

http://www.herbmedpharmacol.com

doi: 10.34172/jhp.2021.04

Journal of Herbmed Pharmacology



A systematic review of herbal medicines to improve the sexual function of menopausal women

Tanya Koliji¹⁰, Zohreh Keshavarz¹⁰, Elham Zare^{1,0}, Faraz Mojab²⁰, Malihe Nasiri³⁰

¹Midwifery and Reproductive Health Research Center, Department of Midwifery and Reproductive Health, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

²School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

³School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article Type: Review

Article History: Received: 3 June 2020 Accepted: 16 August 2020

Kevwords:

Complementary medicine Herbal remedies Menopause Sexual activity

ABSTRACT

Sexual function is one of the most important aspects of menopausal women, and its disorder is a common condition among this group of women. The long-term side effects of hormone replacement therapy to improve this disorder have led women to seek alternative therapies. The purpose of this review is to summarize clinical trials of herbal medicines that improve the sexual function of menopausal women. In this review article the content was searched in 6 databases to identify double- and triple-blind clinical trial studies from January 2000 to April 2020. The search was conducted in English and Persian. Studies were considered if they were related to menopausal woman, sexual function and its various domains. A total of 479 articles were reviewed, 31 of which were included in the study after reviewing the full text. In this study, 3 articles on ginseng, 4 articles on fennel, 2 articles on Fenugreek, 3 articles on bindii, 3 articles on Red clover, 1 article on Schisandra, 2 articles on Hops; 3 articles about Black cohosh, 2 articles about soy, 2 articles about Ginkgo biloba, 1 article about Nigella sativa, 1 article about neroli oil, 1 article about maca, 1 article about Date pollen, 1 article about Aphrodite and 1 article on the combination of St John's wort and vitex were evaluated. Red ginseng, fennel, bindii, Red clover and Black cohosh have the greatest effect on improving the sexual function of menopausal women, and people can be encouraged to use these plants.

Implication for health policy/practice/research/medical education:

This review article presented useful information about herbal medicine to improve sexual function, which could help pharmacists and scientists in the provision of new drugs.

Please cite this paper as: Koliji T, Keshavarz Z, Zare E, Mojab F, Nasiri M. A systematic review of herbal medicines to improve the sexual function of menopausal women. J Herbmed Pharmacol. 2021;10(1):51-60. doi: 10.34172/jhp.2021.04.

Introduction

Sexual desire is the main aspect of human beings throughout life, and sexual health is defined as a state of physical, emotional, mental, and social well-being related to sexual desire, not merely the absence of disease, dysfunction, or disability (1). Sexual dysfunction is characterized by the fact that a person is unable to enjoy this relationship due to difficulty during the sexual response and sexual intercourse stage (2). This disorder is a common condition that includes the four primary areas

of hypoactive sexual desire disorder, arousal disorder, orgasm, and pain during sexual intercourse. The incidence and prevalence vary, and reported to be between 30 and 50 percent, but are under estimated due to the fact that this problem is a taboo (3).

Sexual function is one of the most important aspects of menopausal women (4). There is a common misconception that women lose interest in sex as they get older and will not be able to behave sexually (5). But for many middleaged women, sexual desire is considered a moderate or very important element, so sexual dysfunction is an important health issue among this group of women (6). Menopause usually occurs between the ages of 45 and 55, and the average age is 51 in developed countries and 48 in poor and developing countries (7). Due to these issues, appropriate treatment is required in this field (6).

Hormone replacement therapy is the most intuitive way to treat the disorder (8). Hormone therapy is not an effective treatment option for all women. Because hormone therapy is not only contraindicated for estrogen receptor cancers, but also for women at risk for breast and ovarian cancers, cardiovascular and thromboembolic diseases (9). The long-term side effects of hormone replacement therapy have led women to seek alternative therapies (10). Approximately 51% of women use complementary and alternative medicine, and more than 60% believe that complementary medicine is effective in treating sexual dysfunction (11). Complementary medicine includes: herbal medicine, dietary supplements, acupuncture, relaxation techniques, homeopathy, reflexology, and the like, but these are not able to cure all the symptoms of menopause. In recent years, the use of herbal medicine has become one of the most common options for reducing the menopause symptoms (10). Medicinal plants can be taken orally or topically, used alone or in combination (12). Herbal remedies are usually described affordable, suitable for long-term use and with relatively few side effects (13). The purpose of this systematic review is to summarize clinical trials of herbal remedies that improve the sexual function of menopausal women.

Methods

In this review study, databases including PubMed, Google scholar, Science Direct, Ebsco, Springer, Cochrane Central Register of Controlled Trials were searched. Keywords for early studies included climacteric, plants, herbs, menopause, menopausal symptoms, sexual function, sexuality, sexual dysfunction, and medical plants. The Boolean operators used were AND, NOT, OR, and the operators of each database were also used. The databases were searched in English and Persian. There were no restrictions on the use of medicinal plants, including oral, vaginal, and aromatherapy, or the use of these plants alone or in combination. Criteria for selecting studies included all of the studies published in the form of a double blind and triple blind clinical trial with control group, from January 2000 to April 2020. The inclusion criteria for these studies consisted of menopause for 12 months, age between 45 and 65 years, no history of breast and uterine cancer, and no chronic disease during the study. Exclusion criteria included use of hormone therapy or other medication to treat sexual dysfunction, potential allergy to herbal medicines and missing treatment for more than a week. In order to select the studies, in the first stage, article titles and abstracts were evaluated, and after studying the summary of each article, the unrelated

articles were removed and the possible related articles were identified so that their full text could be read. To evaluate the quality of articles, the CASP checklist (Critical Appraisal Skills Program) was used. Eleven questions were designed in this checklist. The first three questions were screening questions and could be answered quickly. If the answer to both was "yes", it was worth proceeding with the remaining questions (14). According to this checklist, 27 articles included in this study had all the necessary criteria for evaluation and the other 4 studies only lacked one of the items in the checklist (mentioning the type of randomization in the samples) and other items on the checklist were available (15-18).

