

Effect of *Trigonella foenum* (fenugreek) vaginal cream on vaginal atrophy in postmenopausal women

Fakhriyeh Mazalzadeh¹, Khadijeh Hekmat², Foroogh Namjouyan³, Amal Saki⁴

¹Instructor, Department of Midwifery, Menopause Andropause Research Center, ²Instructor, Department of Midwifery, Nursing and Midwifery Faculty, ³Assistant Professor, Department of Pharmacy, School of Pharmacy, ⁴Department of Biostatistics and Epidemiology, School of Public Health, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

ABSTRACT

Background and Objective: Menopause forms one-third of women's lives. During this period, many women continue their sexual activities. One of the most prevalent postmenopausal complications is vaginal atrophy whose symptoms could have destructive effects on the life quality among postmenopausal women. Complications of using estrogen hormone to improve these symptoms are inevitable. One of the objectives of the present study is the assessment of the vaginal cream of Fenugreek on vaginal inflammation of atrophic vaginitis in postmenopausal women. **Materials and Methods:** For assessment of the effect of fenugreek vaginal cream among postmenopausal women who suffer from vaginal atrophy, the present study was carried out in the form of a double-blind clinical trial among sixty postmenopausal women, mainly who had been referred to Health Center 1 located in the east of Ahvaz in 2017. All participants of the present study who were diagnosed with vaginal atrophy were assigned into two groups of 30 randomly. One of these groups received placebo and the other one fenugreek 5% vaginal cream for a period of 8 weeks. Symptoms related to vaginal atrophy were investigated by means of a 4-degree scale (none, mild, moderate, and severe) and maturation vaginal index (MVI) through preparing the vaginal smears technique at baseline and a period of 8 weeks after cytology and intervention experiment. Finally, the process of analyzing statistical data, at a statistical significance level of 0.05, was carried out by means of SPSS Software. **Results:** The results of the present study demonstrated that the fenugreek vaginal cream treatment group experienced a significant improvement in vaginal atrophy symptoms compared to the onset of the study ($P < 0.001$). **Conclusion:** Fenugreek vaginal cream was effective in treating vaginal atrophy; therefore, postmenopausal women are recommended to use this cream instead of synthetic estrogen to reduce the complications of this hormone.

Keywords: Fenugreek vaginal cream, menopause, vaginal atrophy

Introduction

Menopause is one of the most critical periods in a woman's life and one of the most important health concerns among middle-aged women. Women undergo various changes during this period, which can continue for several years. Despite an increase in life expectancy, age of menopause has remarkably remained stable.^[1] As a result, women nowadays spend about

one-third of their life at menopause. Due to the emergence of numerous health problems during this period, investigating factors that reduce and treat these problems play an essential role in improving life quality in postmenopausal women.^[2]

Menopause is associated with various early and late complications.^[3] More than 30% of women who do not receive hormonal therapy experienced symptomatic vaginal atrophy.^[4] Atrophic vaginitis occurs due to estrogen hormone loss.^[5] Estrogen increases the growth of vaginal mucosa and leads to the production of lactic acid by lactobacilli and creation of vaginal pH which prevents excessive growth of bacteria in the vagina and maintains the health of the vagina.^[6]

Address for correspondence: Dr. Fakhriyeh Mazalzadeh, Instructor in Midwifery Department, Menopause Andropause Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
E-mail: Fakhriyehmazal@yahoo.com

Received: 17-02-2020

Revised: 25-04-2020

Accepted: 20-05-2020

Published: 30-06-2020

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_1220_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Mazalzadeh F, Hekmat K, Namjouyan F, Saki A. Effect of *Trigonella foenum* (fenugreek) vaginal cream on vaginal atrophy in postmenopausal women. *J Family Med Prim Care* 2020;9:2714-9.

Due to the fact that vaginal atrophy symptoms are progressive and would not be healed spontaneously, unsuccessful treatment of them would cause the decrement of life quality and also higher levels of vaginal discomfort. However, in spite of the fact that the majority of patients require to be healed, only one-quarter of them follow the treatment appropriately.^[7] The results of the studies that have focused on vaginal atrophy treatment demonstrate that hormone replacement therapy with estrogen in both systemic and topical forms could increase the level of collagen and tissue thickness. Hormone replacement therapy (HRT) is an effective method to treat vaginal atrophy, but it is associated with some hazards.^[8] In a study, the relative risk of breast cancer in women who had used estrogen as a treatment for 1–4 years was reported to be 1.08 times more than the other group that had received no treatment. The risk was reported to be 1.35 among women who had used estrogen for 5 or more years.^[9]

