

**Original Article**

**Comparison of the effect of *Foeniculum vulgare* and St John's wort  
(*Hypericum perforatum*) on the climacteric symptoms and sexual activity in  
menopausal woman**

**Khadijeh Abdali\*<sup>1</sup>, Paria Dowran<sup>2</sup>, Masoumeh Emamghoreishi<sup>3</sup>,  
Maryam Kasraian<sup>2</sup> and Hamidreza Tabatabaei<sup>4</sup>**

<sup>1</sup>Department of Midwifery, Fatemeh College of Nursing and Midwifery,

<sup>2</sup>Department of Obstetrics and Gynecology, School of Medicine,

<sup>3</sup>Department of Pharmacology, School of Medicine,

<sup>4</sup>Department of Epidemiology, Health and Nutrition Faculty,  
Shiraz University of Medical Sciences, Shiraz, Iran

\*Corresponding Author: Email: [abdali\\_kh@yahoo.com](mailto:abdali_kh@yahoo.com), Tel: +989177170129

**ABSTRACT:**

**Background and objective:** Menopause is the permanent ceasing of menstruation for one year and in this period, women potentially suffer from chronic signs and symptoms resulted from estrogen deficiency. With respect to heavy responsibility of women in the society, providing their health is highly required by health system. The objective of the current research is the comparison between the effects of Fennel and Hypiran on severity of climacteric symptoms and sexual performance in menopausal women.

**Methodology:** In a blind placebo-controlled clinical trial, 120 menopausal women of 45-60 of age in Shiraz were randomly categorized in three groups after a checkup for general health. The first group was given the daily dose of three 160mg tablets of Hypiran, the second group was given the daily dose of three 30mg tablets of Fennel and the third group was given three placebo all for the period of 8 weeks. The data was collected by filling out questionnaire for female sexual function and Greene climacteric scale in three phases (before treatment, 4weeks after treatment and 8 weeks after treatment). Thus, 33 individuals in Hypiran group, 33 individuals in Fennel group and 32 individuals in placebo group cooperated until the end of the research. The collected data was analyzed by SPSS software (version 20).

**Findings:** The average age of the participants was 50/52. The score of climacteric symptoms was 42/12±5/1 in Hypiran group before treatment and it decreased to 30/42±4/77 after treatment. The score of climacteric symptoms was 37/81±7/2 in Fennel group before treatment and it decreased to 24/93±6/3 after treatment and regardless of the time, there was a significant difference between the three groups (P≤0.001). The score of sexual function was 18/2±2/61 in Hypiran group before treatment and it increased to 22/78±2/61 after treatment. The score of sexual function was 18/38±2/29 in Fennel group before treatment and it increased to 22/51±2/25 after treatment and there was a significant difference in the mean score of sexual function between the three groups (P≤0.001).

**Conclusion:** Fennel and Hypiran are effective in improvement of menopausal signs and symptoms in women suffering from climacteric symptoms. Also they have positive effect on sexual function of menopausal women.

**Keywords:** Menopause, sexual function, Hypiran, Fennel

## INTRODUCTION:

50% of the population of the world is women and they are the core energy in the family. The health of a woman equals to creation of the required energy and dynamic in the family and it will be effective in the society. With respect to this fact, it is required to recognize the factors causing physical and emotional problems in women and to identify preventive solutions for them so that the health of women, family and society can be improved (1). Menopause is the permanent ceasing of menstruation for one year and retrospectively, it is defined as the period from the last menstruation continuing to 12 months of amenorrhea (2). In today's world, 90% of women experience the age 65. Therefore, menopause is a deniable period in lives of women (3). The average age of menopause is 50 to 52. 95% of women experience menopause at age 44-56 (2). The signs of the estrogen deficiency are defined as climacteric symptoms such as: Hot flash, Urogenital Atrophy, psychic and physiologic effects, cardiovascular diseases, osteoporosis, menstrual irregularity, humor and behavior changes (depression, anxiety and irritability), skin changes, decreased libido and sleep disorder (4-6, 7). But the classical sign and main reason of women to look for menopausal cares is hot flash which accompanies various degrees of flush, sweating and hotness often with palpitation and anxiety in recurrent and transient periods (5). In addition to hot flash, one of the problems of menopause is decreased libido due to dyspareunia and vaginismus resulted by vaginal changes due to estrogen deficiency (4-2). Satisfying sexual instinct not only relieves human by direct effect on nervous system and brain, but also has known useful effects on body. Besides, studies show that lack of enough sexual safety and health leads to outrage, wrath, depression, use of addictive drugs (8). There are different remedies to achieve high quality lives for menopausal women (4). Popular remedies include Hormonal replace therapy (HRT) of