Results

After searching the mentioned databases, 479 articles were found. Based on the title and summary of the articles, 256 articles were irrelevant and 20 articles were deleted due to the type of article design (single blind or nonrandomized). After reviewing the full text of the articles, 172 articles were deleted due to duplication, and finally 31 articles were included in the study. Article selection method is shown in PRISMA Flowchart (Figure 1) (19). Most of the articles in this study were respectively from Iran, Australia, Brazil and South Korea. In this study, 3 articles on ginseng, 4 articles on fennel, 2 articles on Fenugreek, 3 articles on bindii, 3 articles on Red clover, 1 article on Schisandra, 2 articles on Hop, 3 articles about Black cohosh, 2 articles about soy, 2 articles about Ginkgo biloba, 1 article about Nigella sativa, 1 article about neroli oil, 1 article about maca, 1 article about Date pollen, 1 article about Aphrodite and 1 article on the combination of St John's wort and Vitex were evaluated. In these trials, the minimum age of menopausal women was 43 and the maximum was 75 years. The tools used in these trials included FSFI (Female Sexual Function Index), GCS (Green Climacteric Scale), QS-F (Quality of Sexual Function), MRS (Menopause Rating Scale), FIEI (Female Intervention Efficacy Index), MENQOL (Menopause Specific Quality of Life), GRISS (Golombok Rust Inventory of Sexual Satisfaction), GAQ (Global Assessment Questionnaire), VAS (Stress and Sexual Visual Analog Scale), SSRS (Sabbatsberg sexual rating scale), Vaginal Atrophy Checklist and Sexual Satisfaction Questionnaire, among which FSFI and MRS have been used the most in trials. The duration of the study in these trials was at least 5 days with a maximum of 12 months. Table 1 summarizes the articles included in this study and the plants are described below:

Ginseng

Red ginseng, scientifically named *Panax ginseng* C. Meyer, is one of the most common forms of ginseng, which contains phytoestrogens and is widely used in East Asia (20). In a 2019 study by Ghorbani et al, looking at the effect of ginseng on the sexual function of menopausal women,

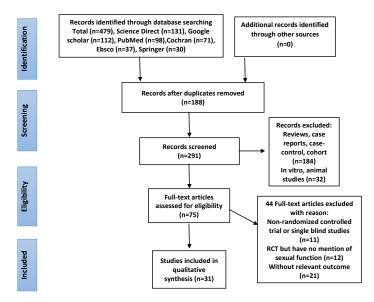


Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of study selection.

sexual function increased in all areas (desire, arousal, orgasm, satisfaction, lubrication, and pain) (P<0.001) (21). In a 2016 study by Kim et al, the MRS in the ginseng group decreased from 12.45 ± 8.79 to 8.32 ± 6.75 , while it decreased from 10.23 ± 7.30 to 9.26 ± 7.51 in the placebo group. The study found that ginseng improved menopausal symptoms, including sexual problems (P=0.035) (20). In a 2010 study by Oh et al, according to the GAQ, ginseng had better therapeutic effects than placebo (P=0.046). The overall score of the FSFI increased slightly from 21.10 \pm 4.40 to 22.95 \pm 4.74 after treatment with Red ginseng, which was not significantly different in all areas between the two intervention and control groups; except for sexual arousal, which increased from 3.10 ± 0.87 to 3.50 ± 0.72 (P=0.006) in the ginseng group (22).

Fennel

Foeniculum vulgare is a plant of the carrot family and native to the shores of the Mediterranean Sea. Iran is one of the producers of this plant. This plant has estrogenic effects. In a 2018 study by Abedi et al, which used fennel vaginal cream, the results showed that sexual desire in the fennel and placebo groups increased after 8 weeks of treatment (from 2 ± 0.53 to 5.3 ± 0.36 in the fennel group, and from 1.8 ± 0.6 to 2.9 ± 0.46 in the control group), and desire in the fennel group increased significantly after the intervention (P<0.001). Also, other areas of sexual function increased based on the FSFI questionnaire in the fennel group (P < 0.001) (23). In another study by Yaralizadeh et al in 2016, the effect of 5% fennel vaginal cream after 8 weeks of treatment was examined. The results showed that vaginal dryness (100% dryness in fennel group versus 3.3% in control group) and dyspareunia (93.3% without dyspareunia in the intervention group versus 0% in the control group) were significantly improved in

the intervention group (P < 0.001) (24). In another study by Rahimikian et al in 2017, the mean score of the MRS questionnaire before treatment with fennel was 20.02% in the intervention group and 20.37 % in the control group. This rate decreased by 9.35 and 18.58, respectively, 8 weeks after the intervention (P < 0.001). The results of the study showed that fennel is able to improves menopausal symptoms, including sexual problems (25). Also, in another study in 2017, Kian et al measured sexual function using the MENQOL questionnaire. Prior to treatment, the score of sexual intercourse in the intervention group was 14.35, which decreased to 10.77 after treatment, and in the control group, it decreased from 16.15 to 14.02 (P = 0.013). As can be seen, the sexual domain score decreased in both groups, but this decrease was higher in the intervention group and based on the results of this study, fennel improved sexual function (26).

Fenugreek

Fenugreek with the scientific name *Trigonella foenum-graecum* is a plant rich in phytoestrogens. In the Shamshad Begum et al study, after the intervention, the menopausal green score (GCS), the last question of which measures sexual desire, decreased after 45 days by 24.82 \pm 5.42 and after 90 days by 19.64 \pm 4.28 in the Fenugreek group. There was also a significant difference between the two groups of intervention and control in all areas of sexual function including sexual desire (P=0.03); orgasm (P<0.001); sexual satisfaction (P<0.001) and dyspareunia (P<0.04). According to this study, sexual problems were less common in the intervention group (27). In a 2017 study by Steels et al, after 12 weeks of treatment with fenugreek, sexual function was improved compared to the control group (P<0.001) (28).

