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Original Article

Evaluating the effect of fennel soft capsules on the quality of life and its different aspects in menopausal women: A randomized clinical trial

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ABSTRACT

Background & Aim: Menopause is one of the natural phases of women's life. At this phase, due to the large fluctuations in hormones, undesirable physical, mental and sexual symptoms would occur that have negative effects on the quality of life of women. Due to the side effects of hormonal therapy, many women would prefer complementary medicine and especially herbal medicine. The present study was conducted to evaluate the effect of fennel on the quality of life in menopausal women.

Methods & Materials: This randomized triple-blind clinical trial was conducted on 90 menopausal women aged 45-60 years in Tehran. Participants were randomly allocated into two groups of fennel and placebo. The participants in the fennel group received oral soft capsules containing 100mg of fennel twice a day for 8 weeks and women in the placebo group received the same doze of placebo capsules containing 100mg of sunflower oil. The measured outcomes in the present study were the quality of life in menopausal women and its different aspects including vasomotor, socio-psychological, physical and sexual aspects which were measures using Menopause-Specific Quality of Life (MENQOL) questionnaire. Data were analyzed using SPSS14.

Results: After 8 weeks of intervention, covariance analysis showed a significant difference in the score of quality of life and its four measured aspects between the two studied groups (for quality of life, vasomotor aspect, physical aspect and socio-psychological aspect: $p < 0.001$, for sexual aspect: $p=0.013$). In the fennel group, the score of quality of life and its aspects had a significant decrease after the intervention compared to before the intervention ($p < 0.001$). In the placebo group the scores of quality of life and socio-psychological, physical and sexual aspects had a significant decrease after the intervention ($p < 0.05$) but the score of vasomotor aspect was increased.

Conclusions: The present study showed that the fennel could decrease the symptoms of menopause with no serious side effects and consequently improve menopausal women's quality of life.

Introduction

Menopause is a general phenomenon in women and, considering the growth in the elderly population, millions of women would experience it globally. It is the permanent cessation of menstruations

following the inactivity of the ovaries (1). The mean age of menopause among Iranian women is 48.2 years and among women of the developed countries is 51 years; therefore Iranian women would experience menopause at a relatively younger age (2-4). Despite the increase in women's life expectancy, the menopause age has significantly remained unchanged and women would spend one third or about 30 years of their lives during postmenopausal period (4). The decrease in the level of

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ovarian hormones (progesterone and especially estrogen) during this period, would lead to occurrence of symptoms such as vasomotor symptoms, genitourinary problems, osteoporosis, mental-cognitive problems, sleep disorders and sexual problems (1, 5). These symptoms could have damaging effects on women's life and impact their quality of life (6). During the menopausal period, quality of life has a close relation with menopausal symptoms and their intensity in a way that menopause would decrease the quality of life and effective interventions after menopause could improve the quality of life in menopausal women (7). Quality of life is a health-related concept and includes different physical, mental, individual and social aspects (8).

Using hormone replacement therapy (HRT) is an old tradition for treating the symptoms of menopause but has various side effects (9). Many menopausal women would prefer complementary and alternative medicine (CAM) to relieve the symptoms of menopause (6). Studies have shown that 32.9% of women around the world are using complementary medicine and about half of them are using this method for treating the symptoms of menopause (10). According to the conducted studies, 37.3% of Iranian obstetricians and midwives would use complementary medicine to prevent gynecological diseases (11).

Herbal medicine is one of the branches of complementary medicine (12) and phytoestrogens or plant estrogens are chemical combinations similar to estrogen in plants (1), which their role in reducing the symptoms of menopause has been proven in many studies (13, 14).

Foeniculum vulgare is globally known as fennel and its different parts such as the fruit (seed), leaves and flowers are being used for different reasons. This plant is native to the Mediterranean region but is cultivated in

almost every country especially Asian, Northern American and European countries. Due to its medical benefits, the cultivation of fennel has been increased globally during the recent years. The main components of fennel are Anethole, Fenchone, Estragole and phenolic combinations (15-18).

In the traditional medicine of many countries, fennel is being used for treating pain, cancer, colic, digestive problems, spasm, dizziness, anorexia, fever, high blood pressure, menstrual problems, insomnia, memory improvement, obesity, ... (16, 17).

