



The effect of ginseng on sexual dysfunction in menopausal women: A double-blind, randomized, controlled trial

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ABSTRACT

Objectives: Sexual problems constitute a largely-overlooked problem for women during menopause. The present study was conducted to determine the effect of *Ginseng* on sexual function (primary outcome), quality of life and menopausal symptoms (secondary outcomes) in postmenopausal women with sexual dysfunction.

Design: This randomized controlled trial was conducted on 62 women who were randomly assigned to the intervention/control groups using block randomization.

Intervention: The intervention group received 500 mg of *Panax Ginseng* and the control group received placebo twice daily for four weeks.

Main outcome measures: Standard questionnaires including the Female Sexual Function Index (FSFI), the Menopause-Specific Quality of Life (MENQOL) and the Greene Menopausal Symptom Scale were completed before and four weeks after the intervention.

Results: There were no statistically significant differences between the two groups in terms of demographic characteristics and the baseline scores of sexual function, quality of life and menopausal symptoms ($P > 0.05$). After the intervention, the mean total score of FSFI (Adjusted Mean Difference = 6.32, 95% CI = 3.48 to 9.16, $P < 0.001$) was significantly higher in the intervention group compared to the control group. The mean total score of quality of life (AMD = -20.79, 95% CI = -25.83 to -15.75, $P < 0.001$) and menopausal symptoms (AMD = -8.25, 95% CI = -10.55 to -5.95, $P < 0.001$) were significantly lower in the treatment group than the control group.

Conclusion: *Ginseng* has significant effects in improving sexual function and quality of life and mitigating menopausal symptoms. As a multipotent plant, *Ginseng* can be a suitable alternative for conventional therapies to promote the health of menopausal women.

1. Introduction

According to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), Female Sexual Dysfunction (FSD) consists of a heterogeneous group of disorders¹ that prevent the individual from responding to sexual stimuli and enjoying sexual experiences.² FSD is a multidimensional and multifactorial disorder with a relatively high prevalence in older ages due to the phenomenon of aging, the high comorbidity of chronic diseases and also the process of menopause, which is considered one of the key factors underlying FSD.³

During menopause, women endure a multitude of complications

and symptoms, from vasomotor symptoms (VMS) to Genitourinary Syndrome of Menopause (GSM), and unlike VSM, which attenuates over time, GSM gradually intensifies, and these symptoms may not even be tangible for the individual.⁴

GSM is a comprehensive concept that includes not only physical changes and symptoms of the lower genitourinary tract but also sexual symptoms (insufficient lubrication, pain, and sexual dysfunction).⁵ FSD is one of the key subsets of GSM, but unlike the other symptoms of this syndrome and VMS, which are mainly caused by circulating estrogen deprivation, in FSD, estrogen deprivation is merely one of the complex multifactorial etiologies of the disorder.⁶

There are interactions between different signs and symptoms of

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GSM. For example, vaginal atrophy and urinary incontinence as urogenital symptoms of GSM can increase the chance of developing sexual dysfunction.^{7,8} VMS and urogenital symptoms are commonly caused as a result of estrogen deficiency. Also, the decline of estrogen and androgen levels during menopause and aging adversely affects a woman's sexual health through direct and indirect pathways. These reasons show that the treatment and prevention of other symptoms are mandatory.⁸

The therapies available for relieving menopausal symptoms or GSM besides hormone therapy (with estrogen, progesterone, tibolone, etc.),^{9–11} include herbal medicine, phytoestrogens (isoflavones, lignans and coumestans)^{12,13} and nutraceuticals (dietary supplements and functional foods).^{14–16} Laser therapy is one of the therapies that has recently proven effective for genitourinary symptoms.⁷ The aforementioned treatment options constitute a small subgroup of complementary and alternative medicine that are commonly used nowadays by menopausal women. Hormone therapy, phytoestrogen therapy and other single-drug therapies, however, are not considered a standard choice of treatment for FSD.^{17,18}

Nowadays, modern pharmacology projects the end for the 'one gene, one target, one disease' paradigm. Its approach is that conventional mono-target drugs are no longer capable of responding to today's chronic, multifactorial and complex diseases,¹⁹ and accordingly, it introduces the concept of polypharmacology, which holds that multi-target medications are required in the process of medication development, so that they can concurrently affect several different receptors^{20,21} and prevent polypharmacy as one of the problems faced by older adults and the cause of many undesirable side-effects and medication interactions.^{22–24}

Ginseng, with the scientific name of *Panax Ginseng C. Meyer*, is considered one of the best-known "health functional foods" and adaptogenic herbs (i.e. plants that boost body resistance against internal and external stresses)²⁵ that has many pharmacological as well as adaptogenic and estrogen-like properties. Consequently, it can be effective as a multi-target plant for not only improving menopausal symptoms and quality of life, but also attenuating or treating the underlying factors of FSD,^{21,26} whether alone or in combination with other medications or plants.^{27,28}

Given the increase in life expectancy, the growth of the phenomenon of aging and the subsequent occurrence of menopause in women and the dramatic effect of FSD on all the qualitative dimensions of their physical and sexual life, the present study was conducted to examine the effect of *Ginseng* on sexual function (primary outcome), quality of life and menopausal symptoms (secondary outcomes).