estrogen and progesterone. However, supplements such as omega-3,6, Calcium and Magnesium, anti-anxiety and anti-depression drugs (2, 6, 7, 9) have also used in different studies. In the current study, Perforan tablet from phytoestrogenic herb of Hypiran and Fennelin soft capsule produced with Fennel which are both available in the market were used.

Hypiran which is used to treat minor and moderate depression, anxiety, PMS, viral infections, mental disorder and dysphoria (10-11).

Fennel is one of the phytoestrogenic herbs used to increase breast milk, improve menstruation, decrease climacteric symptoms in men, ease childbirth and increase libido (12).

With respect to the fact that no researches have made on effects of Fennel on treating climacteric symptoms of menopausal women in the world yet, and considering midwifery community-oriented responsibilities and respecting women health, we decided to study in the aforesaid clinical trial and compare the effects of Fennel and Hypiran on the severity of climacteric symptoms and sexual function in menopausal women referring to the selected obstetric clinics of Shiraz University of Medical Sciences.

## MATERIALS & METHODOLOGY:

The current study is a semi-experimental blind clinical trial. The data was collected in three stages and in a plan of three treated groups including Hypiran group, Fennel group and placebo group. The studied population composed of women of age 45 to 60 eligible for the research referred to clinics affiliated to Shiraz University of Medical Sciences. The number of samples was estimated 33 individuals for each group and with respect to probable elimination of samples and their exit during the study, the volume of samples in each group was considered to be 40 individuals and finally, the total number of samples in each studied group was estimated

to be 120 individuals. After taking a permit from Shiraz University of Medical Sciences for doing the research, the samples were taken from the selected obstetric clinics. The methodology of sampling was purposeful; that is, the samples were selected from the individuals referred to the aforesaid clinics and after an initial review, when the referred individual was not eligible for any reasons to enter the project, the next one was replaced. The particulars of the married women aged 45-60 were listed in form 1 based on the requirements to enter the study included: 1-with 12 months amenorrhea and FSH of more than 40 mIU/ml, 2- history of mild to severe hot flash at least once a day, 3- not taking supplements such as vitamin, soya and hormone therapy for the recent 3 months, 4- not taking anticoagulants, antidepressants, and monoamine oxidase inhibitors (MAOI), 5- not suffering from hepatic, renal, peptic, epileptic diseases, allergic asthma and oophorectomy and be non-alcoholic and non-smoking, 6- with no history of cancerous diseases such as breast cancer, and with no criteria to exit the project: 1- allergic to any types of drugs, 2- not capable of continuous medical intake for any reason, 3- not cooperative, and Goldberg questionnaire was filled out for testing their general health. Whoever acquired the score under 23 (generally healthy), their names were transferred to form 2. Then they were explained enough about the project and its objectives and if expressed their consent, they were filled out the initial questionnaire (greene climacteric scale and FSFI) with a letter of consent and initial information form and demographic form. Then drugs and placebo were prescribed to the studied individuals based on consumption method: 1 tablet three times a day for 8 weeks. 4 and 8 weeks after treatment, the questionnaires of greene climacteric scale and FSFI were filled for the studied individuals. Stability and reliability of the Persian version of the questionnaires was frequently checked by the Iranian researchers (13, 14). Finally, considering probable

elimination, 33 women in Hypiran group, 33 women in Fennel group and 32 women in placebo group finished the study. The methodology included descriptive statistic (mean, standard deviation, tables, diagram) and analytical methods (repeated measurement design with post hoc Bonferroni, One way ANOVA, and Chi-square) by means of SPSS software, version 20.