Different combinations in this plant would cause different properties such as antioxidant and anti-aging, anti-inflammatory, anti-cancer, cardiovascular prevention, arthritis inhibition and strong antinociceptive properties (17, 18). Studies have shown that fennel also has estrogenic properties and its consumption could increase the serum estrogen level and stimulate the secretion of estrogen in body, increase the growth of ovarian follicles, increase the growth of mammary glands and different parts of the reproductive system (vagina, cervix, endometrium, myometrium...) and treat amenorrhea (19-23). Researchers believe that Anethole polymers such as dianethole and photoanethole would function as phytoestrogens (24). However, flavonoids also have estrogenic effects (25, 26). Considering the importance of women's health during the physiologic and yet, sensitive period of menopause and the extended uses of various methods of complementary medicine such as herbal medicine by women to relieve the symptoms of menopause, conducting more researches in this field seems necessary. Therefore, considering the different components of fennel and its benefits and since many studies have mentioned the estrogenic property of fennel but a few studies have evaluated the effect of this phytoestrogen on

the symptoms of menopause and quality of life among menopausal women, the present study was conducted to evaluate the effect of fennel soft capsules on the quality of life and its different aspects in menopausal women.

Methods

The present study was a randomized triple-blind placebo-controlled clinical trial that was conducted to evaluate the effect of oral fennel capsules on the quality of life and its different aspect in menopausal women during 8 weeks. The sample size was calculated to be 39 participants in each group using previously conducted similar studies and the mean of differences formula (assuming that $\alpha = 0.05$ [confidence interval of 95%], $\beta = 0.2$ [test power of 80%], $\delta = 19$ and $e = 14$). And after considering the sample loss at any stage of the study, it was increased to 45 participants in each group. After taking necessary permissions from the ethics committee and relevant authorities, the researcher referred to the Framanfarmayian health center, affiliated to Tehran University of Medical Sciences, every day and started taking the medical history of the visitors. The inclusion criteria were being 45 to 60 years old, being married, passing at least 1 year and at most 5 years from the last menstruation, complaining from the symptoms of menopause, not having any physical or mental diseases, no history of breast cancer, not using any hormonal or herbal drugs or undergoing any complementary medicine therapy to relieve the symptoms of menopause, not having allergy to herbal medicine, not using tranquilizer or antidepressant drugs, not being addicted or smoking, and being illiterate. The exclusion criteria were showing allergic reaction to the fennel or placebo, having a diagnosed disease during the study, unwillingness to

continue the study, not taking the drug or the placebo for 6 days, using other effective methods for relieving the symptoms of menopause. 90 participants with the inclusion criteria who were willing to cooperate were enrolled in the study after taking written informed consent from all of them. Participants were randomly allocated into two groups of A and B using random numbers.

The measured outcomes in the present study were quality of life and its different aspects including vasomotor, socio-psychological, physical and sexual aspects using Menopause-Specific Quality of Life (MENQOL) questionnaire. MENQOL is a valid tool for evaluating the quality of life during menopause which was designed and standardized by Hilditch et al in 1996 at the University of Toronto. This tool contains 29 close questions with a scoring range of 0 to 6 based on the Likert scale and includes four aspects of vasomotor (3 questions), socio-psychological (7 questions), physical (16 questions) and sexual (3 questions). The total score of menopause women's quality of life would be calculated by summing the scores of these four aspects. In this questionnaire, higher scores indicate worse quality of life while lower scores indicate better quality of life in menopausal women (27). Fallahzadeh et al (2006) have approved the validity of the Farsi version of this tool using content validity and approved its reliability with a Cronbach's α of 0.85 (7). Also, using test retest method, Yazdkhasti et al determined that the internal consistency of the questions about quality of life was 0.84, in the vasomotor aspect was 0.80, in the socio-psychological aspect was 0.79, in the physical aspect was 0.82 and in the sexual aspect was 0.83 (28). Participants of both of the intervention and the placebo groups completed the demographic characteristics and MENQOL questionnaires before the intervention. After the primary completion

of the questionnaires, participants of both groups received similar drugs in shape, color, size, smell and packaging (oral fennel capsules and placebo) that were produced by Barij Essence Company and labeled A or B along with a drug consumption checklist.