Table 1. Summary of the articles included in this study

Questionnaire	Results	Side effects	Control group	Intervention group	No. of subjects	Location	Reference
FSFI, MENQOL, GMS	Ginseng progresses sexual function	-	Placebo	500 mg of Ginseng, 2 times daily for 4 weeks	62	Iran	Ghorbani et al (21)
MRS	Ginseng improves sexual problems	-	Placebo	3gr of Ginseng, once a day for 12 weeks	72	South Korea	Kim et al (20)
FSFI GAQ	Improve sexual function, especially in the area of arousal	There were no severe complications, only two cases of vaginal bleeding were observed in the intervention group	Placebo	1 gr of red Ginseng, daily for 8 weeks	28	South Korea	Oh et al (22)
FSFI	Fennel improves sexual function	-	Placebo	5 gr of vaginal Fennel cream every night for 8 weeks	60	Iran	Abedi et al (23)
Vaginal atrophy checklist	Fennel improved vaginal dryness and dyspareunia	No adverse effect	Placebo	5% of vaginal Fennel cream, daily for 8 weeks	60	Iran	Yaralizadeh et al (24)
MRS	Fennel improved sexual function	No adverse effect	Placebo	100 mg of Fennel capsules, two times daily for 8 weeks	90	Iran	Rahimikian et al (25)
MENQOL	Fennel improved sexual function	-	Placebo	100 mg of Fennel capsules, two times daily for 8 weeks	90	Iran	Kian et al (26)
GCS	Sexual problems which were lower in the intervention group	No adverse effect	Placebo	250 mg of Fenugreek capsules, two after breakfast and two after dinner for 12 weeks	88	India	Shamshad Begum et al (27)
MENQOL	Fenugreek improved sexual function	No adverse effect	Placebo	600 mg of Fenugreek capsules, daily for 12 weeks	104	Australia	Steels et al (28)
FSFI, QS-F	Bindii improved sexual function	-	Placebo	$250\ \text{mg}$ of Bindii,, 3 tablets daily (overall 750 mg), for $120\ \text{days}$	36	Brazil	de Souza et al (29)
SQ-F, FIEI	Bindii improved sexual function	No adverse effect	Placebo	250 mg of Bindii, 3 times daily for 90 days	60	Brazil	Postigo et al (30)
Sexual satisfaction questionnaire	Bindii improved sexual satisfaction	-	Placebo	0/9 mg of Bindii, two times daily for 8 weeks	60	Iran	Tadayon et al (31)
MRS	There was no difference in sexual problems before and after the intervention	No adverse effect	Placebo	784 mg of <i>Schisandra</i> , two times daily for 12 weeks	36	China	Park & Kim (32)
GCS	Hop improved sexual function	No adverse effect	Placebo	650 mg of Hop tablet for 90 days	120	Iran	Aghamiri et al (33)
MRS	No significant difference was found in comparison with control group	-	Placebo	75/1 mg of Hop for 16 weeks	50	Finland	Erkkola et al (34)
MRS	Red clover improved sexual function	-	Placebo	Two capsules of Red clover (40 mg) for 12 weeks	72	Iran	Shakeri et al (36)
GRISS	Sexual satisfaction before and after treatment was not significantly different between the two groups	No adverse effect	Placebo	40 mg of Red clover capsules, daily for 12 weeks	100	Brazil	Del Giorno et al (35)
-	Red clover improved libido and dyspareunia	-	Placebo	80 mg of Red clover, two capsules daily for 90 days	53	Australia	Chedraui et al (18)
MENQOL	Black cohosh did not improve sexual function	Liver function tests changed during the intervention in both groups	Placebo	40 mg of Black cohosh, before bedtime for 12 weeks	54	Thailand	Tanmahasamut et al (38)
MRS	Black cohosh improved sexual function	No adverse effect	Placebo	2/5 mg of Black cohosh tablet, for 12 weeks	304	Germany	Ross et al (37)

Table 1. Continued

Questionnaire	Results	Side effects	Control group	Intervention group	No. of subjects	Location	Reference
GCS	Black cohosh improved sexual function	No adverse effect	Placebo	6/5 mg of Black cohosh, daily for 8 weeks	84	Iran	Mohammad-Alizadeh- et al (39)
GCS	Sexual function before and after treatment was not significantly different	No adverse effect. Upper respiratory tract infection that was not related to the intervention	Placebo	300 mg of St John's wort, one in morning and two during the day plus 500 mg of Vitex for 16 weeks	47	Australia	van Die et al (40)
-	Sexual desire was not significantly different between the two groups	-	Placebo	118 mg of Soy, daily for 3 months	94	Australia	Kotsopoulos et al (15)
MRS	Sexual function and vaginal dryness improved in group 1 and 2	Complications were not significantly different between the two groups	Group 3: 1 tablet of placebo + two portions per day of placebo powder	3 groups: Group 1: 1 mg of Estradiol tablet and 0/5 mg of Norethisterone acetate + two portions per day of placebo powder Group 2: 1 tablet of placebo + two portions per day of Soy powder for 16 weeks	60	Brazil	Carmignani et al (41)
FSFI	Ginkgo biloba improved sexual function in all domains except sexual satisfaction and pain during intercourse	-	Group 3: 40 mg of placebo tablet and 2-3 drops of placebo aromatherapy	3 groups: Group 1: 40 mg of <i>Ginkgo biloba</i> , one tablet and 2-3 drops of placebo aromatherapy Group 2: 40 mg of <i>Ginkgo biloba</i> and 2-3 drops of aromatherapy (a combination of Lavender, Rose, Fennel, Geranium), 3 times daily for 6 weeks	180	Iran	Malakouti et al (42)
SSRS	Ginkgo biloba improved sexual desire	-	Placebo	60 mg of Ginkgo biloba, four times daily for 30 days	63	Iran	Amiri Pebdani et al (43)
MENQOL	Sexual function was not significantly different between the groups	No adverse effect	Placebo + 20 mg of Citalopram	500 mg of Black cumin and 1000 mg of vitex, daily + 20 mg of Citalopram after breakfast for 8 weeks	46	Iran	Molaie et al (17)
MENQOL, VAS	Neroli oil improved sexual desire	-	Almond oil	1 ml of Neroli oil that dissolved in Almond oil in two groups ($0/1\%$ and $0/5\%$), 5 cm from nose and inhaled for five minutes	63	South Korea	Choi et al (44)
GCS	Maca improved sexual function	-	Placebo	3/5 mg of Maca for 6 weeks	16	Australia	Brook et al (16)
FSFI	Date palm pollen improved dyspareunia and vaginal lubrication	No adverse effect	Placebo	300 mg of Date palm pollen for 35 days	60	Iran	Sadeghi Goghari et al (45)
MRS	Aphrodite improved sexual function	-	Placebo	Aphrodite containing 40 mg of Bindii + $12/27$ mg of Ginger + 3 mg of Saffron + 11 mg of Cinnamon, 2 times daily for 4 weeks	63	Iran	Taavoni et al (46)