#### **Findings:**

The findings of the current study indicated that considering the average age of 50/52 of the studied women and the average marital age of 11/18, there was not a significant difference between the studied groups (table 1).

Regarding the effect of Hypiran on severity of climacteric symptoms, ANOVA test with repeated measurement design indicated that there is a significant statistical difference between severity of climacteric symptoms before and 4 weeks after treatment and before and 8 weeks after treatment and between 4 and 8 weeks after treatment ( $p \leq 0.001$ ). (Table 2)

Regarding the effect of Fennel on severity of climacteric symptoms, ANOVA test with repeated measurement design indicated that there is a significant statistical difference before and 4 weeks after treatment and before and 8 weeks after treatment and between 4 and 8 weeks after treatment ( $p \leq 0.001$ ). (Table 2)

Regarding placebo and comparison of hot flash before and after treatment, ANOVA test with repeated measurement design indicated that there is a significant statistical difference before and 4 weeks after treatment and before and 8 weeks after treatment and between 4 and 8 weeks after treatment ( $p \leq 0.001$ ). (Table 2)

In comparison of groups, Post hoc Bonferroni test indicated that the severity of climacteric symptoms before treatment in all groups did not have significant statistical difference. Regarding the severity of climacteric symptoms in groups, Post hoc Bonferroni did not indicate significant statistical difference 4 and 8 weeks after

treatment ( $p \leq 0.001$ ). In pairwise comparison of groups, Post hoc Bonferroni indicated that before treatment, there was a significant difference between Hypiran and placebo groups ( $p=0.014$ ) and between Hypiran and Fennel groups ( $p \leq 0.012$ ). 4 weeks after treatment, there was a significant difference between Fennel and placebo groups ( $p \leq 0.001$ ) and between Hypiran and Fennel groups ( $p=0.001$ ). 8 weeks after treatment, there was a significant difference between Hypiran and placebo groups ( $p=0.013$ ) and between Fennel and placebo groups ( $p \leq 0.001$ ) and between Hypiran and Fennel groups ( $p \leq 0.001$ ). (Table 2)

ANOVA with repeated measurement design indicated that there was not a significant

difference between the mean score of sexual function before treatment and 4 weeks after treatment of the three groups ( $p=0.477$ ) but there was a significant difference in mean score of sexual function after treatment of 8 weeks between Hypiran and placebo groups ( $p=0.012$ ) and Fennel and placebo groups ( $p=0.029$ ). Therefore, there was not a significant difference between Hypiran and Fennel groups after treatment of 8 weeks ( $p=0.482$ ) (Table 3)

In intergroup comparison, one way ANOVA indicated that there was a significant difference between the mean score of sexual function in Hypiran group ( $p \leq 0.001$ ), Fennel group ( $p \leq 0.001$ ) and placebo group ( $p \leq 0.001$ ) in three different periods of time. (Table 3)

**Table 1:** Descriptive statistics and demographic and clinical characteristics of menopausal women and their comparisons in three studied groups

| Group characteristic | St John's wort | Foeniculum vulgare | placebo    |
|----------------------|----------------|--------------------|------------|
| Age                  | 52.84±3.63     | 52.03±3.26         | 52.65±3.57 |
| Menopausal age       | 50.3±3.39      | 49.12±2.9          | 49.12±3.64 |
| Duration of marriage | 35.6±6.31      | 32.48±6.01         | 35.12±6.93 |
| Parity(no.children)  | 4.54±1.88      | 4.27±3.21          | 5.12±1.93  |
| BMI                  | 26.7±4         | 26.77±3.21         | 25.68±3.48 |

