was used and each participant was given a unique identifier. In the next step, through random allocation concealment, drug boxes of identical shape and format containing herbal medicines or placebo were randomly coded and numbered. All participants and investigators were blinded to the capsule contents. After 2 months of intervention, the contents of the capsules given to each group were revealed by the pharmacist. After the study was completed, the researchers received information about the numbers and the content of each box.

Fennel, EPO, and placebo were placed inside the same color capsules and were coded by the Barij Essence Pharmaceutical Company, Kashan, and Iran. The method of consumption of capsules in all groups was 2 capsules daily (morning and night), 12 hours after meals for 8 weeks. The major components of fennel essential oils included trans-anethole, fenchone, and estragole (methyl chavicol). Foeniculum vulgare Mill essence was produced by distilling the fennel seeds with water vapor. For this study, pearl-shaped pills (30 mg) were formed from the essence. Fennel drug toxicity has been assessed in a past study and its safety has been reported.[19] Moreover, 1000 mg soft capsules containing 70-140 mg of Gamolenic Acid (GLA) obtained from evening primrose (Oenothera biennis) seeds with concentrations of 7-14% were used in the present study. Numerous studies on EPO have found no toxicity.[20] The placebo contained 100 mg soy starch.

The main outcome was the results of hormonal assessment [Follicle-Stimulating Hormone (FSH), and estradiol]. At the beginning and end of the study period, 5cc venous blood sample was obtained from the studied population. Plasma was detached and maintained at -20ºC until it was assayed using immunoassay kits [Monobind Inc., Germany] according to the manufacturer's instructions. The secondary outcome was questionnaire data that were collected at the start of the study and at the end of the study period. In this study, a demographic characteristics questionnaire and the MRS were used. The demographic characteristics questionnaire included questions about age, menarche age, menopause age, partner's age, weight (kg), and number of gravidity, parity, and children. The MRS is designed to assess menopause-specific health-related Quality of Life (QoL) through measuring the severity of age/menopause-related complaints by rating a profile of symptoms. The MRS scale contains 11 items (symptoms or complaints) in the 3 dimensions of physical, psychological, and urogenital. The items are scored on a scale ranging from 0 (no symptoms) to 4 (severe symptoms) based on the severity of the symptoms perceived by the woman completing the scale. The MRS has been validated to

measure menopausal symptoms in Iranian women with a Cronbach's alpha of 0.931.[21]

The sample size was calculated based on similar previous studies[22] and provided that the ratio of 50% of severe menopausal symptoms (P_0 = 50%) is reduced to 20% (P_1 = 20%) after the intervention with 95% confidence internal (CI) (α =0.05) and power level of 80% (β =0.20), the sample size was determined to be 45 people in each group by predicting a 20% drop.

The analysis of data was accomplished in SPSS software (version 16, SPSS Inc., Chicago, IL, USA). The quantitative variables are presented as mean (SD) and the qualitative variables as frequency (%). The Kolmogorov–Smirnov test was used for assessing the normality of variables. ANOVA and ANCOVA were used to compare variable means, and ANCOVA was used to control for age, menopausal age, and body mass index (BMI). The Benferoni, adjustment of multiple comparisons, was used for groups with significant post-test changes. The significance of the pretest is not important; however, if it is significant, it confirms the used ANCOVA analysis, and the use of this test in this case becomes more valuable and important. The significance level was considered to be less than 0.05.

Ethical considerations

The study was approved by the Ethics and Research Committee of Jahrom University of Medical Sciences (reference number: UMS.REC. 1396.136). Informed consents were obtained from all participants.

Results

In total, 125 participants aged 45-60 years in 3 groups (43 in fennel group, 42 in primrose group, and 40 in placebo group) completed the study and 10 individuals dropped out in the follow-up stage [Figure 1]. The demographic criteria with the highest prevalence were primary school (49.32%), unemployed (85.36%), insufficient income (42.62%), and natural childbirth history (78.72%). The demographic criteria were not significantly different between the 3 groups ($p > 0.05$) [Table 1].

