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The 4-month effect of *Vitex agnus-castus* plant on sexual function of women of reproductive age: A clinical trial

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Abstract:

BACKGROUND: Sexual dysfunction in women is a common disorder. Yet, there is no consensus on its treatment. Few studies have shown that *Vitex agnus-castus* improves sexual dysfunction in postmenopausal women; the present study was conducted to evaluate the effect of *V. agnus-castus* on the female sexual function in the reproductive age.

MATERIALS AND METHODS: This was a double-blinded randomized control clinical trial on the women of reproductive age referred to the gynecology clinic of Al-Zahra Medical Center in Rasht, Iran, from February 2018 to December 2019. The intervention group received Agnugol tablet containing 3.2–4.8 mg dried extract *V. agnus-castus* (51 participants) and the control group received a placebo tablet (51 participants). All participants received one tablet daily for 16 weeks. The participants were asked to complete the Female Sexual Function Index questionnaire at the beginning of the study and after 4, 8, 12, and 16 weeks. Data were analyzed in SPSS statistics (version 21) using Chi-square test, *t*-test, Mann–Whitney U-test, analysis of variance, and mixed model to examine the differences between the groups.

RESULTS: The results showed that the difference between the two groups was not significant in each domain, but there was a significant difference in the overall sexual function mean score so that the intervention group had a higher score than the placebo group after 16 weeks ($P < 0.05$).

CONCLUSION: In the present study, it was observed that the consumption of *V. agnus-castus* during 16 weeks was more effective than the placebo in improving sexual dysfunction. Further studies with larger sample sizes are needed to be able to decide on the prescription of this drug in the clinics.

Keywords:

Female, fertile period, physiological, phytoestrogen, sexual dysfunctions, sexual health, *Vitex agnus-castus*

Introduction

Female sexual dysfunction (FSD) is one of the most effective factors on the quality of marital life[1] that can occur in each stage of sexual response such as sexual desire, arousal, orgasm, and pelvic pain/penetration, or a combination of these.[2] The prevalence of FSD in Iran is reported to be 52% in women of reproductive age.[3] Ignoring sexual problems, especially in women of reproductive age, results in the reduction of life quality, fertility problems, marital discord, and even the separation of couples because they struggle with it for a longer period.[4]

Treating FSD can improve the health of women and society.[5] Although the emphasis of current treatment models is on the biopsychosocial aspects, there is still no

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approved drug for the treatment of FSD. A meta-analysis showed that the effectiveness of current treatments for FSD is as high as or slightly higher than the placebo.[6] Therefore, the discovery of drugs that affect FSD is still of interest.

In recent decades, medicinal plants have been considered for treatment because they are natural, available, and safe.[7] One of these widely used plants is *Vitex agnus-castus* L. from the Verbenaceae family.[8] In traditional medicine, it is used to treat premenstrual syndrome and dysphoric mood disorders,[9] dysmenorrhea,[10] hyperprolactinemia, menopausal disorders,[11] lactation problems, and infertility.[12] Although its exact mechanism has not been established, it seems to affect the hypothalamic–pituitary axis and consequently reduce the release of follicle-stimulating hormone (FSH) and prolactin, and modulate the release of luteinizing hormone (LH) from the pituitary gland. This effect can increase the blood progesterone and modulate the prolactin. The dopaminergic effect of *V. agnus-castus* has been observed *in vitro*[13,14] and *in vivo*,[15] which is due to the presence of chemical compounds such as flavonoids, iridoid glycosides, and essential oil.[16,17] Flavonoid compounds such as extracted apigenin from *V. agnus-castus* were identified as the most active phytoestrogens for estrogen receptors, especially beta-estrogen receptors, and the effectiveness of flavonoids on estrogen receptors was observed experimentally.[18,19] The possible mechanism of the dopaminergic effect of *V. agnus-castus* as an effective neurotransmitter on sexual response can improve sexual function.[20,21] It was also observed in an animal study that flavonoids increased sexual desire, arousal, performance, and pleasure.[22] Moreover, its safety and tolerability have been reported in human studies.[12,23] Since in the recent study, the authors used the safe and minimum effective dose (moderately 4 mg/day) of the drug for 4 months and no significant adverse effect was observed, it seems that there is no concern about the duration of the treatment.[24,25]

Few studies such as the clinical trial of Mirzaii-Najmabdi[26] and Lucks *et al*.[27] on the effectiveness of the *V. agnus-castus* on the sexual function of postmenopausal women showed that the oral, local, and inhalant consumption of *V. agnus-castus* can improve vaginal tone and firmness, increase vaginal lubrication, make intercourse easier,[27] and improve sexual function in perimenopause and postmenopausal women.[26,28] The results of a part of the present study which examined the effect of 1-month consumption of *V. agnus-castus* on female sexual function in reproductive age showed that 1-month consumption did not improve sexual function and its domains.[29] To answer the question of whether longer consumption of this plant for at least 4 months can affect the sexual function, the present study was conducted for 4 months, so that a step can be taken to improve women's health.