One of the drugs was 100mg soft capsules of fennel and the other was 100mg soft capsules of placebo. The 100mg fennel capsules contained fennel essence that was produced through extraction process (distillation and condensation) from the fennel fruits. Each capsule was packed with a basis of 71-90 mg of Anethole in a base of sunflower oil. The placebo capsules contained sunflower oil. The participants took the oral capsules twice a day for 8 weeks. None of the participants, researchers and the statistical analyst had information about the content of the drugs; therefore the study was triple-blind. The researcher got the participants' phone numbers to follow-up their correct drug consumption and also to monitor them for having any adverse side effects; also the participants had the researcher's phone number so that they could contact the researcher in case of any problem. The researcher was contacting the participants through phone calls once a week

during the 8-week intervention. At the end of the 8th week, all the participants filled the Menopause-Specific Quality of Life questionnaire again. The gathered data were analyzed using SPSS14 with a significant level of less than 0.05 using independent t-test, Fisher's exact test, chi-square test, paired t-test and covariance analysis (In order to evaluate the difference between mean scores in posttest with controlling the pretest).

Results

From the 90 selected participants, 80 (40 in the fennel group and 40 in the placebo group) completed the study. No serious side effects were reported by the participants during the study. From the fennel group 2 participants were excluded due to irregular drug consumption, 1 due to having sever hot flashes, 1 for being diagnosed with gallbladder stone during the study, and 1 for having skin rash. The reason for exclusion from the placebo group were 1 for irregular drug consumption, 2 for unwillingness to continue the study, 1 for digestive problems (diarrhea) and 1 for migration.

Table 1. Comparison of demographic and clinical characteristics of menopausal women in two studied groups

Characteristic	<i>Foeniculum vulgare</i>	Placebo	P-Value
Age (Mean ± SD *)	52.33±3.11	51.85±3.71	0.54**
Husband's age (Mean ± SD)	60.90±5.84	59.15±7.02	0.23**
Menopausal age(Mean ± SD)	49.18±2.45	48.18±3.37	0.13**
Years passing from menopause (Mean ± SD)	3.15±1.85	3.71±1.30	0.12**
Number of children (Mean ± SD)	3.08±1.38	2.85±1.03	0.41**
BMI (Mean ± SD)	28.32±3.68	27.14±2.62	0.10**
Employment status N (%)	Housekeeper	39 (97.5)	
	Occupying	1 (2.5)	1***
Husband's employment status N (%)	Occupying	20 (50)	
	Unemployed	20 (50)	0.11****
	Academic	2 (5)	
Educational level N (%)	Primary or guidance school	23 (57.5)	
	High school or diploma	15 (37.5)	1***
	Academic	2 (5)	
Economic status N (%)	Weak	5 (12.5)	
	Normal	30 (75)	0.41***
	Well	5 (12.5)	

*standard division **independent t test ***fisher's exact test ****chi-square test

Table2. Comparison of scores of Quality of Life and its different aspects between the two groups

Quality of life	Time	<i>Foeniculum vulgare</i>	Placebo	P-Value
Vasomotor aspect	Before the intervention	15.17±5.20	13.22±5.39	0.11*
	After 8 weeks	8±5.13	15 ±5.79	<0.001**
	P-Value	<0.001***	0.02***	
Socio-Psychological aspect	Before the intervention	30.77±11.40	28.12±10.18	0.30*
	After 8 weeks	19.48±7.68	25.20±8.58	<0.001**
	P-Value	<0.001***	0.02***	
Physical aspect	Before the intervention	62.35±17.68	63.57±14.92	0.74*
	After 8 weeks	36.40±13.61	58.50±16.77	<0.001**
	P-Value	<0.001***	0.02***	
Sexual aspect	Before the intervention	14.35±6.22	16.15±5.33	0.13*
	After 8 weeks	10.77±4.69	14.02±5.18	0.013**
	P-Value	<0.001***	0.02***	
Total score	Before the intervention	122.65±29.23	121.08±25.45	0.80*
	After 8 weeks	74.60±25.11	112.73±26.39	<0.001**
	P-Value	<0.001***	0.03***	