The mean of FSH, estradiol, and MRS scores in the groups before and after the intervention is presented in Table 2. The study results showed that the mean FSH score in the fennel group decreased 14 IU/L compared to the placebo group (p = 0.00). In addition, the mean FSH score in the EPO group decreased 20 IU/L compared to the placebo group ($p < 0.05$). The mean estradiol score significantly increased (33 pg/ml) in the fennel group and the EPO group (25 pg/ml) compared to the placebo group [Table 3]. Moreover, the mean estradiol score in the fennel group (7 pg/ml) significantly increased compared to the EPO group. The difference in the mean FSH score between the fennel and EPO groups after the intervention was not significant.

Table 1: Demographic characteristics of participants

Mean (SD*)	Fennel	EPO**	Placebo	*p****
Age	54.41 (4.41)	52.85 (4.33)	53.35 (4.57)	0.257
Partner's age	59.18 (6.38)	59.71 (7.25)	60.72 (6.52)	0.575
Menarche age	13.44 (2.33)	13.16 (1.76)	13.17 (2.02)	0.783
Gravidity	4.88 (2.43)	5.23 (2.51)	6.30 (6.63)	0.298
Parity	4.33 (1.93)	4.57 (1.97)	4.62 (1.91)	0.788
Weight	70.38 (9.28)	72.28 (11.4)	72.00 (12.07)	0.690

*SD: Standard Deviation, **EPO: Evening primrose oil, ***P: ANOVA test

The mean MRS score significantly decreased in the fennel and EPO groups compared to placebo [Table 4], but this difference was only significant in the psychological dimension. The physical and urogenital dimensions did not change after the intervention. The difference in the mean MRS score between the fennel and EPO groups after the intervention was not significant.

Discussion

Based on this study, FSH level significantly decreased and estradiol level significantly increased in the Fennel and EPO groups 2 months after the intervention. In animal studies, use of fennel[23] and EPO[24] increased FSH and decreased luteinizing hormone in rats with Polycystic Ovary Syndrome (PCOS). Moreover, another animal study demonstrated that fennel extract enhanced the serum level of estrogen, progesterone, and prolactin[25] and EPO elevated prolactin, testosterone, and decreased gonadotropin levels.[26]

However, in a human study, the use of fennel for 3 months did not change the FSH score in girls with PCOS.[27] In menopausal women, estradiol level increased after the use of fennel for 8 weeks, but this was not statistically significant.[28] Furthermore, the use of a phytoestrogen such as Cimicifuga racemosa in infertile women had positive effects on mid-cycle estradiol level and pregnancy rate.[29] In some researches, Chinese Herbal Medicines have been recommended for decreasing FSH level before menopause and for preventing premature menopause.[30,31]

Given that the sex hormone balance changes before and after menopause, the effectiveness of herbal medicines, especially phytoestrogens, on hormonal changes should be different.[13] It appears that stimulation of estrogen receptors or mechanisms other than estrogen pathways (antioxidant and anti-inflammatory activities) may contribute to the beneficial impact of herbal therapy in women's health.[32]

The present study results showed that the usage of fennel and EPO can decrease the MRS score, especially in the psychological dimension, after 8 weeks. In the same studies, the use of fennel for 8-10 weeks reduced the MRS score in Iranian[33] and Indonesian menopausal women.[34]