Materials and Methods

Study design and setting

This randomized double-blind controlled trial was conducted from February 2018 to December 2019 at Al-Zahra Education, Research and Remedial Center, Guilan University of Medical Sciences, Rasht, Iran.

Study participants and sampling

All women of reproductive age who referred to the gynecological clinic of Al-Zahra Hospital for routine gynecological examinations were invited to study if they had a sexual problem and wanted to improve their sexual function. Individuals read and signed the consent form if they met the inclusion criteria. Inclusion criteria were an age of 15–44 years, no disease based on a gynecologist's opinion (thyroid problems, diabetes and mental illness, hyperprolactinemia, liver disease, abnormal bleeding, cervicitis, and vaginitis), no depression (Beck score below 9), and no premenstrual syndrome. Furthermore, no conflict between the couples leading to the decision to separate based on the woman's statement, no alcohol or drug addiction in husband or wife based on the woman's statement, the ability of the husband to have normal sex during the intervention (such as no erectile dysfunction or premature ejaculation), and no consumption of hormonal contraceptive tablets were the inclusion criteria.

Exclusion criteria were unwillingness to continue participating in the study, use of any chemical drug that interferes with sexual function (antipsychotics, benzodiazepines, and selective serotonin reuptake inhibitors), pregnancy, any complication or allergic symptoms caused by the intervention, and any stressful event (such as death and separation) for the subject during the study according to Holmes-Rahe Scale.[30] They were then evaluated for premenstrual syndrome and depression. All of them completed the form of diagnosis of premenstrual syndrome. If they had 5 out of 11 criteria during the last 7 days of the menstrual cycle, they were considered as women with premenstrual syndrome and due to its confounding effect, these patients were not included in the study.[2] Then, subjects without premenstrual syndrome were asked to complete the Beck Depression Inventory. If they did not have depression (a score of below 9), individuals were asked to complete the Female Sexual Function Index (FSFI) questionnaire. In the end, the gynecology and demographic questionnaires were completed.

In the first session and before taking the tablets, the stages of the natural sexual response and the effective factors on it were taught to subjects within one hour.

To randomly divide subjects into groups, the random number function of Excel was used. In Excel software, groups A and B were first arranged in order. Then, random numbers were generated in the next column using the RAND command. In the next step, the generated random numbers were sorted from small to large using the SORT command which changed the order of the groups. Finally, subjects were assigned to the intervention and placebo groups using the new order.

Based on a randomized grouping, each subject was given a tablet (Agnugol tablet containing 3.2–4.8 mg dried extract *V. agnus-castus* or placebo) to use one tablet daily for 16 weeks and without interruption.[31]

For *V. agnus-castus* group (group A), Agnugol® tablets made by Goldaru Herbal Pharmaceutical Company were used which are coated tablets containing dried extract of the fruit of *V. agnus-castus* in the amount of 3.2–4.8 mg dried extract (with the license number of 1228030321). For the placebo group (group B), tablets made by Hakim Pharmaceutical Company were used which contain starch with the same color, shape, taste, and weight of Agnugol tablets.[31] The tablets were packed in sealed opaque envelopes by a noninvolved colleague. The researcher, gynecologist, and patient were unaware of the type of intervention.

A part of the results of the study was evaluated after 1 month and showed the ineffectiveness of tablets. Therefore, the study lasted up to 4 months to comply with the effectiveness guidelines of phytoestrogen plants, as early studies showed that long-term use (between 4 and 6 months) was essential for the effectiveness of phytotherapy.[32,33]

At the end of every 4 weeks (4, 8, 12, and 16 weeks), participants were asked to come to the clinic to complete the FSFI questionnaire again and submit a daily record of medication. Changes in the number of intercourses and possible side effects of medications were asked of participants at the end of each month. The researcher contacted the subjects once a week to assure they were taking the tablets regularly and to ask about possible side effects. The researcher called the subjects once a week to ask if they were taking the tablets regularly and if there were any possible side effects. Participants were asked to complete a complication registry form and a daily medication registry form during the intervention. Both groups received counseling and medication under the supervision of a gynecologist. During the research, individuals were asked to contact the researcher in case of acute complications such as abnormal bleeding, digestive problems, and headache to be referred to the relevant specialist for treatment and necessary measures. During the study, the ethics supervisor of Guilan University of Medical Sciences supervised the study and sampling process three times.