*independent t test ** covariance test *** paired t test

Considering the demographic characteristics, independent t-test showed no significant statistical difference between both groups regarding their quantitative variables including age, husband’s age, the age of the last menstrual cycle, the years passing from menopause, number of children and body mass index. Fisher’s exact test and chi-square test also showed no significant difference between both groups regarding their qualitative variables including employment status, husband’s employment status, educational level and economic status (Table 1). According to table 2, independent t-test showed no significant difference between the fennel and the placebo groups regarding the quality of life in menopausal women and its different aspects before the intervention and both groups were homogenous regarding in these variables. But according to covariance analysis, after the intervention, there was a significant difference between the scores of quality of life and its four different aspects of the fennel and the placebo groups (for quality of life and 3 aspects of socio-psychological, physical and vasomotor: $p < 0.001$ and for sexual aspect: $p = 0.013$).

Comparing the before and after the intervention scores revealed that after 8

weeks of intervention the scores of quality of life and each of its four aspects were significantly decreased in the fennel group ($p < 0.001$). In the placebo group also after the intervention the scores of quality of life and 3 aspects of socio-psychological, physical and sexual were significantly decreased ($p < 0.05$) but the score of vasomotor aspect increased (the quality of life in the domain of vasomotor was worsen for the placebo group).

Discussion

The aim of this study was to evaluate the effect of fennel on the quality of life of menopausal women. Results of the present study showed that fennel and placebo both decreased the total score of Menopause-Specific Quality of Life questionnaire (decreased the symptoms of menopause) and consequently improved the quality of life in menopausal women; however, this decrease was more significant in the fennel group compared to the placebo group. The present study showed that fennel could significantly improve different aspects of vasomotor, socio-psychological, physical and sexual of quality of life while in the placebo group only three aspects of socio-psychological, physical and sexual were significantly

improved and no improvement was observed in the aspect of vasomotor.

Comparing the scores after the intervention showed a significant difference between both the fennel and the placebo groups in their total score of quality of life and the scores of its four aspects. This significant difference indicates that fennel has been more effective in improving the quality of life in menopausal women. The effect of placebo on decreasing the symptoms of menopause and consequently improving women's quality of life could be due to the Placebo effect because placebo could also improve the symptoms of menopause to some extent (29). Results of the present study were in line with the results of previous studies that evaluated the effect of phytoestrogens on the symptoms of menopause and confirmed the positive effect of these plants on reducing the symptoms of menopause. Results of the present study were similar to the results of Chedraui et al (2011) who evaluated the effect of soy on flushing and symptoms of menopause using the MRS tool (30). Rostock et al (2011) evaluated the effect of black cohosh on the symptoms of menopause using the MRS tool and their results confirmed the positive effect of this phytoestrogen on the symptoms of menopause (31). Abdali et al (2016) in their study compared the effect of fennel and St John's wort on the symptoms of menopause and sexual performance of menopausal women and their results indicated the effect of fennel on reducing the symptoms of menopause (32). Although the used tool in the present study was different than the three mentioned studies, but the results were in line with their results and fennel has been effective in reducing the symptoms of menopause like the phytoestrogens used in these three studies.

In the study of Basaria et al (2009) using soy significantly improved all the subgroups of the Menopause-Specific Quality of Life

questionnaire (33). Welty et al (2007) in a study evaluated the effect of soy on the quality of life in menopausal women and resulted that soy consumption would decrease the symptoms of menopause and improve the quality of life in menopausal women (34). Results of the present study were also in line with these two studies. The similarity between the results of the present study and the mentioned studies could be due to the similarity in the estrogenic property of fennel and the used plants in these studies.

Norozi et al (2016) in a study evaluated the effect of soy milk on the quality of life in menopausal women using MENQOL. They observed no significant difference between the both groups of soy milk and placebo after the intervention (35). Amato et al (2013) also evaluated the effect of soy on the quality of life in menopausal women and found no significant difference between the intervention and the placebo groups comparing the scores of MENQOL (36). Results of the present study were in conflict with the results of these two studies. It is probable that the differences in the type or the dose of the used phytoestrogen have been effective in the resulted conflict. Also in the present study cases of early or synthetic menopause (due to hysterectomy or oophorectomy) were not enrolled so this could also be effective in this difference.