**Table 2:** Comparison of total score of Greene climacteric symptoms between the three groups in three different periods of treatment

| Group              | Before intervention |                    | 4 weeks after intervention |                    | 8 weeks after intervention |                    | P-value |
|--------------------|---------------------|--------------------|----------------------------|--------------------|----------------------------|--------------------|---------|
|                    | Mean                | Standard deviation | Mean                       | Standard deviation | Mean                       | Standard deviation |         |
| St John's wort     | 42.12               | 5.1                | 35.3                       | 4.78               | 30.42                      | 4.77               | <0.001  |
| Foeniculum vulgare | 37.81               | 7.2                | 30.06                      | 6.72               | 24.93                      | 6.3                | <0.001  |
| placebo            | 38.09               | 5.27               | 36.65                      | 5.45               | 34.21                      | 5.35               | <0.001  |
| P-value            | ≤0.006              |                    | ≤0.001                     |                    | ≤0.001                     |                    |         |

**Table 3:** Comparison of scores of female sexual function of the three groups in three different periods of treatment

| Group              | Before intervention |                    | 4 weeks after intervention |                    | 8 weeks after intervention |                    | P-value |
|--------------------|---------------------|--------------------|----------------------------|--------------------|----------------------------|--------------------|---------|
|                    | Mean                | Standard deviation | Mean                       | Standard deviation | Mean                       | Standard deviation |         |
| St John's wort     | 18.2                | 2.61               | 20.74                      | 2.55               | 22.78                      | 2.61               | <0.001  |
| Foeniculum vulgare | 18.38               | 2.29               | 20.03                      | 2.17               | 22.51                      | 2.25               | <0.001  |
| placebo            | 19.39               | 3.18               | 19.95                      | 3.07               | 20.79                      | 3                  | <0.001  |
| P-value            | 0.172               |                    | 0.477                      |                    | 0.007                      |                    |         |

**DISCUSSION:** Phytoestrogens are estrogen-like chemicals in plants (15). The three major groups of phytoestrogens include Isoflavin, Comestan

and Lignan. There are a lot of evidence for using plants to relieve hot flash and other menopausal symptoms (16). Phytoestrogens decrease the risk

of cardiovascular diseases, breast cancer and endometrium, osteoporosis and relieve menopausal symptoms, especially, hot flash and improve memory, humor and sleeping patterns. Phytoestrogens act as an estrogen agonist in postmenopausal women and may have estrogen-like effects. Lower percentage of epidemiology of cardiovascular diseases in part of Asian people who use food dietary including high phytoestrogens indicates protective effects of phytoestrogens (17). Hypiran plant has been known as the herbal drug for curing different neurological diseases for over 2000 years. Hypiran effects have been observed on treating mild to average depression, anxiety, PMS, viral infections, dysphoria and mental disorders in numerous clinical studies (10-11). Hypiran chemical compounds include: Hypericin with flavoniods, xanthone derivates (chlorogenic acid and caffeic acid), tannins (catechin) and phloroglucin hyperforin (18). Hypiran also contains phytoestrogens which replaces estrogens in menopausal women with contradictions to hormone therapy (19).

Fennel is another type of phytoestrogenic herbs. Fennel essence obtained from distillation of its fruit by means of water steam is pale yellow and aromatic liquid which gradually turns brown (20-22). Fennel chemicals include: 10% fat, slightly sweet and mucilage and about 4% essence. Fennel oil composes of 4% palmitic acid, 22% oleic acid, 14% linoleic acid and 60% petroselinic acid (22).

In the current study, Hypiran and fennel both had effects on severity of climacteric symptoms and sexual function of menopausal women. In Hypiran group, the total score of Greene climacteric symptoms decreased about 7 units after 4 weeks and 12 units after 8 weeks. In fennel group, the total score of Greene climacteric symptoms decreased about 7 units after 4 weeks and 11 units after 8 weeks of treatment. In Hypiran group, the mean score of sexual function increased 4.56 score after 8

weeks of treatment in comparison with before treatment and in Fennel group, the mean score increased to 4.13 while in placebo group, it increased for 1.4 score; it indicates a significant difference in the treated group. There are various studies on the effects of phytoestrogens on menopausal symptoms. Ebdali et al showed that the severity, frequency and period of hot flash in menopausal women remarkably decreased after a 2-month treatment by Hypiran (23). Fahami et al in their study on 59 menopausal women to determine the effects of Hypiran and Passion flower on menopausal symptoms showed that Passion flower and Hypiran had a remarkable effect on decreasing the menopausal symptoms (24).