Due to dangerous side effects associated with hormonal therapy, some women have turned to nonhormonal and herbal therapies and use of high-dose vitamins in spite of the benefits of estrogen therapy in postmenopausal women. Among these non hormonal methods, the use of herbal medicines, vaginal moisturizers and lubricants, and vitamins as well as certain changes in lifestyle leads to an improvement in vaginal atrophy.^[10] Applying plant-based compounds of phytoestrogen is one of the main alternative therapies. These plant-based compounds mainly have estrogenic properties. The safety of these compounds was reported years ago.^[11]

The main herbal sources of phytoestrogens are licorice, red clover, fenugreek, and soybeans.^[12] *Trigonella foenum* (fenugreek) belongs to fabaceae family native to the Mediterranean and South Asia.^[13]

One of the most important plants that contain estrogen and are effective in the hormonal balance of the body is Fenugreek. The isoflavones in Fenugreek are considered to give estrogenic beneficial effects to this plant. In their study entitled “Investigating the effect of fenugreek extract on early menopausal complications,” Basirat *et al.* (2010) proposed that this plant is better to control the symptoms of menopause due to its higher estrogenic properties, and at the same time, it is safer than other plants.

Hakimi *et al.* (2015) have investigated the most possible effects of fenugreek seed on hot flash among menopausal women and indicated that using fenugreek seeds for 4 to 8 weeks is effective in decreasing the times of experiencing hot flash and the score of vasomotor symptoms.^[14]

Nowadays, applying topical and synthetic estrogen is necessary to reduce vaginal atrophy and maintain the natural performance and structure of genitourinary tissue, and using hormonal and nonhormonal methods to reduce such changes is inevitable, because lack of estrogen is the main cause of such changes.^[7]

Long-term use of estrogen is associated with some complications; therefore, using synthetic estrogen is less acceptable, which is mainly attributed to the complications caused by estrogen. Synthetic estrogen has various side effects such as breast cancer, endometrial hyperplasia, and cardiovascular disease; hence, there has been an increasing tendency to use alternative therapies.^[15]

The major objective of the present study is to investigate the effect of vaginal cream of Fenugreek on vaginal inflammation of atrophic vaginitis among postmenopausal women. The results showed that fenugreek was effective; therefore, it is suggested that alternative hormonal therapies such as phytoestrogens be utilized to improve menopausal symptoms including vaginal atrophy.

Materials and Methods

Procedures

This study was performed as a randomized double-blind controlled study with the objective of investigating the effect of fenugreek vaginal cream on vaginal atrophy among postmenopausal women who were complaining about vaginal atrophy and had been referred to Health Center 1 located in the east of Ahvaz. A total number of 60 women who had been diagnosed with vaginal atrophy received fenugreek 5% vaginal cream and placebo for 8 weeks [Figure 1]. The participants of the