Many studies have mentioned the estrogenic effect of fennel but only a few has evaluated the effect of this phytoestrogen on the symptoms of menopause. Therefore, the present study could be considered as one of the first studies that has evaluated the effect of fennel on the quality of life in menopausal women. The present study showed that consuming two 100mg oral capsules of fennel for 8 weeks would significantly decrease the symptoms of menopause and improve the quality of life in menopausal

women. Therefore, considering women's approach toward using herbal medicine, this available and inexpensive plant could be used as a treatment for reducing the intensity of menopause symptoms and improving the quality of life in menopausal women. However, considering the few number of studies about the effect of fennel on the symptoms of menopause, it seems that more studies in this regard are necessary to decisively confirm these results. One of the limitations of the present study was that due to lack of cooperation and willingness of the excluded participants to complete the questionnaires, it was not possible to perform intention to treat analysis. It is recommended to perform more studies with larger sample sizes and longer periods using intention to treat analysis for achieving more accurate results.

Results of the present study showed that fennel as an inexpensive phytoestrogen could decrease the vasomotor, socio-psychological, physical and sexual symptoms menopause and improve the quality of life in menopausal women. More studies should be conducted to confirm these results.

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Conflict of Interest

None reported.

References

1. Fritz MA, Speroff L. Clinical gynecology endocrinology and infertility, Philadelphia: Lippincott Williams & Wilkins; 2011. 673-857.
2. Rajaeefard A, Mohammad-Beigi A, Mohammad-Salehi N. Estimation of natural age of menopause in Iranian women: A meta-analysis study. *Koomesh*. 2011. 13(1): 1-7. [Persian]
3. Nahidi F, Karman N, Vallaei N, Fazli Z. Studying incidence of menopause and its effective factors in Tehran. *Research in Medicine*. 2010. 33(4): 258-265. [Persian]
4. Berek JS. Berek and Novak's Gynecology. Philadelphia: Lippincott Williams & Wilkins; 2012. 1320-1340.
5. Rahman SA, Zainudin SR, Mun VL. Assessment of menopausal symptoms modified Menopause Rating Scale (MRS) among middle age women in Kuching, Sarawak, Malaysia. *Asia Pacific Family Medicine*. 2010. 9(1): 5.
6. Bayer HealthCare Pharmaceuticals ,Menopausal complaints. Available at: <http://pharma.bayer.com/en/treatment-care/womens-health/menopausal-complaints/> Accessed 2.12.2016.
7. Fallahzade, H. Dehghani Tafti, A. Dehghani Tafti, M. Hoseini, F. Hoseini, H. Factors Affecting Quality of Life after Menopause in Women ,Yazd, 2008. *Journal of Shaheed Sadoughi University of Medical Sciences*. 2011. 18(6): 552-558. [Persian]
8. Fayers PM, Machin D. Quality of Life - Assessment, Analysis & Interpretation. England: John Wiley & Sons Ltd; 2000. 3-10.
9. Edelman JS. Menopause Matters: Your Guide to a Long and Healthy Life. United stat of America: Johns Hopkins Press Health Book; 2010. 41-53.