Data collection tool and technique

In this double-blind randomized study, the Persian version of the FSFI questionnaire was used after measuring its validity and reliability.[34] The validity and reliability of this instrument were approved by Rosen *et al*.[35] In Iran, the validity of the Persian version of this questionnaire was reported by Mohammadi and Faghizadeh.[34] In the current study, the results of Cronbach's alpha for the domains of sexual desire, arousal, vaginal moisture, orgasm, satisfaction, and pain were, respectively, 0.86, 0.94, 0.91, 0.89, 0.97, and 0.92. The total sexual function score was 0.97, which was more than 0.7 and acceptable. FSFI is a 19-item questionnaire that measures female sexual function in six domains of sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. The overall score of an individual is the sum of her scores in each domain, which varies from 2 to 36. A higher score in each domain indicates more desirable sexual function. The pain domain in this scoring questionnaire is reversed and higher scores note better sexual condition and less pain. A higher score indicates better sexual function and a score of <26.55 indicates sexual dysfunction. This questionnaire was used for evaluation before and after the intervention.[35,36]

Demographic and obstetric characteristics included the age of the couple, woman's education, woman's employment status, monthly income of the family, gravidity (number of pregnancies), parity (number of deliveries), type of delivery, marriage duration, and number of intercourses during 1 month before the intervention and during the intervention.

The primary outcome of the present study was an increase in the mean score of sexual function in both groups and one of its secondary outcomes was determining the number of intercourses and satisfaction with the intervention.

Based on the mean score of female sexual function in the intervention and control groups with a confidence level of 95%, a test power of 90%, observed effect size of 0.7, and a 20% probability of sample volume drop, the required sample size in each group was 51 participants.[21] After receiving the necessary permissions, sampling was conducted by easy or accessible sampling method from women referring to the gynecological clinic of AL-Zahra hospital from February 2018 to December 2019.

The sample size was estimated based on the effective size of sexual function scores $(\mu_1 - \mu_2)/\sigma = 0.650$ of both intervention and control groups in the study by Akbarzadeh *et al*.[21] Considering 95% confidence interval,

90% test power, and 10% drop rate, at least 55 samples were needed in each group.

The obtained data from the samples were analyzed by SPSS version 21(SPSS Inc., Chicago, IL, USA). Kolmogorov–Smirnov test was used to investigate the normal distribution of quantitative data. *T*-test was employed to compare the quantitative demographic and obstetric variables with normal distribution between the two groups. Mann–Whitney U test was used for data with nonnormal distribution and ordinal variables. The qualitative variables were analyzed by the Chi-square test. The independent *t*-test was used to compare the mean score of sexual function before intervention for all domains. Analysis of variance (ANOVA) with repeated measurement of one factor was used for intragroup comparisons. To examine the differences between groups, a mixed model was employed. Before this analysis, its assumptions including the normal distribution of the response variable and the homogeneity of variances were evaluated. The significance level in this study was 0.05.

Ethical consideration

This randomized double-blind case–control trial was approved by the Ethics Committee of the faculties of pharmacy and nursing and midwifery, Shahid Beheshti University of Medical Sciences (Ethics Code IR.SBMU.PHARMACY.REC.1397.155 on November 5, 2018) and was registered at the Iranian Registry of Clinical Trials with the code IRCT20100503003860N36.

Results

In the present study, 205 women were interviewed and invited to the study, of which 93 women did not enter the study due to noncompliance with the inclusion criteria and unwillingness to participate. In sum, 112 women were eligible to enter the study. During the study, 10 women including four in the control group (fear of complication[1] and lack of follow-up [3]) and six in the intervention group (fear of complication [1], nausea [2], spotting [1], and no follow-up [2]) were excluded from the study. Finally, 51 women in each group were analyzed [Figure 1].

The personal, social, and obstetric characteristics of the women in the intervention and placebo groups are shown in Table 1. There was no significant difference between the two groups in terms of personal, social, and obstetric characteristics and they were homogeneous ($P \geq 0.05$) [Table 1].

There was no significant difference between the two groups of intervention and placebo before the intervention in terms of six domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain) and the mean score of overall sexual function ($P \geq 0.05$) and the two groups was homogeneous [Table 2].

ANOVA with repeated measurement was used for intragroup comparison. The results showed that the mean scores of all variables in the intervention group changed over time ($P < 0.001$). However, in the control group, only the mean score of pain changed over time ($P < 0.001$) and the time trend was not significant for other variables ($P > 0.05$) [Table 2 and Figures 2-8].