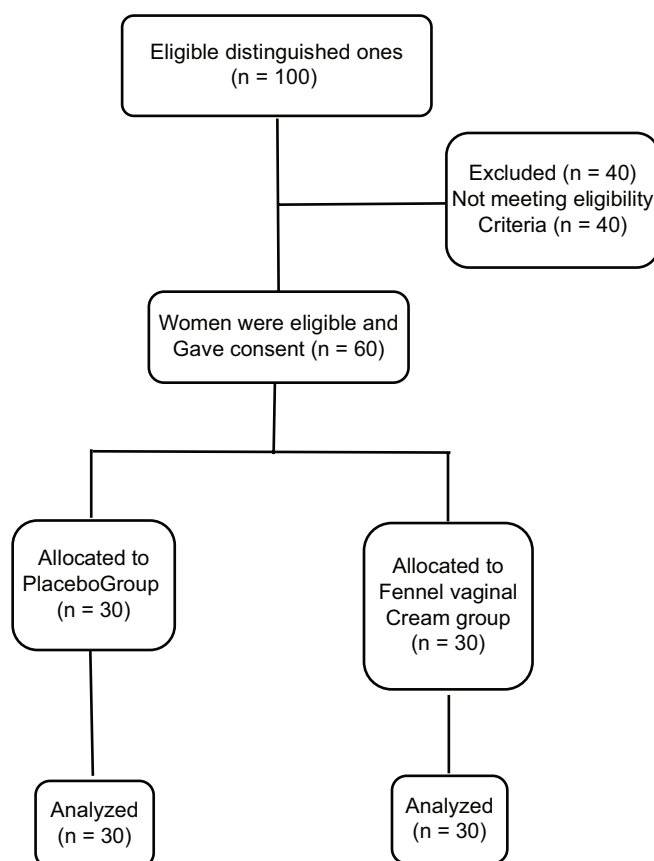


Figure 1: Flowchart of retention and recruitment of this study participants

present study were assigned in two equal groups of 30 people randomly: Group A or intervention (fenugreek 5% vaginal cream) and Group B or control (placebo vaginal cream). The patients were required to refer back to the center 14, 28, and 56 days after the onset of the therapy for reexamination and follow-up. The measurement of vaginal PH and smear were performed mainly in the first and last referral, and other measurements (clinical examinations) were repeated every other week. The symptoms of vaginal atrophy inflammation were mainly investigated by means of a 4-degree scale (none, mild, moderate, and severe) and maturation vaginal index (MVI) by preparing vaginal smears at baseline and 8 weeks after cytology experiment and intervention. Finally, by means of SPSS software at a statistical significance level of 0.05, all the data were analyzed.

Inclusion criteria

1. Having the postmenopausal symptoms for at least one year
2. The presence of vaginal atrophy symptoms
3. Being monogamous and also being engaged with extra sexual activity
4. Being literate.

Exclusion criteria

1. Genital tract abnormalities
2. Vaginal infection that should be treated
3. Nasal and uterine bleeding induced by unknown causes
4. Women who tolerated hormonal therapy at a period of 2 months before the starting of the study
5. Women with breast diseases induced by unknown causes
6. Women who used a high amount of phytoestrogens such as fenugreek, flaxseed, red clover, and soybean during the last month
7. Women with the disease of cholestatic liver
8. Women with end-stage kidney disease
9. Improper use of cream.

Data analysis

Independent *t*-test and its nonparametric equivalent, i.e., Mann–Whitney test, were utilized to compare the means of the two groups based on the normality of the data. Chi-square test was employed to analyze the qualitative variable. Since the data were qualitative, GEE analysis was used to analyze the treatment improvement trend over 8 weeks and compare it between the two groups. In addition, Mann–Whitney test was run every other week to compare the improvement in follow-up periods between these two groups. Statistical analysis of the data was carried out by means of SPSS 22.0.

Results

Within placebo and fenugreek groups, the mean age was 55.1 ± 4.6 and 54.1 ± 4.4 years, respectively, and their mean age of menopause was 48.3 ± 2.8 and 48.1 ± 2.1 years, respectively, and with this regard, the two groups were not significantly different ($P > 0.05$).

Discussion

Tables 1 and 2 indicate the effect of fenugreek on maturation vaginal index (MVI). The results showed that, the average of MVI before and 8 weeks after the therapy has a significant difference in the fenugreek group ($P < 0.001$). Among the fenugreek group, the average of MVI was significantly higher in comparison with the placebo group ($P < 0.000$).

The results of this study are mainly in line with those of the study performed by Lima *et al.*^[16] who carried out an investigation to examine the effect of soybean vaginal gel on vaginal atrophy and reported that MVI had a significant improvement in the soybean group 12 weeks after the therapy ($P < 0.001$).

In their study, Tedeschi *et al.* (2012) have investigated the effect of isoflavones of red clover on symptoms of vaginal cytology and menopause in postmenopausal women and pointed out that red clover had a great effect on the improvement of menopausal symptoms.^[17]

According to Table 3, the average vaginal acidity before the experiment was almost equal in the two groups ($P < 0.27$). However, after 8 weeks, there was a significant decrease within the therapy group in comparison with the placebo group ($P < 0.001$). This reduction could have an impressive role in the improvement of vaginal atrophy. As a result of a decrease in vaginal acidity, lactobacilli became more active, which reduced vaginal infection.