2. Methods

2.1. Study design and participants

This study was a double-blind, randomized, placebo-controlled, clinical trial conducted at the health centers of Tabriz, Iran, in January–June 2018. The participants were all married postmenopausal women aged 45 to 60 years who had a steady sexual partner without any medical problems that could affect their sexual function and had at least two sexual intercourses per month. Their last menstruation had occurred a minimum of 12 months ago and a maximum of ten years ago and their FSFI score was lower than 28 in the initial evaluation.

The study exclusion criteria consisted of having a self-reported psychological problem, sexual dysfunction related to psychiatric disorders, hormonal treatment due to sexual dysfunction during the last two weeks, cardiovascular disorders, uncontrolled diabetes and hypertension, low blood pressure, radical hysterectomy, external genitalia deformity, a history of chemotherapy or pelvic radiotherapy, central nervous system diseases, liver or kidney dysfunction, having dietary restrictions or nutritional deficiencies because of financial or medical problems, having motor impairment and activity limitations, taking medications known to have interactions with *Ginseng* (such as

amlodipine, valerian and lorazepam), post-coital bleeding and the current consumption of phytoestrogens and other herbal medications.

2.2. Sample size

The sample size was determined based on the variable under study (i.e. sexual function) using G-power software. Based on the results obtained by Nazarpour et al.²⁹ in relation to the biggest standard deviation of the subdomain of pain out of all the subdomains of FSFI and considering $M_1 = 24.11$ (the mean pre-intervention score) and assuming a 20% reduction in the score due to the intervention $M_2 = 19.23$ (the mean post-intervention score), $SD_1 \approx SD_2 = 6.04$, $\alpha = 0.05$, and power = 90%, the sample size was calculated as 28. To take account of a potential 10% sample loss, 31 people were ultimately allocated to each group.

2.3. Sampling

After the study protocol was approved by the Ethics Committee of Tabriz University of Medical Sciences and permission was obtained for performing sampling, ten out of the 90 health centers of Tabriz were selected from areas with different socio-economic statuses and larger numbers of patients.

Since the women's data were entirely available through the health centers' electronic system, all the postmenopausal women were selected as the study samples. The researcher invited the eligible women to take part in the study by phone calls. Upon the invitation, the women presenting to these centers were fully assessed in terms of meeting the inclusion and exclusion criteria and were also fully briefed on the study objectives by the researcher. The eligible women willing to take part were included in the study as the initial samples, and the FSFI was completed by the patients after they were briefed on the phases of sexual activity. The participants scoring less than 28 in this questionnaire were identified as cases with sexual dysfunction and were entered into the study upon giving their informed written consent.

2.4. Randomization and intervention

Using block randomization with four and six blocks and an allocation ratio of 1:1, the participants were assigned to the intervention and control groups. For the purpose of allocation concealment, the medications and placebos were put in sealed opaque envelopes sequentially numbered. The process of randomization and the preparation of the envelopes was carried out by a person not involved in the sampling process or the data analysis. The intervention group received 500 mg of *Panax Ginseng* (containing ginsenoside Rg1 = 0.3% and Rb1 = 0.2%) twice daily for four weeks. These capsules were procured from Ghaem Darou Herbal Pharmaceutical Company under the commercial name of Ru*Ginseng*. The control group received placebo capsules (no active ingredients) with the same instructions as the intervention group. The empty placebo capsules of exactly the same color, shape and size as Ru*Ginseng* were procured from a pharmaceutical company, and the placebo was prepared by a collaborating pharmacist at the Pharmacy School of Tabriz University of Medical Sciences. These capsules were of the same weight as the *Ginseng* capsules but contained lactose and starch. The participants and the researcher responsible for data collection were completely blinded to the intervention type or participants' allocation to the study groups. Prior to the intervention with either the medications or the placebos, the participants received checklists of medication use and side-effects. Two weeks after the intervention, telephone follow-ups were used to instruct the regular use of the medications and assess the side-effects and potential withdrawals.