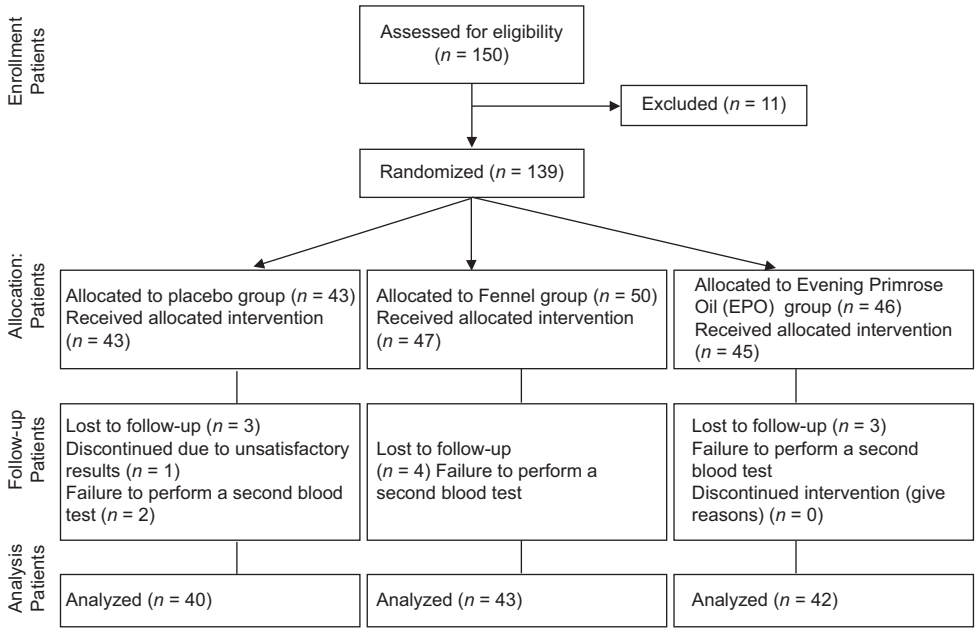

Figure 1: CONSORT flow diagram

Table 2: Comparison of mean (FSH), estradiol, and the (MRS) score between the groups before and after the intervention

	FSH*		Estradiol		MRS**	
	Before Mean(SD)	After Mean(SD)	Before Mean(SD)	After Mean(SD)	Before Mean(SD)	After Mean(SD)
Fennel	77.57(25.45)	59.51(37.08)	52.37(47.01)	74.03(21.42)	21.33(2.82)	17.96(3)
EPO***	77.97(30.64)	54.23(32.01)	41.61(26.88)	66.26(34.45)	21.36(4.12)	18.84(3.27)
Placebo	74.47(33.48)	74.41(43.23)	43.23(21.24)	40.43(25.07)	20.39(3.29)	20.13(2.90)
*p*****	0.846	0.019	0.292	0.003	0.877	0.010

*FSH: Follicle-stimulating hormone, **MRS: Menopause Rating Scale, *** EPO: Evening primrose oil, ****ANCOVA test

Table 3: Pairwise comparisons of means (FSH) and estradiol levels between the groups after the intervention

	FSH*				Estradiol			
	Mean difference (SE)	95% Confidence Interval for Difference		*p***	Mean difference (SE)	95% Confidence Interval for Difference		*p***
		Lower bound	Upper bound			Lower bound	Upper bound	
Fennel vs. placebo	-14.90 (3.24)	-2.77	-7.02	<0.001	33.60 (3.101)	26.06	41.13	<0.001
EPO*** vs. placebo	-20.18 (3.255)	-8.08	-2.27	<0.001	25.83 (3.166)	18.14	33.59	<0.001
EPO vs. Fennel	-5.28 (3.20)	-3.04	2.49	0.30	-7.77 (3.130)	- 5.37	-0.17	0.043

Based on estimated marginal means. *FSH: Follicle-stimulating hormone, **Adjustment for multiple comparisons: Bonferroni correction, ***EPO: Evening Primrose Oil

One study has suggested that fennel consumption does not improve vaginal atrophy in postmenopausal women,[35] but another study reported beneficial impact on sexual function in postmenopausal women.[36]

Other studies showed that EPO affected psychological symptoms after 8 weeks,[37] and its combination with other herbal supplements after 4 weeks reduced headache, urinary incontinence, and dry vaginal problems.[38] However, one research reported that EPO has no benefits in treating hot flashes compared with placebo.[39] Menopause symptoms are correlated with reduced levels of sex hormones, but other symptoms such as sleep disturbance, fatigue, and anxiety are multifactorial symptoms. Although the cause of menopausal problems is a decrease in sex hormones, the severity of these problems is a multifactorial variable.[40] Sociodemographic characteristics, such as being unemployed or a housewife, lifestyle factors, attitudes toward menopause, marital relationship, and the psychological status, can affect the severity of menopause symptoms[41,42] during herbal treatment and can be considered as confounder factors in these studies.