Table 1: Comparison of maturation vaginal index before and 8 weeks after the therapy among the participants

Time	Group	Fenugreek n=30	Placebo n=30	P
	MVI	n (%)		
Before therapy	0-49	30 (100)	30 (100)	1
	50-64	0	0	
	65-100	0	0	
After therapy	0-49	0	22 (73.6)	<0.001
	50-64	0	8 (26.4)	
	65-100	30 (100)	0	
P		<0.001	<0.001	

Table 2: Comparison of the percentage of vaginal mucus cells before and after the treatment in the two groups

Vaginal mucus cells	Group Follow-up time	Fenugreek	Placebo	P
		n=30	n=30	
M±SD				
Surface cells	Before therapy	8.7±7.2	8.7±7.2	1
	After therapy	64.3±14.1	14.26±8.5	
	P	0.001	0.002	
Intermediate cells	Before therapy	18.3±14.3	17.8±9.5	0.4
	After therapy	25.7±17.1	46.9±20.1	
	P	<0.001	0.33	
Base cells	Before therapy	73.4±20	73.7±13.6	0.06
	After therapy	9.4±8.7	38.5±21.9	
	P	<0.001	0.006	

Table 3: Comparison of the average vaginal acidity before and after the therapy in the two groups

Time	Group PH	Fenugreek n=30 n (%)	Placebo n=30 n (%)	P
Before therapy	<5	0	0	0.27
	5-5.49	5 (16.8)	2 (7.6)	
	5.5-6.49	21 (69.9)	14 (46.2)	
After therapy	>6.49	4 (13.3)	14 (46.2)	<0.001
	<5	30 (100)	4 (13.5)	
	5-5.49	0	15 (50)	
P	5.5-6.49	0	3 (9.9)	<0.001
	>6.49	0	8 (26.6)	
		<0.001	<0.002	

Table 4: Comparison of dyspareunia severity before and on the 2nd, 4th, and 8th week after the study

Time	Group Dyspareunia	Fenugreek n=30 n (%)	Placebo n=30 n (%)	P
	None	0	0	0.83
	Mild	2 (6.6)	4 (13.3)	
	Moderate	4 (13.3)	3 (10)	
	Severe	24 (80.1)	23 (76.7)	
2 nd week	None	2 (6.6)	0	<0.001
	Mild	8 (27.4)	1 (3.3)	
	Moderate	18 (59.4)	16 (53.8)	
	Severe	2 (6.6)	13 (42.9)	
4 th week	None	24 (80.1)	0	<0.001
	Mild	5 (16.6)	3 (10)	
	Moderate	1 (3.3)	17 (56.1)	
	Severe	0	10 (33)	
8 th week	None	29 (96.7)	0	<0.001
	Mild	1 (3.3)	3 (10)	
	Moderate	0	22 (73.4)	
	Severe	0	5 (16.6)	
P		<0.001	0.001	

In their study, Yaralizadeh *et al.*^[18] by investigating the effect of vaginal cream on vaginal atrophy in a group of postmenopausal women observed a significant decrease in vaginal acidity within the both placebo and fennel groups 8 weeks after the therapy ($P < 0.001$).

In a study carried out by Lima *et al.*^[16] after investigating the effect of soybean vaginal cream for the treatment of vaginal atrophy, there was a significant decrease observed in vaginal acidity in both soybean and placebo groups ($P < 0.001$).

Based on the data presented in Table 4, through investigating the effect of fenugreek vaginal cream on vaginal dyspareunia, in accordance with the Friedman test results, a significant difference between dyspareunia before and after the study could be seen ($P < 0.001$). Vaginal dyspareunia improvement was observed from a combined 4-degree score of vaginal symptoms from the second week of therapy onward ($P < 0.001$). Moreover, in the first visit, 80.1% of the individuals reported

Table 5: Comparison of severe vaginal dryness before and on the 2nd, 4th, and 8th week after the study

Time	Group Dryness intensity	Fenugreek n=30 n (%)	Placebo n=30 n (%)	P
Before the therapy	None	0	0	0.38
	Mild	1 (3.3)	2 (6.7)	
	Moderate	5 (16.7)	4 (13.3)	
	Severe	24 (80)	24 (80)	
2 nd week	None	2 (6.7)	0	0.001
	Mild	6 (20)	2 (6.7)	
	Moderate	21 (70)	15 (50)	
	Severe	1 (3.3)	13 (43.3)	
4 th week	None	7 (23.3)	0	<0.001
	Mild	23 (76.7)	3 (10)	
	Moderate	0	17 (57)	
	Severe	0	10 (33)	
8 th week	None	30 (100)	2 (6.7)	<0.001
	Mild	0	5 (16.6)	
	Moderate	0	16 (53.4)	
	Severe	0	7 (23.3)	
P		<0.001	<0.001	
P		<0.001	0.21	
B (SE)		1.79 (0.25)		

to have severe dyspareunia, 13.3% moderate dyspareunia, and 6.6% mild dyspareunia.