2.5. Tools

The data collection tools included a socio-demographic

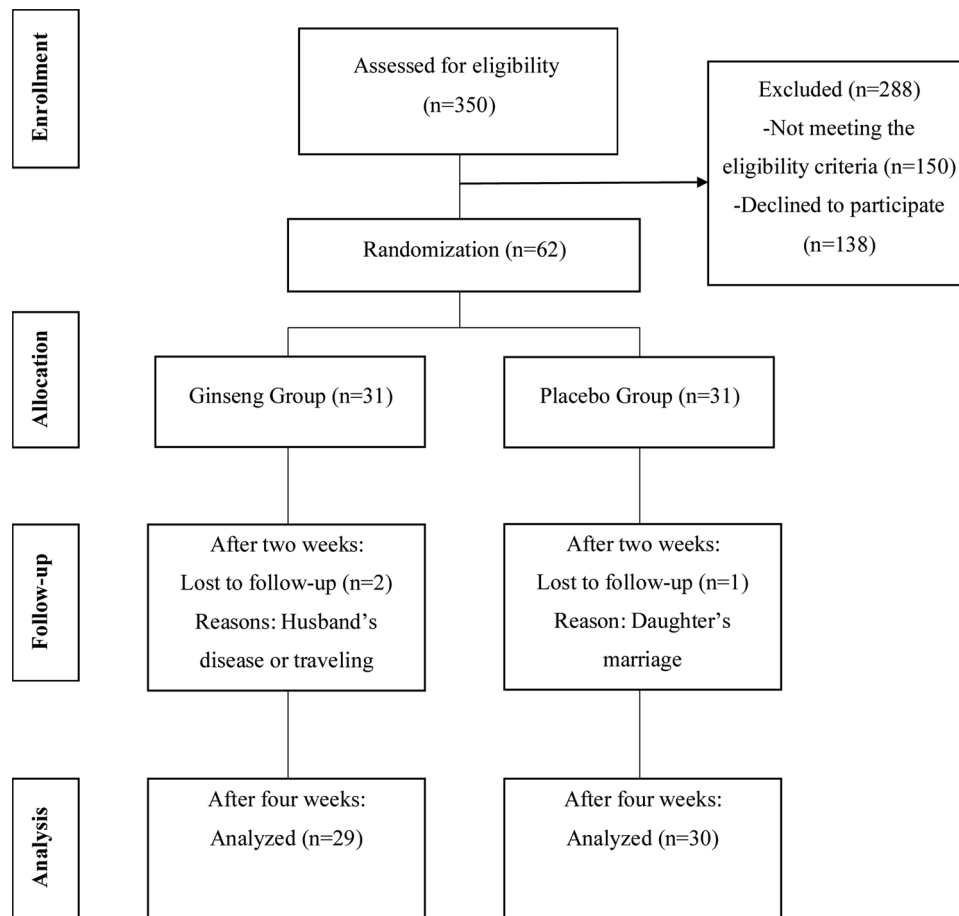


Fig. 1. The study flowchart.

questionnaire, the Female Sexual Function Index (FSFI), the Menopause-Specific Quality of Life (MENQOL) questionnaire and the Greene Menopausal Symptoms Scale and a checklist of side-effects.

The FSFI consists of 19 items in six main domains [desire (two items), arousal (four items) lubrication (four items), orgasm (three items), satisfaction (three items) and pain (three items)]. Each item is scored from zero (or one) to five, and higher scores indicate better sexual function. Participants' responses to the items before and four weeks after the intervention comprised the basis of scoring and the total score was calculated as the sum of the scores in these six domains after applying a specific weight factor for each domain (0.6 for desire, 0.4 for arousal and lubrication and 0.3 for orgasm, satisfaction and pain) and ranged from 2 to 36. It has been used in several studies.^{9, 15,30} The validity and reliability of this questionnaire have been confirmed by Rosen et al. (2000)³¹ and also by Fakhri et al. (2012) in Iran.³²

The MENQOL Questionnaire was developed and used by the Faculty of Medicine of the University of Toronto in Canada to assess the quality of life in postmenopausal women.³³ This questionnaire contains 29 closed-ended items in four domains (three items in the vasomotor domain, seven in the psycho-social domain, 16 in the physical domain and three for sexual symptoms), with scores ranging from 0 to 6 based on a Likert-type scale. The MENQOL score is calculated as the sum of the scores in these four domains. The validity and reliability of this questionnaire were confirmed in Iran in a study by Yazdkhasti et al.³⁴ Based on a six-point Likert scale and the number of items in the questionnaire, the minimum, and maximum scores in the vasomotor, psycho-social, physical and sexual domains are 0-18, 0-42, 0-96 and 0-18, respectively. The total MENQOL score is the sum of the scores in these domains and varies from 0 to 174. Approaching the maximum score indicates a greater severity of menopause symptoms and a lower quality

of life in post-menopause.

Menopausal symptoms were evaluated by the standard Greene scale, which has been developed by Professor Greene and has already been used in several studies in Iran and its validity and reliability have been confirmed by Askari et al.³⁵ This scale is a 21-item measure for examining the presence and severity of menopausal symptoms, including psychological (items 1-11), physical (items 12-18), vasomotor (items 19 and 20) and sexual (item 21) symptoms. Each item in this scale is scored from zero ('no symptoms') to three ('extremely bothered') based on the respondent's experiences during the last four weeks. The Greene score is calculated as the sum of the scores in these four domains. Higher scores indicate more severe menopausal symptoms.