In a research on benefits of diet therapy by soy Isoflavones, Kyung et al studied its effect on menopausal symptoms and cardiovascular risk factors in 80 women for 4 months and concluded that the diet therapy can be efficiently healthy treatment for menopausal symptoms and has a pleasant effect on cardiovascular system (25).

In a study by Van die et al, there was not a remarkable difference between placebo, Hypiran and Vitex agnus in decreasing hot flash, depression and menopausal symptoms (26). Also Al-Akoum et al reports that Hypiran can have a remarkable effect on hot flash and also improvement of life quality (27).

Regarding the effect of phytoestrogen on sexual function of menopausal women, there have not made particular studies in the world so far. As already mentioned, the reason for most menopausal symptoms is the sudden deficiency of estrogen. The estrogen deficiency causes hot flash, anxiety, insomnia, tenderness of vaginal cells, etc. (4-5). Prescription of vaginal estrogen due to hormonal effects and side effects are not acceptable for most women. Malini studied the estrogenic effect of Fennel on genital system of male and female mice. Prescription of Fennel in male mice increased the endometrial and myometrial diameter and led to an estrogenic

cycle (28), No studies have been made on the effect of Hypiran on sexual function of menopausal women yet.

It can be briefly concluded that Fennel and Hypiran can probably be a suitable alternative for treating menopausal symptoms and improvement of sexual function due to estrogenic effects.

#### ACKNOWLEDGEMENT:

The current study is the outcome of the research project approved by Shiraz University of Medical Sciences. Hereby, we thank and appreciate the honorable deputy of research and respected guiding and advising professors of the university and the helpful personnel of gynecology ward of Shahid Motahari Clinic and dear patients for all assistance and support in the study.

#### REFERENCES:

1. Rapkin AJ. Vasomotor symptoms in menopause: physiologic condition and central nervous system approaches to treatment. *Am J Obstet Gynecol.* 2007;196(2):97–106.
2. Danforth B. *Danforth's obstetrics and gynecology.* 2 ed: asar sobhan; 2008:434-44.
3. Hakimi S, Mohammad Alizadeh S, Delazar A, Abasalizadeh F, Bamdadmoghadam R. Possible Effects of fenugreek seeds on menopausal flushing. *Herb Quarterly of Medical science of Tabriz.* 2006;5(19).
4. Speroff L, Marc A. *Clinical gynecology endocrinology and infertility.* 7 ed: golban; 2005:541-645, 469-70.
5. Kajori M 555D, Safavi SH, Saeed fatemi N, Mohammadi R, Samani L N. Women's health in life cycle. 1<sup>th</sup> ed :Nordansh; 1388:222-246
6. Berek J. Berek & Novak's gynecology. 14 ed: golban; 2007:1203-120.
7. Ryan KJ, Berquetz RS. *Kistner's gynecology and women's health.* 7<sup>th</sup> ed: golban; 1997:633-666.
8. Brezsnayk M, Wisman MA. Sexual desire and relationship functioning the effects of marital satisfaction and power. *Journal of Sex & marital therapy* May-Jun 2004;30(3):199-217.
9. Secreto G, Chiechi LM, Amadori A, Miceli R, Venturelli E, Valerio T, et al. Soy isoflavones and melatonin for the relief of climacteric symptoms a multicenter, double-blind, randomized study. *Maturitas* Jan 2004;47(1):11-20.
10. Lecrubier Y, Clerc G, Didi R, Kieser M. Efficacy of St. John's wort extract WS 5570 in major depression: a double-blind, placebo-controlled trial. *Am J Psychiatry* 2002;159:1361-1366.
11. Blumel JE, Castelo-Branco C, Cancelo M, et al. Relationship between psychological complaints and vasomotor symptoms during climacteric. *Maturitas* 2004;49:205-210.
12. Puleo MA. Fennel and Anise as estrogenic agents. *Journal of Ethnopharmacology* 1980 Des;2(4): 337–44.
13. Mohammadi H, Heidari M, Faghihzadeh S. The Female Sexual Function Index (FSFI) : validation of the Iranian version. *Fasnameh Payesh* 2008;7(2): 269-278.
14. Hakimi C, Mohammad alizadeh charandaie C, Delazar Y, Abasalizade F, Bamdad moghadam R va hamkaran. *barasi asar ehtmalidane shanbalile bar gorgreftgi zanan yaese.* *Fasname geiahan daroie* 1385;9(1):14-19.
15. Savino F, Cresi F, Castagno E, Silvestro L, Oggero R. A randomized double-blind placebo-controlled trial of a standardized extract of *Matricariae recutita*, *Foeniculum vulgare* and *Melissa officinalis* (ColiMil) in the treatment of breastfed colicky infants. *Phytother Res* 2005;19(2):335-40.
16. Porabbas S, Kesmati M, Rasekh AR. *Barasi asarate zed eztrabi giahe raziane va naghsh ehtmalidane system gabaarzhic va girandehaie estrogeny dar in asrat dar mosh sahraie made.* *physiology & pharmacology* 1390spring;15(1):134-43.
17. MacLusky N J, Mechanisms of gonadal steroid action New concepts in hormone management Selective estrogen receptor