The diet of menopausal women should be considered in future studies in the evaluation of herbal medicine, because

Table 4: Pairwise comparisons of mean (MRS) score between the groups after the intervention

	MRS*		
	Fennel vs. placebo	EPO *** vs. Placebo	EPO vs. Fennel
Mean difference (Std.Error)	-2.17 (0.54)	-1.29 (0.55)	0.88 (0.54)
95% Confidence interval for difference			
Lower bound	-3.48	-2.63	-0.44
Upper bound	-0.86	0.04	2.20
*p***	<0.001	0.055	0.322

*MRS: Menopause Rating Scale, **Adjustment for multiple comparisons: Bonferroni Correction,***Evening Primrose Oil

a high-fat, low-fiber diet causes a rise in estrogen levels during menopause.[43]

Health care providers should realize that hormone replacement therapy is not recommended due to the cancer tsunami, and many postmenopausal women seek to alleviate the physical and psychological problems caused by hormonal changes during menopause through complementary medicine. Thus, using herbal supplements along with psychotherapy interventions can be one of the integrated health approaches to managing menopausal symptoms.[44] Therefore, all midwives should be familiar with herbal supplement therapy and effective medications in this regard.

Based on the results of this study, herbal phytoestrogens such as fennel and EPO can be effective in treating menopausal symptoms and none of them is superior to the other. Therefore, health care providers, especially midwives, should prescribe herbal medicine for postmenopausal women. Then, herbal medicines such as EPO and fennel can be used to alleviate menopause problems and can be recommended by health care providers.

Some limitations of this study were small sample size, low generalizability, short time of treatment, and failure to assess all sex hormones. Although we were well aware of these problems, we were not able to overcome them due to financial and logistic obstacles. Thus, we suggest for future studies that combined use of herbal supplements during menopause may be more effective than single use in improving menopausal symptoms, and it is possible to achieve better outcomes in a shorter duration.

Conclusion

The data of the present study demonstrated significant changes in FSH, estradiol, and psychological menopausal symptoms in postmenopausal women in the fennel group and evening primrose oil group.

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Conflicts of interest

Nothing to declare.

References

1. Dalal PK, Agarwal M. Postmenopausal syndrome. Indian J Psychiatry 2015;57:222-32.
2. Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T. Symptoms of menopause—global prevalence, physiology and implications. Nat Rev Endocrinol 2018;14:199-215.
3. Tempfer CB, Hilal Z, Kern P, Juhasz-Boess I, Rezniczek GA. Menopausal hormone therapy and risk of endometrial cancer: A systematic review. Cancers (Basel) 2020;12:2195. doi: 10.3390/cancers12082195.
4. Riazi H, Ghazanfarpour M, Taebi M, Abdolahian S. Effect of vitamin D on the vaginal health of menopausal women: A systematic review. J Menopausal Med 2019;25:109-16.
5. Hunter M, Melanie Smith In Collaboration With The British Menopause Society. Cognitive Behaviour Therapy (CBT) for menopausal symptoms: Information for GPs and health professionals. Post Reprod Health 2017;23:83-4.
6. Ghazanfarpour M, Sadeghi R, Abdolahian S, Latifnejad Roudsari R. The efficacy of Iranian herbal medicines in alleviating hot flashes: A systematic review. Int J Reprod Biomed 2016;14:155-66.
7. Kargozar R, Azizi H, Salari R. A review of effective herbal medicines in controlling menopausal symptoms. Electron Physician 2017;9:5826-33.
8. Ebrahimi A, Tayebi N, Fatemeh A, Akbarzadeh M. Investigation of the role of herbal medicine, acupressure, and acupuncture in the menopausal symptoms: An evidence-based systematic review study. J Family Med Prim Care 2020;9:2638-49.
9. Castelo-Branco C, Gambacciani M, Cano A, Minkin MJ, Rachoń D, Ruan X, *et al*. Review and meta-analysis: Isopropanolic black cohosh extract iCR for menopausal symptoms-An update on the evidence. Climacteric 2021;24:109-19.
10. Khadivzadeh T, Najafi MN, Kargarfard L, Ghazanfarpour M, Dizavandi FR, Khorsand I. Effect of fennel on the health status of menopausal women: A systematic and meta-analysis. J Menopausal Med 2018;24:67-74.
11. Christelle K, Zulkfili M, Noor N, Draman N. The effects of evening-primrose oil on menopausal symptoms: A systematic review and meta-analysis of randomized controlled trials. Curr Womens Health Rev 2020;16:265-76.
12. Nazari A, Roozbehani A. Influence of fennel Foeniculum vulgar extract on fertility, growth rate and histology of gonads on guppy Poecilia reticulata. Turk J Fish Aquat Sci 2015;15:457-63.
13. Sunita P, Pattanayak S. Phytoestrogens in postmenopausal