A checklist was also used for assessing any adverse events experienced by the women and included items about vaginal bleeding, diarrhea or digestive symptoms, elevated blood pressure, breast enlargement, migraine or other headaches, etc.

The reliability of the tools was assessed by test-retest at a two-week interval on 20 women of menopausal age, and the Cronbach's alpha coefficient and Intraclass Correlation Coefficient were calculated as 0.94 and 0.74 for the FSFI, 0.87 and 0.99 for MENQOL and 0.79 and 0.99 for the Greene scale.

2.6. Statistical analysis

Data were analyzed in SPSS-22. The normal distribution of the quantitative data was assessed using the Kolmogorov-Smirnov test. In assessing participants' demographic details, quantitative variables were reported as a mean and qualitative variables as a percentage. The sociodemographic-test

3. Results

3.1. Baseline characteristics

Of the 350 women initially assessed, 150 were excluded for not satisfying the inclusion criteria and due to different medical problems in the women themselves or their husbands, which tend to be common in the examined age range, and 138 were excluded for unwillingness to take part, and 62 women ultimately entered the study and were randomly assigned to the *Ginseng* or placebo groups (n = 31 per group). In a telephone follow-up two weeks after beginning the study, two women from the *Ginseng* group (due to their husband's illness or traveling) and one from the placebo group (due to her daughter's marriage) were unwilling to continue cooperation. The study was thus completed with the participation of 59 women. All the questionnaires were re-completed by the patients after the termination of the study. The statistical analysis was carried out on the data from 29 women in the intervention group and 30 women in the control group (Fig. 1).

Blood pressure and BMI were assessed in the two groups before and after the intervention, and systolic blood pressure was found to have reduced significantly in the *Ginseng* group compared to the placebo group four weeks after the intervention. Diastolic blood pressure and BMI had also reduced in the *Ginseng* group four weeks after the intervention compared to before; however, the difference between the two groups was not statistically significant (Table 1).

3.2. Sexual function

The mean (standard deviation) total score of FSFI increased from 16.82 (5.66) before the intervention to 21.73 (5.46) in the *Ginseng* group and decreased from 18.08 (4.32) before the intervention to 15.99 (7.72) four weeks after the intervention in the placebo group. There were no significant differences between the two groups in terms of the mean scores of sexual function at baseline, but the mean post-intervention scores adjusted for baseline were significantly higher in the *Ginseng* group compared to the control group (AMD = 6.32; 95% CI = 3.48 to 9.16; P < 0.001). Moreover, the intervention group showed significant improvements in all the domains of the FSFI (desire, arousal, lubrication, orgasm, satisfaction and pain) compared to the control group (P < 0.001; Table 2).

3.3. Quality of life

The mean total score of quality of life before the intervention was 72.65 in the *Ginseng* group and 68.90 in the placebo group. Also, four weeks after the intervention, the mean score was 50.62 in the *Ginseng* group and 66.97 in the placebo group. In terms of the mean overall quality of life, there were no significant differences between the groups' mean scores at baseline (P = 0.554), but the mean post-intervention score adjusted for baseline was significantly higher in the *Ginseng* group compared to the control group (AMD = -20.79; 95% CI = -25.83 to -15.75; P < 0.001). Significant improvements were observed in all the dimensions of quality of life (vasomotor, psychosocial, physical and sexual) in the *Ginseng* group (P < 0.001; Table 3).

3.4. Menopausal symptoms

The mean total score of menopausal symptoms decreased from 29.00 to 19.48 in the *Ginseng* group and from 28.19 to 26.27 in the placebo group (AMD = -8.25; 95% CI = -10.55 to -5.95; P < 0.001). The mean post-intervention score adjusted for baseline was significantly lower in the *Ginseng* group compared to the placebo group (P < 0.001). The *Ginseng* group showed improvements in symptoms in all the dimensions of the Greene scale compared to the control group (P < 0.001; Table 4).

A positive adjusted mean difference on the FSFI and a negative

Table 1

The demographic characteristic of the participants in the *Ginseng*/Placebo groups.