- modulators. *Obstet Gynaecol J* 1997;15(2):4-20.
18. Gaster B, Holroyd J. St John's wort for depression. *Arch Intern Med* 2000;160:152-156.
  19. Appt S E, Usefulness of the monkey model to investigate the role of soy in postmenopausal womans health. *ILAR J* 2004;45(1):200-211.
  20. Jaffary F, Ghannadi A, Najafzadeh H, Evaluation of the Prophylactic Effect of Fennel Essential Oil on Experimental Osteoporosis Model in Rats. *Int J Pharmol* 2006;2(1):588-592.
  21. Mark A, Moy AD. Complementary / alternative therapies for reducing hot flashes in prostate cancer patients. *Urology* 2002Apr; 59(4 Suppl 1):20-33.
  22. Daryaie MR. *Daneshname teb ahle bait*. 2<sup>nd</sup> ed. Tehran:entsharate payam ketab;1338.506-508.(in Persian)
  23. Abdali KH, Khajehei M, Tabatabaee H. Effect of St John's wort on severity, frequency, and duration of hot flashes in premenopausal, perimenopausal and postmenopausal women: a randomized, double-blind, placebo-controlled study. *The Journal of The North American Menopause Society* 2010 July;17(2): 326-331
  24. Fahami F, Asali Z, Aslani A, Fathizadeh N. A comparative study on the effects of *Hypericum Perforatum* and passion flower on the menopausal symptoms of women referring to Isfahan city health care centers. *Iranian Journal of Nursing and Midwifery Research* 2010 July;15(4):202-207
  25. Kyung K.; Man JM.; Soarcs JR. Benefits of soy isoflavone therapeutic regimen on menopausal symptoms. *Obstet Gynecol*,99(3):389-93,2002.
  26. van Die M, Burger HG, Bone KM, , Cohen MM, Teede HJ. *Hypericum perforatum* with *Vitex agnus-castus* in menopausal symptoms: a randomized controlled trial. *The Journal of The North American Menopause Society* 2009 MAY;16(1):156-163
  27. Al-Akoum M, Maunsell E, Verreault R, Provencher L, Otis H, Dodin S. Effects of *hypericum perforatum* (St. John 's wort) on hot flashes and quality of life in perimenopausal women: a randomized pilot trial. *Menopause* 2009;16:307-314.
  28. 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 J Physiol Pharmacol*. 1985 Jan-Mar;29(1):21-6.