Bindii

Bindii, scientifically named Tribulus terrestris, is a plant from the Caltrops family that has long been used as a drug to enhance sexual potency due to its effect on sex hormones. In a 2016 study by de Souza et al, after intervention, all areas of the questionnaire were enhanced in two groups (P<0.05), except for lubrication in the control group, which did not change. Then, they compared the effect of bindii with the control group using the SQ-F questionnaire. The questionnaire score before intervention was 1.83 \pm 0.76 in the bindii group and 1.79 \pm 0.89 in the placebo group, and after 120 days of treatment, the questionnaire score was enhanced for the bindii group in all areas including desire (P<0.01), arousal/lubrication (P<0.05) and pain (P<0.05). The results of the study showed that using bindii improved sexual desire (29). In another study by Postigo et al in 2016 on bindii, using the SQ-F questionnaire, sexual desire and excitement (7.6 \pm 3.2 vs. 10.2 ± 3.2) (P < 0.001), stimulation (3.3 ± 1.5 vs. 4.2 \pm 1.0) (P<0.01), arousal (5.7 \pm 2.1 vs. 7.2 \pm 2.6) (P<0.01), comfort during intimacy (6.5 \pm 2.4 vs. 8.0 \pm 1.9) (P<0.01) increased after intervention, but there was no significant change in orgasm and sexual satisfaction between the two groups (P=0.28). Also, using the FIEI, sexual function increased in all areas and the ability to reach orgasm increased by 73.3% compared to the SQ-F questionnaire, indicating the effectiveness of bindii (30). Another study conducted by Tadayon et al in 2017 examined the effect of bindii on the sexual satisfaction of menopausal women, and the results showed that after 8 weeks of bindii syrup intake, the average score of sexual satisfaction increased from 34.8 to 37.56 after intervention (P<0.05). Therefore, based on the study results, bindii increases sexual satisfaction (31).

Schisandra chinensis

Schisandra chinensis is a type of berry known in China having 5 flavors (salty, sour, bitter, spicy and sweet), and is traditionally used as a tea to treat colds, kidney problems and memory loss. The Park and Kim study in 2016 found no difference in the number of sexual problems before and after intervention in the placebo and intervention groups. Only the amount of estradiol in the active drug group increased non-significantly (P=0.441) (32).

Hop

Hop, scientifically known as *Humulus lupulus*, is a plant of the Hemp genus, which contains phytoestrogens, and its estrogen is 8 times stronger than other estrogen containing plants. In a 2016 study by Aghamiri et al, on sexual function of menopausal women after 4 weeks (-0.4, -0.1- -0.6), 8 weeks (-0.7, -0.5- -0.9) and 12 weeks (-1.2, -0.9- -1.4) of treatment with hops, there was a significant difference compared to the placebo group (P < 0.001) (33). In another 2010 study by Erkkola et al, which examined the effect of hops on menopausal problems, the mean

total score decreased from 23 to 21 in the intervention group and from 21 to 17 in the control group after 16 weeks of treatment. The results showed that hops did not have a significant effect on the improvement of MRS questionnaire domain compared to placebo (P=0.06) (34).

Red clover

Red clover with the scientific name of *Trifolium pratense* is a plant that contains phytoestrogens and is used for various therapeutic purposes including menopausal symptoms. In addition, the plant contains coumarin and cyanogenic glycosides, which reduce blood coagulation (35). In a 2014 study by Shakeri et al, using MRS questionnaire, the total questionnaire score in the intervention group reduced from 20.41 ± 6.32 to 10.08 ± 2.28 and in the control group, reduced from 20.77 \pm 6.15 to 17.25 \pm 6.59 (P=0.0001), indicating that red clover improves menopausal symptoms, including sexual problems (36). In a 2010 study by Del Giorno et al, after 12 months of treatment for the intervention and control group, sexual satisfaction was not significantly different according to the GRISS questionnaire (intervention group: 34.54 ± 18.18, control group: 34.78 ± 17.94) (35). In a 2006 study by Chedraui et al, the effect of treatment was assessed 90 days after intervention, and the results showed that dyspareunia decreased from 78.8% before intervention to 34.6% after intervention, and this rate was 69.2% in the placebo group after intervention. Also, after intervention with red clover, a significant effect on sexual desire was observed, so that before treatment, the decrease in sexual desire was 94.3%, and after treatment it was 52.8% in the intervention group and 73.6% in the placebo group (P = 0.05) (18).

Black cohosh

Black cohosh, scientifically known as Cimicifuga racemose, is a plant from the Buttercup family, native to the eastern United States and Canada. It is used to treat menopausal symptoms (37). In a 2015 study by Tanmahasamut et al, after 12 weeks of using black cohosh, there was no change in the sexual performance score based on the Menopause Specific Quality of Life Questionnaire (P =0.174) (38). In a 2012 study by Ross et al, after 12 weeks of using black cohosh, sexual problems were improved in postmenopausal women (P=0.012) (37). In a 2013 study by Mohammad-Alizadeh-Charandabi et al, which examined the effect of black cohosh on menopausal symptoms, the GCS questionnaire found that the rate of sexual function in the intervention group was 29% after 4 weeks and 36% after 8 weeks, and it was 8 and 10 percent in the control group, respectively. According to the results of the study, black cohosh improves sexual function (39).