Variable	Ginseng Group (n = 31) Number (Percent)	Placebo Group (n = 31) Number (Percent)	P-Value
Age (year)			0.562 ^b
45-50	7 (22.6)	8 (25.8)	
51-55	17 (54.8)	12 (38.7)	
56-60	7 (22.6)	11 (35.5)	
Mean (SD) ^a	52.9 (53.5)	53.5 (4.1)	
Menopausal Age (year)			0.201 ^b
45-50	18 (58.1)	21 (67.7)	
51-55	13 (41.9)	10 (32.3)	
Mean (SD) ^a	48.1 (3.1)	49.1 (2.7)	
Education			0.931 ^c
Primary school	25 (80.6)	23 (74.2)	
Secondary school	2 (6.5)	3 (9.7)	
High school diploma and university education	4 (12.9)	5 (16.1)	
Spouse's Education			0.519 ^c
Primary school	21 (67.7)	24 (77.6)	
Secondary school	7 (22.6)	5 (16.1)	
High school diploma and university education	3 (9.7)	2 (6.5)	
Occupation			0.300 ^d
Housewife	27 (87.1)	23 (74.2)	
Employed	4 (12.9)	8 (25.8)	
Spouse's Occupation			0.379 ^e
Unemployed	4 (12.9)	0	
Employed	4 (12.9)	4 (12.9)	
Retired	7 (22.6)	8 (25.8)	
Self-employed	16 (51.6)	19 (61.3)	
Parity			0.444 ^e
Less than 4	16 (51.6)	12 (38.7)	
4 or higher	15 (48.4)	19 (63.1)	
Delivery Type			0.729 ^e
Vaginal	23 (74.2)	23 (74.2)	
Cesarean section	3 (9.7)	1 (3.4)	
Both	5 (16.1)	5 (17.2)	
Family Size			0.822 ^e
1-3	17 (54.8)	15 (48.4)	
4-6	14 (44.1)	16 (51.6)	
Monthly Income Adequacy			1.000 ^e
Inadequate	18 (58.1)	19 (61.3)	
Relatively adequate	12 (38.7)	10 (32.3)	
Adequate	1 (3.2)	2 (6.5)	
Satisfaction with Life			0.631 ^e
Satisfied	27 (87.1)	25 (80.6)	
No comments	3 (9.7)	4 (12.9)	
Dissatisfied	1 (3.2)	2 (6.5)	
Pre-Intervention BP^f			
Systolic ^g	124.84 (14.80)	124.19 (13.42)	0.858 ^b
Diastolic ^g	80.32 (8.75)	80.00 (8.56)	0.884 ^b
Post-Intervention BP^f			
Systolic ^g	114.83 (12.71)	123.17 (13.68)	0.019 ^b
Diastolic	75.86 (9.17)	80.17 (9.78)	0.087 ^b
Pre-Intervention BMI^{g,a}	31.04 (4.16)	31.59 (3.48)	0.573 ^b
Post-Intervention BMI^{g,a}	30.69 (4.26)	31.20 (3.30)	0.605 ^b

^a Mean (Standard Deviation).

^b Independent-t-test

^c Chi-square for trend test.

^d Fisher's-t-test

^e Chi-square test.

^f Blood Pressure (mmHg).

^g Body Mass Index (kg m⁻²).

adjusted mean difference on the MENQOL and Green scale were observed, which reveal the improvements in the intervention group.

3.5. Side-effects

The side-effects reported included one case of insomnia and

Table 2The mean total score of FSFI and the mean scores of its dimensions in the *Ginseng*/Placebo groups.

Variable (Score Range)	Ginseng Mean (SD)	Placebo Mean (SD) ^a	Mean Difference 95% CI ^b	P-Value
Desire (1-5)				
Baseline	1.72 (0.75)	2.11 (0.89)	-0.39 (-0.81 to 0.32)	0.069
4 weeks	2.69 (0.78)	2.32 (0.80)	0.37 (0.24 to 0.93)	< 0.001
Arousal (0-5)				
Baseline	2.53 (1.16)	2.65 (0.90)	-0.13 (-0.65 to 0.40)	0.634
4 weeks	3.47 (1.12)	2.23 (1.51)	1.30 (0.76 to 1.85)	< 0.001
Lubrication (0-5)				
Baseline	3.16 (1.16)	3.19 (1.00)	-0.03 (-0.58 to 0.52)	0.916
4 weeks	3.63 (0.01)	2.53 (1.66)	0.98 (0.37 to 1.59)	< 0.001
Orgasm (0-5)				
Baseline	2.83 (1.39)	2.90 (0.94)	-0.08 (-0.68 to 0.53)	0.798
4 weeks	3.35 (1.32)	2.33 (1.62)	0.98 (0.38 to 1.58)	< 0.001
Satisfaction (0-5)				
Baseline	2.88 (1.29)	2.98 (0.98)	0.10 (0.98 to 0.48)	0.721
4 weeks	3.97 (1.14)	2.81 (1.25)	1.22 (0.80 to 0.64)	< 0.001
Pain (0-5)				
Baseline	3.75 (1.76)	4.39 (1.46)	1.37 (-1.41 to 4.15)	0.130
4 weeks	4.62 (1.45)	3.76 (2.23)	1.07 (0.23 to 1.92)	< 0.013
Total FSFI Score (2-36)				
Baseline	16.82 (5.66)	18.08 (4.39)	-1.26 (-3.84 to 1.31)	0.330
4 weeks	21.73 (5.45)	15.99 (7.72)	6.32 (3.48 to 9.16)	< 0.001

t-test compare the mean scores of sexual function and its dimensions before the intervention. After the intervention, the ANCOVA adjusted for baseline scores was used to compare the scores.