indications: A theoretical perspective. Pharmacogn Rev 2011;5:41-7.
14. Albert-Puleo M. Fennel and anise as estrogenic agents. J Ethnopharmacol 1980;2:337-44.
15. Shewchuk BM. Prostaglandins and n-3 polyunsaturated fatty acids in the regulation of the hypothalamic–pituitary axis. Prostaglandins Leukot Essent Fatty Acids 2014;91:277-87.
16. Holloway D. Update on non-hormonal treatment options during the menopause. Nurse Prescribing 2017;15:28-32.
17. Najaf Najafi M, Ghazanfarpour M. Effect of phytoestrogens on sexual function in menopausal women: A systematic review and meta-analysis. Climacteric 2018;21:437-45.
18. Glaser R, York AE, Dimitrakakis C. Beneficial effects of testosterone therapy in women measured by the validated Menopause Rating Scale (MRS). Maturitas 2011;68:355-61.
19. Badgujar SB, Patel VV, Bandivdekar AH. Foeniculum vulgare mill: A review of its botany, phytochemistry, pharmacology, contemporary application, and toxicology. Biomed Res Int 2014;2014:842674. doi: 10.1155/2014/842674.
20. CHAPTER 16: Romm A. Labor and Birth, in Botanical Medicine for Women's Health. In: Romm A, Hardy ML, Mills S, editors. Botanical Medicine for Women's Health - Elsevier eBook on VitalSource, 2nd Edition. Saint Louis, U.S.A.: Churchill Livingstone; 2010. p. 398-415.
21. Jahangiry L, Parviz R, Mirghafourvand M, Khazaee-Pool M, Ponnet K. The psychometric properties of the Persian menopause rating scale. BMC Womens Health 2020; 20:172.
22. Tavoni S, Shakeri F, Haghani H, Gooshehgir A. The effect of red clover on severity of physical menopause symptoms. Journal of Research Development in Nursing and Midwifery 2013;10:75-80.
23. Karampoor P, Azarnia M, Mirabolghasemi G, Alizadeh F. The effect of hydroalcoholic extract of fennel (foeniculum vulgare) seed on serum levels of sexual hormones in female wistar rats with polycystic ovarian syndrome (PCOS). Journal of Arak University of Medical Sciences 2014;17:70-8.
24. 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. J Armaghane danesh 2018;22:714-24.
25. Sadeghpour N, Montaseri A, Najafpour A, Dolatkhah H, Rajabzadeh A, Khaki A. Study of foeniculum vulgare (fennel) seed extract effects on serum level of estrogen, progesterone and prolactin in mouse. Crescent Journal of Medical and Biological Sciences 2015;2:23-7.
26. Atteia HH, Alzahrani S, El-Sherbeeny NA, Youssef AM, Farag NE, Mehanna ET, *et al*. Evening primrose oil ameliorates hyperleptinemia and reproductive hormone disturbances in obese female rats: Impact on estrus cyclicity. Front Endocrinol (Lausanne) 2020;10:942. doi: 10.3389/fendo.2019.00942.
27. Ghavi F, Taghizadeh M, Taebi M, Abdolahian S. Effect of Foeniculum vulgare essence on symptoms of polycystic ovarian syndrome (PCOS): A randomized double-blind, placebo-controlled trial. J Herb Med 2019;17:100277.
28. Ghaffari P, Hosseininik M, Afrasiabifar A, Sadeghi H, Hosseininik A, Tabatabaei S, *et al*. The effect of fennel seed powder on estradiol levels, menopausal symptoms, and sexual desire in postmenopausal women. Menopause 2020;27:1281-6.