In the second visit, 6.6% of the participants reported severe dyspareunia, 59.4% moderate dyspareunia, 27.4% mild dyspareunia, and 6.7% lack of dyspareunia, and this difference was significant ($P < 0.001$). At the end of the intervention, 96.7% of the participants reported the lack of dyspareunia and only 3.3% reported mild dyspareunia, which indicates the positive effect of fenugreek vaginal cream.

Based on the observations of Yaralizadeh *et al.*^[18] after 8 weeks of treatment with fennel vaginal cream, there was a significant decrease in vaginal dyspareunia in fennel and placebo groups ($P < 0.001$). In the fenugreek group, 83.3% of the participants reported 80% of severe vaginal dryness, 16.7% moderate vaginal dryness, and 0% lack of vaginal dryness before the study. After the study, however, 0% reported severe vaginal dryness, 0% moderate vaginal dryness, 23.3% lack of vaginal dryness, and 76.6% mild vaginal dryness, which shows the improvement of vaginal dryness after 4 weeks of medicine use ($P < 0.001$). In the end of the intervention (after 8 weeks) and after reexamination of the symptoms, 100% of the participants reported signs of vaginal dryness. Since the data were qualitative, GEE analysis was used in order to analyze the treatment improvement trend over 8 weeks, and the results showed the tendency of improvement could be very different among these two groups ($P < 0.001$).

Based on the results presented by Lima *et al.*^[16] there was a significant effect of applying soybean vaginal cream on vaginal

Table 6: Comparison of color of vagina before and on the 2nd, 4th, and 8th week after the study

Time	Group	Fenugreek n=30	Placebo n=30	P
	Paleness	n (%)		
Before the therapy	None	0	0	0.67
	Mild	2 (6.6)	3 (10)	
	Moderate	7 (23.3)	6 (20)	
2 nd week	Severe	21 (69.3)	21 (70)	0.18
	None	1 (3.3)	0	
	Mild	4 (13.3)	3 (10)	
4 th week	Moderate	9 (30)	6 (20)	<0.001
	Severe	16 (53.3)	21 (70)	
	None	5 (16.7)	0	
8 th week	Mild	24 (80)	3 (10)	<0.001
	Moderate	1 (3.3)	6 (20)	
	Severe	0	21 (70)	
P		30 (100)	0	<0.001
P		0	3 (10)	
P		0	6 (20)	
P		0	21 (70)	
P		<0.001	0.11	
P		0.001		
B (SE)		1.92 (0.38)		

dryness after a period of 12 weeks ($P < 0.001$). In the soybean group, 70% of the participants reported severe vaginal dryness and 30% moderate dryness, while after 4 weeks of treatment, 66.7% reported moderate vaginal dryness, 23.3% mild vaginal dryness, and 10% lack of vaginal dryness, and after 12 weeks, 56% reported mild vaginal dryness, 40% lack of vaginal dryness, and 3.3% mild vaginal dryness.^[16] These results are in line with those of the present study.

Based on the data presented in Table 5, after applying fenugreek vaginal cream, a remarkable improvement after 4 weeks of therapy could be seen ($P < 0.001$). In the fenugreek group, 69.3% of the participants had severe vaginal paleness, 23.3% moderate vaginal paleness, 6.6% mild vaginal paleness, and 0% lacked vaginal paleness before the study [Table 6]. After 4 weeks, 0% of the participants had severe vaginal paleness, 3.3% moderate vaginal paleness, and 80% mild vaginal paleness, and after the symptoms were measured in the end of the study, it was observed that 100% had no vaginal paleness. Due to the changes in the vascular structure of the mucosa in postmenopausal women, the vagina becomes thin and pale.

Conclusion

Based on the data from the present study, it could be seen that using the proposed fenugreek vaginal cream can greatly help improve vaginal atrophy. Moreover, this cream has been proved to bring about no side effects; because it is new and local, the plants are accessible; it is an innovation, has industrial use, and has the potential to be present in the market; and this product can be successful in the present market which lacks a suitable herbal medicine for vaginal atrophy.

Fenugreek vaginal cream with the mentioned combinations and properties is introduced into Iran and the world for the first time. This product is 100% natural, and there is no domestic or foreign equivalent at all; therefore, it was patented by the National Invention Organization.

Limitations of the study

Vaginal atrophy symptoms are mental phenomena, and different individuals may understand them differently. Moreover, different factors such as culture, socioeconomic situation, and so on can affect this understanding; therefore, controlling this self-report scale was out of the researcher's control.