The number of women examined before the intervention was 31 in both groups; after the intervention, it reduced to 29 in the *Ginseng* group and 30 in the placebo group.

Higher sexual function scores indicate more favorable conditions.

^a Mean (Standard Deviation)

^b Mean Difference (95% Confidence Interval)

palpitations and two cases of flushing in the *Ginseng* group and one case of gastric discomfort and change in urine color and smell in the control group.

4. Discussion

The results obtained in the present study showed that *Ginseng* has significant effects in improving sexual function and quality of life and mitigating menopausal symptoms in women.

Although *Ginseng* was associated with a significant improvement in

the total FSFI score, four weeks after the intervention, the mean total score was still lower (worse) in the intervention group given the threshold of 28 and the cut-off point of 24.75, extracted from a study validating the Persian version of the scale.³²

Three studies have so far been conducted on the effects of *Ginseng* on women's sexual function.^{36–38} The present study is the first to investigate the multi-purpose effects of *Ginseng* with an all-inclusive approach.^{28,39} The majority of studies on *Ginseng* have been conducted in Korea, which is the main producer of *Ginseng* in the world, and the present study is the first human clinical trial on *Ginseng* in Iran.

Table 3The mean total score of MENQOL and the mean scores of its dimensions in the *Ginseng*/Placebo groups.

Variable (Score Range)	Ginseng Mean (SD)	Placebo Mean (SD) ^a	Mean Difference 95% CI ^b	P-Value
Vasomotor Symptoms (0-18)				
Baseline	10.84 (3.58)	9.19 (5.01)	-1.65 (-0.57 to 3.86)	0.142
4 weeks	7.62 (3.40)	9.37 (5.12)	-1.75 (-4.19 to -1.84)	< 0.001
Psychological Symptoms (0-42)				
Baseline	15.42 (8.55)	15.58 (8.88)	-0.16 (-4.59 to 4.27)	0.942
4 weeks	11.07 (6.68)	14.93 (8.58)	-4.28 (-5.50 to -3.06)	< 0.001
Physical Symptoms (0-96)				
Baseline	34.58 (13.06)	31.07 (15.64)	3.48 (-3.84 to 10.81)	0.345
4 weeks	22.45 (9.25)	29.73 (15.49)	-10.74 (-13.06 to -8.40)	< 0.001
Sexual Symptoms (0-18)				
Baseline	11.81 (5.17)	13.03 (4.27)	-1.23 (-3.63 to 1.18)	0.313
4 weeks	9.48 (4.82)	12.93 (3.92)	-2.35 (-3.36 to -1.33)	< 0.001
Total MENQOL Score (0-174)				
Baseline	72.65 (21.54)	68.90 (27.64)	3.74 (-8.85 to 16.33)	0.554
4 weeks	50.62 (16.46)	66.97 (27.37)	-20.79 (-25.83 to -15.75)	< 0.001

t-test compare the mean scores of quality of life and its dimensions before the intervention. After the intervention, the ANCOVA adjusted for baseline scores was used to compare the scores.

The number of women examined before the intervention was 31 in both groups; after the intervention, it reduced to 29 in the *Ginseng* group and 30 in the placebo group.

Higher scores indicate poorer qualities of life.

^a Mean (Standard Deviation).

^b Mean Difference (95% Confidence Interval).

Table 4
The mean total score of the Greene scale and the mean scores of its dimensions in the *Ginseng*/Placebo groups.

Outcome (Score Range)	<i>Ginseng</i> Mean (SD) ^a	Placebo Mean (SD) ^a	Mean Difference 95% CI ^b	P-Value
Psychological Symptoms (Anxiety) (0-18)				
Baseline	7.84 (3.22)	8.23 (3.67)	-0.39 (-2.14 to 1.37)	0.660
4 weeks	6.14 (2.76)	7.90 (3.50)	-1.62 (-2.34 to -0.91)	< 0.001
Psychological Symptoms (Depression) (0-15)				
Baseline	7.16 (3.62)	6.29 (4.26)	0.87 (-1.14 to 2.88)	0.389
4 weeks	4.41 (2.27)	5.57 (4.08)	-1.97 (-2.80 to -1.15)	< 0.001
Physical Symptoms (0-21)				
Baseline	7.45 (4.04)	7.61 (4.92)	-0.16 (-2.45 to 2.13)	0.888
4 weeks	4.48 (3.41)	6.70 (4.12)	-2.60 (-3.51 to -1.68)	< 0.001
Vasomotor Symptoms (0-6)				
Baseline	4.13 (1.67)	3.71 (1.97)	0.42 (-0.51 to 1.35)	0.369
4 weeks	2.52 (1.50)	3.77 (2.05)	-1.55 (-2.15 to -0.95)	< 0.001
Loss of Interest in Sex (0-3)				
Baseline	2.42 (0.72)	2.35 (0.84)	0.06 (-0.33 to 0.46)	0.762
4 weeks	1.93 (0.75)	2.33 (0.71)	-0.44 (-0.68 to 0.19)	< 0.001
Total Greene Score (0-63)				
Baseline	29.00 (9.52)	28.19 (11.88)	0.81 (-4.66 to 6.27)	0.769
4 weeks	19.48 (7.01)	26.27 (10.52)	-8.25 (-10.55 to -5.95)	< 0.001