The mixture of St John's Wort and Vitex

Hypericum perforatum is a genus of hypricas, vitex with the scientific name of Vitex agnus-castus, which is of the Vervain genus, have been proven to work through neurotransmitters, and the effectiveness of factors affecting the central nervous system has been shown to relieve menopausal symptoms. According to a 2009 study by van Die et al, the effect of the combination of St John's wort and Vitex on menopausal symptoms, including sexual problems, the result of study for sexual problem (0.34, 95% CI: 0.07, to 0.75, P=0.11) had no significant difference between the intervention and placebo groups (40).

Soy

Soy is a powerful source of isoflavones that are similar to estradiol in structure, although they are more biologically active and less potent than endogenous or artificial estrogens. In a 2000 study by Kotsopoulos et al, after 3 months of intervention, sexual desire was improved in the intervention (P=0.09) and control groups (P=0.015), but there was no significant difference between the two groups (15). Also, in the 2010 Carmignani et al study, according to the MRS questionnaire, after 16 weeks of intervention, genitourinary symptoms, including sexual problems, bladder problems, and vaginal dryness reduced from 4.5 to 3 in the hormone therapy group and from 4.8 to 3.3 in the soy supplement group. This rate decreased in the placebo group from 4.6 to 3.9 indicating statistically significant improvement in hormone therapy and soy supplement group compared to placebo (P = 0.04) (41).

Ginkgo biloba

The Maidenhair tree, scientifically known as Ginkgo biloba, contains flavonoid glycosides and phytoestrogens that improve blood flow and relax smooth muscle tissues. A number of studies have shown the plant's effectiveness on sexual function. In 2017, Malakouti et al examined the effect of Ginkgo biloba tablets and aromatherapy on the sexual function of menopausal women. The results of the study showed that the sexual performance score was significantly different between the three groups in all areas of sexual performance, except for sexual satisfaction and pain during intercourse. Thus, the overall sexual performance score in the Aroma group increased from 18.4 (5.4) to 22.9 (3.3), from 17.5 (6.8) to 21.6 (4.5) in the Ginkgo biloba group, and from 15.8 (5.7) to 17.2 (4.2) in the placebo group. According to the results of the study, *Ginkgo biloba* improves sexual function (P = 0.003) (42). In another study conducted by Amiri Pebdani et al in 2014, the results of the study showed that after intervention, a significant difference was observed between the groups in terms of sexual desire (P=0.02) (43).

Black cumin

Black cumin, scientifically known as *Nigella sativa* is a multi-purpose plant with many properties for the organs of the body. It also improves breastfeeding and menstrual problems and appears to be effective for

hormone deficiency, including menopausal hormones. In a 2018 study by Molaie et al, which looked at the effect of a combination of fennel and vitex on menopausal symptoms, the results showed that sexual function did not have a statistically significant difference effect between groups (P=0.231) (17).

Neroli oil

Neroli oil, scientifically known as Citrus aurantium L., is known for its anti-anxiety, anti-depressant and sedative properties. Limonene is one of the most chemical compounds in neroli oil with anti-anxiety effects. In a 2014 study by Choi et al, they examined the effect of neroli oil inhalation on menopausal symptoms, in which participants were divided into three groups. One group received 0.1 percent neroli oil, second group received 0.5 percent neroli oil, both dissolved in almond oil, and the control group received almond oil. The results of the study showed that after 5 days of inhaling oils, sexual desire in the control group decreased (P=0.013). The 0.1% neroli oil group (P = 0.049) and the 0.5% neroli oil group (P=0.001) showed an increase in sexual desire, which according to statistical analyzes, the rate of sexual desire in the two neroli oil groups was significantly increased after intervention (P=0.001) (44).

Maca

Maca is the root of the *Lepidium meyenii* plant, which grows exclusively at high altitudes in the Andean region of Peru and is used for fertility enhancement and aphrodisiac effect. In a 2008 study by Brooks et al, which looked at the effect of mace on the sexual dysfunction of menopausal women, after 6 weeks of consuming 3.5 mg of mace powder, using the GCS questionnaire, sexual problems were significantly reduced (P=0.05) (16).

Date palm pollen

The palm tree (Phoenix dactylifera) is a plant of the Palmaceae family, whose different parts have various healing properties. Date pollen is used in China and Greece to treat infertility and improve sexual function. All parts of this plant contain carbohydrates, vitamins, tannins, steroids, alkaloids and flavonoids. In a 2015 study by Sadeghi Goghari et al, which looked at the effect of date pollen capsules on dyspareunia and vaginal lubrication, after 35 days of using 300 mg of date pollen capsules, the results showed that the average change in dyspareunia score for intervention group was significantly higher than the control group (P=0.48). Also, the mean vaginal lubrication score did not differ significantly between the two groups before intervention, but after intervention, it was significantly higher in the intervention group than the control group (P=0.045). As the results of the study indicated, date pollen capsules were able to reduce dyspareunia and increase vaginal lubrication without any side effects (45).

Aphrodite

Aphrodite is an herbal supplement that contains ginger, saffron, cinnamon and bindii, each of which has different healing properties. In a 2014 study by Taavoni et al, which looked at the effect of Aphrodite on menopausal symptoms, the results showed that after 4 weeks of taking Aphrodite, which included 40 mg of bindii, 12.27 mg of ginger, 3 mg of saffron and 11 mg. cinnamon, the MRS questionnaire average score in the Aphrodite group before intervention was 21.93 and after intervention decreased to 13.11, and for the placebo group before intervention was 22.13, which after taking the placebo, this rate was still 22.13. Significant differences were observed before and after intervention in the Aphrodite group (P=0.01), while this difference was not observed in the placebo group (P=1.0) (46).

Discussion

Almost all of the articles about herbal medicines on the treatment of sexual dysfunction in menopausal women had a positive effect, which might be due to the fact that the probability of publishing articles with a positive effect is higher, which in itself increases the bias in publishing. In almost half of the reviewed articles, the side effects of herbal medicines were not mentioned, which is very important. Because an herbal medicine, can be dangerous like a chemical, it has been shown that excessive and uncontrolled use of herbal products, especially phytoestrogens, to treat menopausal symptoms, can endanger people's health, especially because many extracts are not prepared in a standard manner (47).