10. Posadzki P, Lee MS, Moon TW, Choi TY, Park TY, Ernst E. Prevalence of complementary and alternative medicine (CAM) use by menopausal women: a systematic review of surveys. *Maturitas*. 2013. 75(1): 34-43.
11. Fahimi F, Hrgovic I, El-Safadi S, Münstedt K. Complementary and alternative medicine in obstetrics: a survey from Iran. *Archive of Gynecology and Obstetrics*. 2011. 284(2): 361-4.
12. Fraser DM, Cooper MA. *Myles textbook for midwives*. England: Churchill Livingstone ;2009. 550-552.
13. Thomas AJ, Ismail R, Taylor-Swanson L, Cray L, Schnall JG, Mitchell ES, Woods NF. Effects of isoflavones and amino acid therapies for hot flashes and co-occurring symptoms during the menopausal transition and early postmenopause: a systematic review. *Maturitas*. 2014. 78(4): 263-76.
14. Chen M-N, Lin C-c, Liu C-f. Efficacy of phytoestrogens for menopausal symptoms: a meta-analysis and systematic review. *Climacteric*. 2015. 18(12): 260-269.
15. Crowley, Catherin. 101+ Recipes from the herb lady. USA: Lulu; 2006. 85-96.
16. Badgular SB, Patel VV, Bandivdekar AH. *Foeniculum vulgare Mill: A Review of Its Botany, Phytochemistry, Pharmacology, Contemporary Application, and Toxicology*. *BioMed research international*. 2014;2014:32.
17. Parthasarathy VA, Chempakam B, Zachariah TJ. *Chemistry of spices*: Cabi; 2008..
18. Rahimi R, Ardekani MRS. Medicinal properties of *Foeniculum vulgare Mill*. in traditional Iranian medicine and modern phytotherapy. *Chinese journal of integrative medicine*. 2013;19(1):73-9.
19. Rose J. *The aromatherapy book: applications and inhalations*: North Atlantic Books; 2013.
20. Khazaei M, Montaseri A, Khazaei MR, Khanahmadi M. Study of *Foeniculum vulgare* effect on folliculogenesis in female mice. *International journal of fertility & sterility*. 2011;5(3):122.[Persian]
21. Turkyılmaz Z, Karabulut R, Sönmez K, Basaklar AC. A striking and frequent cause of premature thelarche in children: *Foeniculum vulgare*. *Journal of pediatric surgery*. 2008;43(11):2109-11.
22. Malini T, Vanithakumari G, Megala N, Anusya S, Devi K, Elango V. Effect of *Foeniculum vulgare Mill*. seed extract on the genital organs of male and female rats. *Indian Journal of Physiology and Pharmacology*. 1985 Jan-Mar ; 29(1): 21-6.
23. Mohebbi-kian E, Mohammad-Alizadeh-Charandabi S, Bekhradi R. Efficacy of fennel and combined oral contraceptive on depot medroxyprogesterone acetate-induced amenorrhea: a randomized placebo-controlled trial. *Contraception*. 2014;90(4):440-6.
24. Puleo M. Fennel and anise as estrogenic agents. *Journal of Ethnopharmacology*. 1980 Dec; 2(4): 337-44.
25. Karabin M, Hudcova T, Jelinek L, Dostalek P. Biotransformations and biological activities of hop flavonoids. *Biotechnology advances*. 2015;33(6):1063-90.
26. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. *The Scientific World Journal*. 2013;2013.
27. Hilditch JR, Lewis J, Peter A, van Maris B, Ross A, Franssen E, et al. A menopause-specific quality of life questionnaire: development and psychometric properties. *Maturitas*. 1996 Jul;24(3):161-75
28. Yazdkhasti M, Keshavarz M, Merghati Khoei E, Hosseini AF. The effect of structured educational program by support group on menopause women's quality of life. *Iranian Journal of Medical Education*. 2012;11(8):986-94.[Persian]
29. Miller HG, Li RM, editors. *Measuring hot flashes: summary of a National Institutes of Health workshop*. Mayo Clinic Proceedings; 2004: Elsevier.
30. Chedraui P, San Miguel G, Schwager G. The effect of soy-derived isoflavones over hot flashes, menopausal symptoms and mood in climacteric women with increased body mass index. *Gynecological endocrinology*. 2011;27(5):307-13.
31. Rostock M, Fischer J, Mumm A, Stammwitz U, Saller R, Bartsch HH. Black cohosh (*Cimicifuga racemosa*) in tamoxifen-treated breast cancer patients with climacteric complaints—a prospective observational study.

Gynecological endocrinology. 2011;27(10):844-8.

32. 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. *International Journal of Biological Research*. 2016;7:148-154.

33. Basaria S, Wisniewski A, Dupree K, Bruno T, Song M, Yao F, et al. Effect of high-dose isoflavones on cognition, quality of life, and lipoprotein in post-menopausal women. *Journal of endocrinological investigation*. 2009;32(2):150-5.

34. Welty FK, Lee KS, Lew NS, Nasca M, Zhou J-R. The association between soy nut consumption and decreased menopausal symptoms. *Journal of women's health*. 2007;16(3):361-9.

35. Nourozi M, Haghollahi F, Ramezanzadeh F, Hanachi P. Effect of Soy Milk Consumption on Quality of Life in Iranian Postmenopausal Women. *Journal of family & reproductive health*. 2015;9(2):93. [Persian]

36. Amato P, Young RL, Steinberg FM, Murray MJ, Lewis RD, Cramer MA, et al. Effect of soy isoflavone supplementation on menopausal quality of life. *Menopause*. 2013;20(4):443-7.