t-test compare the mean scores of quality of life and its dimensions before the intervention. After the intervention, the ANCOVA adjusted for baseline scores was used to compare the scores.

The number of women examined before the intervention was 31 in both groups; after the intervention, it reduced to 29 in the *Ginseng* group and 30 in the placebo group.

Higher scores indicate more severe menopausal symptoms.

^a Mean (Standard Deviation).

^b Mean difference (95% Confidence Interval).

In a study conducted by Kim et al. ³⁷ on 24 premenopausal women on the effects of *Ginseng* on sexual function and quality of life, despite the significant improvement observed in the *Ginseng* recipients, the results showed no significant differences between the two groups. The results of a clinical trial conducted by Oh et al. ³⁶ to assess the effect of *Ginseng* on sexual arousal in postmenopausal women showed that *Ginseng* increases the score of the arousal subdomain of the FSFI significantly ($P = 0.006$).

The last study on this subject was conducted by Chung et al., ³⁸ who assessed the effect of *Ginseng* on sexual function in 41 premenopausal women. The results showed a significant increase in the overall score of sexual function and the scores of all its dimensions, but no significant differences were observed between the two groups ($P = 0.702$), and Chung et al. attributed this lack of difference to the significant placebo effect reported by the placebo group.

The positive effect of *Ginseng* on sexual function may be due to its effectiveness in increasing the release of NO (Nitric Oxide) from the arterial walls and the increased sensitivity of tissues to it or the increased physical energy levels and the anti-fatigue properties of *Ginseng* (which is proven to affect the fatigue caused by cancer as well).^{40,41}

By way of various pharmacological activities, *Ginseng* can be effective in the treatment and mitigation of the factors underlying FSD. ⁴² In one animal study, *Ginseng* was found to relax the vaginal smooth muscles and the Corpus cavernosum clitoris in rabbits, as mediated by NO, Guanosine Monophosphate (GMP) and the polarization of the calcium-potassium channel. *Ginseng* also increases NO synthesis from the epithelial cells of the vascular walls, and with its protective effects, acts as an antioxidant.^{43,44}

In a review study, Coleman et al. (2003) examined the effects of *Ginseng* on quality of life, and although eight out of the nine eligible studies in that review article had reported improvements in the overall quality of life, the study was not capable of identifying the properties that could be definitely attributed to *Ginseng*.⁴⁵ This lack may have been due to a large number of studies that had used unreliable tools to assess the quality of life and also the fact that *Ginseng* had been used in them as a supplement in combination with vitamins and other herbal medicines.

A multi-center clinical trial conducted over 16 weeks by Wiklund

et al. in Sweden to determine the effects of standard *Ginseng* extract on quality of life and physiological parameters in 382 symptomatic postmenopausal women with a mean age of 53 years who were randomly assigned to the intervention and control groups showed significant differences between the two groups in terms of the depression, self-control and mental health dimensions ($P = 0.03$), but no significant improvements were observed in the remaining dimensions in either group ⁴⁶.

Ellis et al. (2003) conducted a study on the effects of *Ginseng* on the health-related quality of life over eight weeks and randomly assigned 30 women to their intervention and control groups. The results showed significantly higher scores in the social function ($P = 0.017$) and mental health ($P = 0.019$) subdomains of the SF-36 in the intervention group compared to the controls. ⁴⁷ These findings agree with the results obtained in the present study.

The positive effect of *Ginseng* on the quality of life is probably due to its positive effects on various body systems, including effects such as strengthening the immune system, improving cognitive function (anti-Alzheimer's disease and anti-depression),^{48,49} inhibiting cardiovascular risk factors,⁵⁰ improving sleep quality, inhibiting oxidative stress as an antioxidant ⁵¹ and reducing musculoskeletal pain ⁵².