There are a variety of herbs available for menopausal women with sexual dysfunction. However, few studies have been done on each plant, so it is recommended that more studies be performed. Also, studies on fennel had the highest number of articles, and articles related to red ginseng, bindii, red clover, and black cohosh where at next. Most of them had a positive effect, and it is recommended that menopausal women be encouraged to use these 5 herbs to solve sexual problems.

In the Najafi et al study, a systematic review and subsequent meta-analysis was conducted on the effect of phytoestrogens on the sexual function of menopausal women in 2017. The study found that soy had no effect on sexual function but improved dyspareunia. Maca and fenugreek also promoted sexual function, while red ginseng did not significantly improve sexual function (48). As mentioned, this study examined only medicinal plants that contained phytoestrogens, while the present study examined both phytoestrogens and non-phytoestrogens plants. In a study by Niazi et al, a systematic review of medicinal plants affecting sexual satisfaction and sexual function in menopausal women was conducted in 2019. The results showed that bindii, fennel, fenugreek, ginseng, red clover and Aphrodite had a positive effect

on dyspareunia, sexual satisfaction and sexual function. But Date palm pollen and Ginkgo biloba had no effect on sexual satisfaction (49). Also in this study we found that these plants are useful for sexual function but studies examining Fenugreek and Aphrodite are less than to say that these plants are useful for sexual function. In another study by Mazaro-Costa et al in 2010, a review article on medicinal plants affecting female sexual dysfunction, they suggested Ginkgo biloba, ginseng and saffron for arousal disorders, and black cohosh, vitex and red clover were recommended for several sexual dysfunctions, and hops and bindii have been suggested for desire disorder (50). The study looked at the PubMed search database, but the present study looked at more databases to find related articles. Finally, the inconsistency in the duration of studies, doses, and specific products makes it impossible to perform meta-analyzes in this study.

Conclusion

In the present study, which was conducted to investigate the effect of medicinal plants on the sexual function of menopausal women, it was found that the articles conducted in this field were very diverse in terms of the type of plant that used for intervention and there was a maximum of 3 acceptable articles for each plant. More studies should be performed with a higher sample size. Among the examined studies, red ginseng, fennel, bindii, red clover, and black cohosh had the highest number of articles, most of which had a positive effect on the sexual function of menopausal women, who can be encouraged to take these herbs.

Acknowledgments

This study was a research project in School of Nursing and Midwifery of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Authors' contribution

TK conducted the literature search and data extraction. TK and EZ wrote the first draft of the manuscript. ZK, MN, and FM helped with data collection and agreed with manuscript results and conclusions. EZ, ZK, MN, FM made critical revision and approved the final version.

Conflict of interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical considerations

Ethical issues including text plagiarism, misconduct, manipulation or appropriation, data fabrication, falsification, redundant publication as well as duplicate submissions have been carefully observed by authors.

Funding/Support

This study was conducted with financial support that was provided by the Midwifery and Reproductive Research Center, Shahid Beheshti University of Medical Science, Tehran, Iran. (Grant number: 22230)

References

- Freak-Poli R, Kirkman M, De Castro Lima G, Direk N, Franco OH, Tiemeier H. Sexual activity and physical tenderness in older adults: cross-sectional prevalence and associated characteristics. J Sex Med. 2017;14(7):918-27. doi: 10.1016/j.jsxm.2017.05.010.
- Tong J, Zhang C, Zhu L, Zhang L, Jinghe L. Sexual dysfunction in perimenopausal women based on a national epidemiological survey in China. Climacteric. 2019;22(2):190-4. doi: 10.1080/13697137.2018.1547699.
- 3. Weinberger JM, Houman J, Caron AT, Anger J. Female sexual dysfunction: a systematic review of outcomes across various treatment modalities. Sex Med Rev. 2019;7(2):223-50. doi: 10.1016/j.sxmr.2017.12.004.
- 4. Sobecki-Rausch J, Lindau ST. New treatments for female sexual dysfunction: are they safe and effective for older postmenopausal women? Curr Sex Health Rep. 2019;11(1):21-8. doi: 10.1007/s11930-019-00187-x.
- Jackson SE, Yang L, Koyanagi A, Stubbs B, Veronese N, Smith L. Declines in sexual activity and function predict incident health problems in older adults: prospective findings from the English longitudinal study of ageing. Arch Sex Behav. 2020;49(3):929-40. doi: 10.1007/s10508-019-1443-4.
- Naeij E, Moosazadeh M, Khani S, Firouzi A, Barzegari S. Effect of counseling and educational interventions on sexual functioning of women with natural menopause: a systematic review and meta-analysis. J Adv Pharm Educ Res. 2019;9(S2):40-51.
- 7. Golshiri P, Akbari M, Abdollahzadeh MR. Age at natural menopause and related factors in Isfahan, Iran. J Menopausal Med. 2016;22(2):87-93. doi: 10.6118/jmm.2016.22.2.87.
- 8. Chen LR, Ko NY, Chen KH. Isoflavone supplements for menopausal women: a systematic review. Nutrients. 2019;11(11). doi: 10.3390/nu11112649.
- 9. Ralph A, Webley G. A prospective audit of pragmatic herbal treatment of women experiencing menopausal symptoms using measure yourself medical outcome profile (MYMOP2) questionnaires. J Herb Med. 2019;17-18:100286. doi: 10.1016/j.hermed.2019.100286.
- Mahdavian M, Mirzaii Najmabadi K, Hosseinzadeh H, Mirzaeian S, Badiee Aval S, Esmaeeli H. Effect of the mixed herbal medicines extract (fennel, Chamomile, and Saffron) on menopause syndrome: a randomized controlled clinical trial. J Caring Sci. 2019;8(3):181-9. doi: 10.15171/ jcs.2019.026.
- 11. Johnson A, Roberts L, Elkins G. Complementary and alternative medicine for menopause. J Evid Based Integr Med. 2019;24:2515690x19829380. doi: 10.1177/2515690x19829380.
- 12. Wang Y, Cao HJ, Wang LQ, Lu CL, Yan YQ, Lu H, et al. The effects of Chinese herbal medicines for treating diabetic foot ulcers: a systematic review of 49 randomized controlled trials. Complement Ther Med. 2019;44:32-43. doi: 10.1016/j.ctim.2019.03.007.
- 13. Cheng CF, Lin YJ, Tsai FJ, Li TM, Lin TH, Liao CC, et al.