Other limitation of the present study was the patients' failure to follow the treatment after they stopped using this vaginal cream; therefore, the results of the present study cannot show the effects of quitting the treatment.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Mazalzadeh F, Hekmat K, Namjoyan F, SakiMalehi A. Effect of fenugreek vaginal cream on dyspareunia and sexual satisfaction in menopausal women: A randomized clinical trial. *Iran J Obstet Gynecol Infertil* 2018;21:22-30.
- Ziaghham S, Abbaspoor Z, Abbaspoor MR. Effect of hyaluronic acid and vitamin E vaginal tablets on atrophic vaginitis: A randomized controlled trial. *Afri J Pharm Pharmacol* 2012;6:3124-9.
- Palacios S, Nappi R, Bruyniks N, Particco M, Panay NJ. The European vulvovaginal epidemiological survey (EVES): Prevalence, symptoms and impact of vulvovaginal atrophy of menopause. *Climacteric* 2018;21:286-91.
- Utian W, Maamari R. Attitudes and approaches to vaginal atrophy in postmenopausal women: A focus group qualitative study. *Climacteric* 2014;17:29-36.
- Grodstein F, Stampfer MJ, Colditz GA, Willett WC, Manson JE, Joffe M, *et al.* Postmenopausal hormone therapy and mortality. *N Engl J Med* 1997;336:1769-76.
- Holman DM, Benard V, Roland KB, Watson M, Liddon N, Stokley S. Barriers to human papillomavirus vaccination among US adolescents: A systematic review of the literature. *JAMA Pediatr* 2014;168:76-82.
- Nilsson K, Risberg B, Heimer G. The vaginal epithelium in the postmenopause—cytology, histology and pH as methods of assessment. *Maturitas* 1995;21:51-6.
- Huang AJ, Brown JS, Kanaya AM, Creasman JM, Ragins AI, Van Den Eeden SK, *et al.* Quality-of-life impact and treatment of urinary incontinence in ethnically diverse older women. *Arch Inter Med* 2006;166:2000-6.
- Sinha A, Ewies A. Non-hormonal topical treatment of vulvovaginal atrophy: An up-to-date overview. *Climacteric* 2013;16:305-12.

10. Abdolahi F, Azadbakht M, Shabankhani B, Rezaie Abhari F, Moslemizadeh N. Effect of aqueous glycyrrhiza globra extract on menopausal symptoms. *J Mazandaran Univ Med Sci* 2007;16:75-82.
11. Albertazzi P, Purdie DW. The nature and utility of the phytoestrogens: A review of the evidence. *Maturitas* 2002;42:173-85.
12. Rioux JE, Devlin MC, Gelfand MM, Steinberg WM, Hepburn DS. 17 β -estradiol vaginal tablet versus conjugated equine estrogen vaginal cream to relieve menopausal atrophic vaginitis. *Menopause* 2018;25:1208-13.
13. Niazi A, Moradi M. Sexual satisfaction and function in postmenopausal women treated with herbal medicines: A review of clinical trials. *Evidence Based Care* 2019;9:7-16.
14. Hakimi S, Mohammad Alizadeh S, Delazar A, Abbasalizadeh F, Bamdad Mogaddam R, Siiahi M, *et al.* Probable effects of fenugreek seed on hot flash in menopausal women. *J Med Plant* 2006;3:9-14.
15. Wharton W, E Gleason C, Sandra O, M Carlsson C, Asthana S. Neurobiological underpinnings of the estrogen-mood relationship. *Curr Psychiatry Rev* 2012;8:247-56.
16. Lima SMRR, Bernardo BFA, Yamada SS, Reis BF, da Silva GMD, Galvão MAL. Effects of *Glycine max* (L.) Merr. soy isoflavone vaginal gel on epithelium morphology and estrogen receptor expression in postmenopausal women: A 12-week, randomized, double-blind, placebo-controlled trial. *Maturitas* 2014;78:205-11.
17. Tedeschi C, Benvenuti C, EG RG. Comparison of vaginal gel isoflavones versus no topical treatment in vaginal dystrophy: Results of a preliminary prospective study. *Gynecol Endocrinol* 2012;28:652-4.
18. Yaralizadeh M, Abedi P, Najar S, Namjoyan F, Saki A. Effect of *Foeniculum vulgare* (fennel) vaginal cream on vaginal atrophy in postmenopausal women: A double-blind randomized placebo-controlled trial. *Maturitas* 2016;84:75-80.