In the present study, the symptoms of menopause improved significantly in the *Ginseng* group compared to the controls, which may have been largely due to *Ginseng*'s estrogen and estrogen-like activities. These properties of *Ginseng* have been confirmed in a study conducted by Xu et al., who investigated the effect of *Ginseng* on oophorectomized rats and showed a reversal of uterine and vaginal atrophy, increased estrogen receptors and reduced circulating FSH and LH, which all have a major role in reducing menopausal symptoms and the revival of the genital tissues ^{52,53}.

In a review study conducted by Lee et al. (2016) to investigate the effects of *Ginseng* on the management of postmenopausal women's health, of the ten eligible studies reviewed, one study showed no significant differences in the frequency of hot flushes between the placebo and *Ginseng* groups. The second study reported positive effects for *Ginseng* on the symptoms of menopause. The third RCT reported beneficial effects for *Ginseng* on depression and general health and well-being. The fourth trial had compared hormonal changes between the

two groups and could not prove any significant differences between them. The other two RCTs had investigated the effect of *Ginseng* on endometrial thickness in postmenopausal women and found no significant differences between the two groups in this regard. The remaining trials had reported no positive effects for *Ginseng* on oxidative stress markers and antioxidant levels. The overall results of this review study provided positive evidence on the effects of *Ginseng* on sexual function, sexual arousal and the overall score of hot flushes,⁵⁴ which agrees with the present findings.

In a clinical trial conducted over 12 weeks by Kim et al. (2009–2010) in Korea to determine the effects of *Ginseng* supplements on postmenopausal symptoms and cardiovascular risk factors, 72 postmenopausal women aged 40 to 60 years were randomly allocated to the *Ginseng* and placebo groups. The results showed significant improvements in the scores of menopausal symptoms based on the Kupperman Index ($P = 0.032$) and Menopause Rating Scale ($P = 0.035$) in the *Ginseng* group compared to the placebo group,⁵⁵ which agrees with the present findings regarding the mitigation in menopausal symptoms caused by *Ginseng*.

In this study, the *Ginseng* group reported side-effects including insomnia, palpitations and flushing, and the placebo group reported gastric discomfort and changes in urine color and odor. The side-effects of *Ginseng* were also investigated in two different review studies conducted by Shergis et al. and Lee et al. and included insomnia, palpitations, headache, mild liver dysfunction,⁵⁶ nausea, headache and migraine, cold and flu, diarrhea and digestive disorders and vaginal bleeding.⁵⁴ In another review study, Seely et al. noted that side-effects such as hypertension, vaginal bleeding, breast pain, insomnia, acne and diarrhea are often caused by the inappropriate and long-term use of this medication.⁵⁷ Similarly, Seigle described a syndrome called the *Ginseng* abuse syndrome that is characterized by hypertension, irritability, diarrhea, insomnia, skin rash, dizziness and symptoms of bipolar (manic-depressive) disorder⁵⁸.

With the increasing population of postmenopausal women, the complications of menopause and its interactions with women's physical and sexual quality of life, and with the knowledge that most postmenopausal women rarely seek treatment for sexual dysfunctions and consider menopause the end of their sexual life, and since the treatment and prevention of these complications are possible with effective training and interventions and with no adverse side-effects, it is the duty of health care workers involved in promoting women's health during menopause to prioritize the provision of high-quality services to this age group. The results of the present study show that *Ginseng* can be recommended as a treatment option for middle-aged women, sex therapists, and health planners.

4.1. Strengths and limitations

The strengths of this study include observing all the principles of conducting clinical trials, including random allocation, allocation concealment, blinding and also the use of standard and valid tools for assessing sexual function, quality of life and menopausal symptoms. Another limitation was that most of the women in the present study were housewives and had primary school education, and the generalizability of the results to women with higher levels of education or employed women may be impossible. The researchers recommend assessing the effects of concurrent verbal training, because most postmenopausal women have no knowledge of their natural sexual cycle. Moreover, since genitourinary disorders are common in older men, the concurrent assessment of both sexual partners is recommended. The greatest limitation of this study, however, was the short duration of the intervention and follow-up compared to previous studies.

In addition, most studies on this plant have used the cross-over design, been conducted in Korea, which is the native land of *Ginseng*, and been supported or funded by pharmaceutical companies such as Pharmaton. Meanwhile, *Ginseng* is considered a non-native and

expensive plant in Iran.

5. Conclusion

According to the results obtained, *Ginseng* has significant effects in improving the quality of sexual function (rather than the frequency of sexual intercourse) and quality of life and mitigating menopausal symptoms in women. Given that no side-effects mandating the discontinuation of the medication regimen were reported in this study, and since this plant is an over-the-counter alternative medicine available throughout the world, it can be recommended as a suitable alternative for improving the function of postmenopausal women. Nonetheless, further studies, including systematic review studies, are required for a definitive decision about the effectiveness of *Ginseng*.

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Conflicts of interest

None to be declared.

Ethical approval

The Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1396.715) approved this study.

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