- Effects of Chinese herbal medicines on the risk of overall mortality, readmission, and reoperation in hip fracture patients. Front Pharmacol. 2019;10:629. doi: 10.3389/fphar.2019.00629.
- Critical Appraisal Skills Programme. CASP (randomised controlled trial) checklist. Available from: https://casp-uk.net/.
- 15. Kotsopoulos D, Dalais FS, Liang YL, McGrath BP, Teede HJ. The effects of soy protein containing phytoestrogens on menopausal symptoms in postmenopausal women. Climacteric. 2000;3(3):161-7. doi: 10.1080/13697130008500108.
- Brooks NA, Wilcox G, Walker KZ, Ashton JF, Cox MB, Stojanovska L. Beneficial effects of *Lepidium meyenii* (maca) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content. Menopause. 2008;15(6):1157-62. doi: 10.1097/gme.0b013e3181732953.
- 17. Molaie M, Darvishi B, Jafari Azar Z, Shirazi M, Amin G, Afshar S. Effects of a combination of *Nigella sativa* and *Vitex agnus-castus* with citalopram on healthy menopausal women with hot flashes: results from a subpopulation analysis. Gynecol Endocrinol. 2019;35(1):58-61. doi: 10.1080/09513590.2018.1499086.
- Chedraui P, Hidalgo L, San Miguel G, Morocho N, Ross S. Red clover extract (MF11RCE) supplementation and postmenopausal vaginal and sexual health. Int J Gynaecol Obstet. 2006;95(3):296-7. doi: 10.1016/j.ijgo.2006.08.013.
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151(4):264-9. doi: 10.7326/0003-4819-151-4-200908180-00135.
- 20. Kim SY, Seo SK, Choi YM, Jeon YE, Lim KJ, Cho S, et al. Effects of red ginseng supplementation on menopausal symptoms and cardiovascular risk factors in postmenopausal women: a double-blind randomized controlled trial. Menopause. 2012;19(4):461-6. doi: 10.1097/gme.0b013e3182325e4b.
- 21. Ghorbani Z, Mirghafourvand M, Charandabi SM, Javadzadeh Y. The effect of ginseng on sexual dysfunction in menopausal women: a double-blind, randomized, controlled trial. Complement Ther Med. 2019;45:57-64. doi: 10.1016/j.ctim.2019.05.015.
- 22. Oh KJ, Chae MJ, Lee HS, Hong HD, Park K. Effects of Korean red ginseng on sexual arousal in menopausal women: placebo-controlled, double-blind crossover clinical study. J Sex Med. 2010;7(4 Pt 1):1469-77. doi: 10.1111/j.1743-6109.2009.01700.x.
- 23. Abedi P, Najafian M, Yaralizadeh M, Namjoyan F. Effect of fennel vaginal cream on sexual function in postmenopausal women: a double blind randomized controlled trial. J Med Life. 2018;11(1):24-8.
- 24. Yaralizadeh M, Abedi P, Najar S, Namjoyan F, Saki A. Effect of *Foeniculum vulgare* (fennel) vaginal cream on vaginal atrophy in postmenopausal women: a doubleblind randomized placebo-controlled trial. Maturitas. 2016;84:75-80. doi: 10.1016/j.maturitas.2015.11.005.
- Rahimikian F, Rahimi R, Golzareh P, Bekhradi R, Mehran A. Effect of *Foeniculum vulgare* Mill. (fennel) on menopausal symptoms in postmenopausal women: a randomized, triple-blind, placebo-controlled trial. Menopause. 2017;24(9):1017-21. doi: 10.1097/gme.00000000000000881.
- Rahimi Kian F, Bekhradi R, Rahimi R, Golzareh P, Mehran A. Evaluating the effect of fennel soft capsules on the quality