29. Shahin AY, Mohammed SA. Adding the phytoestrogen cimicifugae racemosae to clomiphene induction cycles with timed intercourse in polycystic ovary syndrome improves cycle outcomes and pregnancy rates-A randomized trial. Gynecol Endocrinol 2014;30:505-10.
30. Teng B, Peng J, Ong M, Qu X. Successful pregnancy after treatment with chinese herbal medicine in a 43-year-old woman with diminished ovarian reserve and multiple uterus fibrosis: A case report. Medicines (Basel) 2017;4:7. doi: 10.3390/medicines4010007.
31. Elliott D. The treatment of elevated FSH levels with Chinese medicine. Journal of Chinese Medicine 2009;91:5-11.
32. Mahboubi M. Foeniculum vulgare as valuable plant in management of women's health. J Menopausal Med 2019;25:1-14. doi: 10.6118/jmm. 2019.25.1.1.
33. Golzareh P, Rahimi R, Rahimikian F, Bekhradi R, Mehran A. The effect of fennel oral capsules on physical symptoms caused by menopause in women. The Iranian Journal of Obstetrics, Gynecology and Infertility2017;20:41-8.
34. Emilda E, Nora V. Analysis of the effect foiliculum vulgare seeds on the menopausal score rating scale on menopause women in District Langsa–Indonesia. J Med Rev Case Rep 2020;4:114-7.
35. Ghazanfarpour M, Shokrollahi P, Khadivzadeh T, Baharian Sharghi N, Mirzaii Najmabadi K, Babakhanian M, *et al*. Effect of foeniculum vulgare (fennel) on vaginal atrophy in postmenopausal women: A double-blind, randomized, placebo-controlled trial. Post Reprod Health 2017;23:171-6.
36. Abdali K, Dowran P, Emamghoreishi M, Kasraian M, Tabatabaei H. Comparison of the effect of Foeniculum vulgare and St John's wort (Hypericum perforatum) on the climacteric symptoms and sexual activity in menopausal woman. Int J Adv Biotechnol Res 2016;7:148-54.
37. Sharif S, Darsareh F. Impact of evening primrose oil consumption on psychological symptoms of postmenopausal women: A randomized double-blinded placebo-controlled clinical trial. Menopause 2020;27:194-8.
38. Yakoot M, Salem A, Omar AM. Effectiveness of a herbal formula in women with menopausal syndrome. Forsch Komplementmed 2011;18:264-8.
39. Farzaneh F, Fatehi S, Sohrabi MR, Alizadeh K. The effect of oral evening primrose oil on menopausal hot flashes: A randomized clinical trial. Arch Gynecol Obstet 2013;288:1075-9.
40. Pimenta F, Leal I, Maroco J, Ramos C. Menopause symptoms' predictors: The influence of lifestyle, health- and menopause-related, and sociodemographic characteristics. J Women Aging 2012;24:140-51.
41. Lee MS, Kim JH, Park MS, Yang J, Ko YH, Ko SD, Joe SH. Factors influencing the severity of menopause symptoms in Korean post-menopausal women. J Korean Med Sci 2010;25:758-65.
42. Capistrano E, Dombek K, da Costa A, Marinheiro L. Factors associated with the severity of menopausal symptoms in postmenopausal Brazilian women. Reproducao e Climaterio2015;30:70-6.
43. Aubertin-Leheudre M, Gorbach S, Woods M, Dwyer JT, Goldin B, Adlercreutz H. Fat/fiber intakes and sex hormones in healthy premenopausal women in USA. J Steroid Biochem Mol Biol 2008;112:32-9.
44. Johnson A, Roberts L, Elkins G. Complementary and alternative medicine for menopause. J Evid Based Integr Med 2019;24:1-14.