- of life and its different aspects in menopausal women: a randomized clinical trial. Nurs Pract Today. 2017;4(2):87-05
- 27. Shamshad Begum S, Jayalakshmi HK, Vidyavathi HG, Gopakumar G, Abin I, Balu M, et al. A novel extract of fenugreek husk (FenuSMART™) alleviates postmenopausal symptoms and helps to establish the hormonal balance: a randomized, double-blind, placebo-controlled study. Phytother Res. 2016;30(11):1775-84. doi: 10.1002/ptr.5680.
- Steels E, Steele ML, Harold M, Coulson S. Efficacy of a proprietary *Trigonella foenum-graecum* L. de-husked seed extract in reducing menopausal symptoms in otherwise healthy women: a double-blind, randomized, placebocontrolled study. Phytother Res. 2017;31(9):1316-22. doi: 10.1002/ptr.5856.
- 29. de Souza KZ, Vale FB, Geber S. Efficacy of *Tribulus terrestris* for the treatment of hypoactive sexual desire disorder in postmenopausal women: a randomized, double-blinded, placebo-controlled trial. Menopause. 2016;23(11):1252-6. doi: 10.1097/gme.0000000000000766.
- 30. Postigo S, Lima SM, Yamada SS, dos Reis BF, da Silva GM, Aoki T. Assessment of the effects of *Tribulus terrestris* on sexual function of menopausal women. Rev Bras Ginecol Obstet. 2016;38(3):140-6. doi: 10.1055/s-0036-1571472.
- Tadayon M, Shojaee M, Afshari P, Moghimipour E, Haghighizadeh MH. The effect of hydro-alcohol extract of *Tribulus terrestris* on sexual satisfaction in postmenopause women: a double-blind randomized placebo-controlled trial. J Family Med Prim Care. 2018;7(5):888-92. doi: 10.4103/jfmpc.jfmpc_355_17.
- 32. Park JY, Kim KH. A randomized, double-blind, placebocontrolled trial of *Schisandra chinensis* for menopausal symptoms. Climacteric. 2016;19(6):574-80. doi: 10.1080/13697137.2016.1238453.
- 33. Aghamiri V, Mirghafourvand M, Mohammad-Alizadeh-Charandabi S, Nazemiyeh H. The effect of Hop (*Humulus lupulus* L.) on early menopausal symptoms and hot flashes: a randomized placebo-controlled trial. Complement Ther Clin Pract. 2016;23:130-5. doi: 10.1016/j.ctcp.2015.05.001.
- 34. Erkkola R, Vervarcke S, Vansteelandt S, Rompotti P, De Keukeleire D, Heyerick A. A randomized, double-blind, placebo-controlled, cross-over pilot study on the use of a standardized hop extract to alleviate menopausal discomforts. Phytomedicine. 2010;17(6):389-96. doi: 10.1016/j.phymed.2010.01.007.
- 35. del Giorno C, Fonseca AM, Bagnoli VR, Assis JS, Soares JM Jr, Baracat EC. Effects of *Trifolium pratense* on the climacteric and sexual symptoms in postmenopause women. Rev Assoc Med Bras (1992). 2010;56(5):558-62. doi: 10.1590/s0104-42302010000500017.
- Shakeri F, Taavoni S, Goushegir A, Haghani H. Effectiveness of red clover in alleviating menopausal symptoms: a 12-week randomized, controlled trial. Climacteric. 2015;18(4):568-73. doi: 10.3109/13697137.2014.999660.
- Ross SM. Menopause: a standardized isopropanolic black cohosh extract (remifemin) is found to be safe and effective for menopausal symptoms. Holist Nurs Pract. 2012;26(1):58-61. doi: 10.1097/HNP.0b013e31823d1f67.
- 38. Tanmahasamut P, Vichinsartvichai P, Rattanachaiyanont M, Techatraisak K, Dangrat C, Sardod P. Cimicifuga racemosa extract for relieving menopausal symptoms: a

- randomized controlled trial. Climacteric. 2015;18(1):79-85. doi: 10.3109/13697137.2014.933410.
- 39. Mohammad-Alizadeh-Charandabi S, Shahnazi M, Nahaee J, Bayatipayan S. Efficacy of black cohosh (*Cimicifuga racemosa* L.) in treating early symptoms of menopause: a randomized clinical trial. Chin Med. 2013;8(1):20. doi: 10.1186/1749-8546-8-20.
- 40. van Die MD, Burger HG, Bone KM, Cohen MM, Teede HJ. Hypericum perforatum with *Vitex agnus-castus* in menopausal symptoms: a randomized, controlled trial. Menopause. 2009;16(1):156-63. doi: 10.1097/gme.0b013e31817fa9e0.
- 41. Carmignani LO, Pedro AO, Costa-Paiva LH, Pinto-Neto AM. The effect of dietary soy supplementation compared to estrogen and placebo on menopausal symptoms: a randomized controlled trial. Maturitas. 2010;67(3):262-9. doi: 10.1016/j.maturitas.2010.07.007.
- 42. Malakouti J, Jabbari F, Asghari-Jafarabadi M, Javadzadeh Y, Farshbaf-Khalili A. The impact of *Ginkgo biloba* tablet and aromatherapy inhaler combination on sexual function in females during postmenopausal period: a double-blind randomized controlled trial. Int J Womens Health Reprod Sci. 2017;5:129-36. doi: 10.15296/ijwhr.2017.24.
- 43. Amiri Pebdani M, Taavoni S, Seyedfatemi N, Haghani H. Triple-blind, placebo-controlled trial of *Ginkgo biloba* extract on sexual desire in postmenopausal women in Tehran. Iran J Nurs Midwifery Res. 2014;19(3):262-5.
- 44. Choi SY, Kang P, Lee HS, Seol GH. Effects of inhalation of essential oil of *Citrus aurantium* L. var. *amara* on menopausal symptoms, stress, and estrogen in postmenopausal women: a randomized controlled trial. Evid Based Complement Alternat Med. 2014;2014:796518. doi: 10.1155/2014/796518.
- 45. Sadeghi Goghari S, Yousefzadeh S, Rakhshandeh H, Dadghar S, Mazloom SR. The impact of date palm pollen capsule on vaginal iubrication and dyspareunia in menopausal woman. J Midwifery Reproductive Health. 2018;6(4):1399-408. doi: 10.22038/jmrh.2018.23071.1246.
- 46. Taavoni S, Ekbatani NN, Haghani H. Effect of *Tribulus terrestris*, ginger, saffron, and Cinnamomum on menopausal symptoms: a randomised, placebo-controlled clinical trial. Prz Menopauzalny. 2017;16(1):19-22. doi: 10.5114/pm.2017.67366.
- 47. Karimian Z, Keramat A. sHot flashes of menopause and herbal medicine in Iran: a systematic review. Iran J Obstet Gynecol Infertil. 2014;17(111):1-11. doi: 10.22038/ijogi.2014.3278.
- 48. Najaf Najafi M, Ghazanfarpour M. Effect of phytoestrogens on sexual function in menopausal women: a systematic review and meta-analysis. Climacteric. 2018;21(5):437-45. doi: 10.1080/13697137.2018.1472566.
- Niazi A, Moradi M. Sexual satisfaction and function in postmenopausal women treated with herbal medicines: a review of clinical trials. Evid Based Care. 2019;9(2):7-16. doi: 10.22038/ebcj.2019.38679.2016.
- Mazaro-Costa R, Andersen ML, Hachul H, Tufik S. Medicinal plants as alternative treatments for female sexual dysfunction: utopian vision or possible treatment in climacteric women? J Sex Med. 2010;7(11):3695-714. doi: 10.1111/j.1743-6109.2010.01987.x.