In the comparison of mean scores of sexual domains between the two groups, only the overall score of sexual function in the placebo group was 3.88 points lower than the intervention group over 16 weeks and a statistically significant difference was observed between the two groups [Table 3].

There was no difference between the two groups of intervention and placebo in terms of satisfaction with the drug over a period of time. The majority of subjects in the intervention group (82%) were almost satisfied in the 4th month.

Discussion

By examining the effect of time and type of intervention in the intervention group, it was revealed that mean scores of all sexual function domains (desire, arousal, lubrication, orgasm, satisfaction, pain, and the overall score of FSFI) had a significant increase over 16 weeks ($P < 0.05$). But in the placebo group, only the mean scores of pain and overall sexual function significantly increased ($P < 0.05$). Furthermore, the effect of the type of intervention was evaluated between the two groups and showed that the overall score of sexual function in the intervention group was higher than the placebo group during 16 weeks and a statistically significant difference was observed between the two groups ($P < 0.05$).

These intragroup changes can be explained by the effectiveness of counseling for both groups of intervention and placebo and the feeling of being treated because of the placebo effect.[37] As Bradford reported, more than 40% of subjects in the placebo group with hyperactive sexual problems showed improvement in desire and arousal after receiving a placebo.[38] However, to justify the lack of significant differences between the two groups in terms of scores of each sexual domain, it can be said that in order to improve sexual function as an issue that was influenced by various factors, comprehensive interventions considering the biopsychosocial model as well as attention to couples were required.[39,40] When the solution to the sexual problem was focused only on one couple or one treatment method, the result was probably unsatisfactory.[6]

Table 1: The comparison of personal, social, and obstetric characteristics between the two groups

Variable	Intervention group, *n* (%)	Placebo group, *n* (%)	*P*
Woman's age, years (mean±SD)	33.62±6.82	33.96±6.31	0.79*
Husband's age, years (mean±SD)	38.84±8.95	39.00±7.97	0.92*
Gravidity (mean±SD)	2.15±1.25	2.07±1.42	0.76**
Parity (mean±SD)	1.75±1.15	1.71±1.18	0.86**
Duration of marriage, years (mean±SD)	12.13±7.77	12.07±7.30	0.96*
BMI (mean±SD)	26.41±2.72	25.83±3.03	0.30*
Woman's education			
Middle school	17 (33.3)	21 (41.2)	0.47**
Diploma	27 (52.9)	12 (23.5)	
University	7 (13.7)	18 (35.5)	
Woman's occupation			
Housewife	40 (78.4)	36 (70.6)	0.36***
Employed	11 (21.6)	15 (29.4)	
Private room			
Yes	39 (76.5)	43 (84.3)	0.31***
No	12 (23.5)	8 (15.7)	
Income			
Enough	36 (70.6)	37 (72.5)	0.94**
Less than enough	10 (19.6)	7 (13.7)	
Above enough	5 (9.8)	7 (13.7)	
Type of delivery			
Vaginal	23 (45.1)	26 (51)	0.71***
C-section	21 (41.2)	17 (33.3)	
No delivery	7 (13.7)	8 (15.7)	
Number of intercourses during 1 month before the intervention (mean±SD)	5.19±2.18	4.94±2.02	0.54**

**T*-test, **Mann–Whitney test, ***Chi-Square test. SD=Standard deviation, BMI=Body mass index

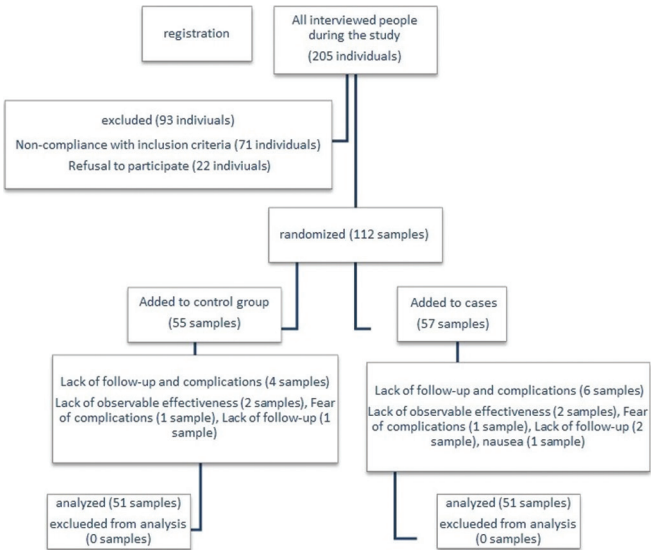

Figure 1: CONSORT flow diagram

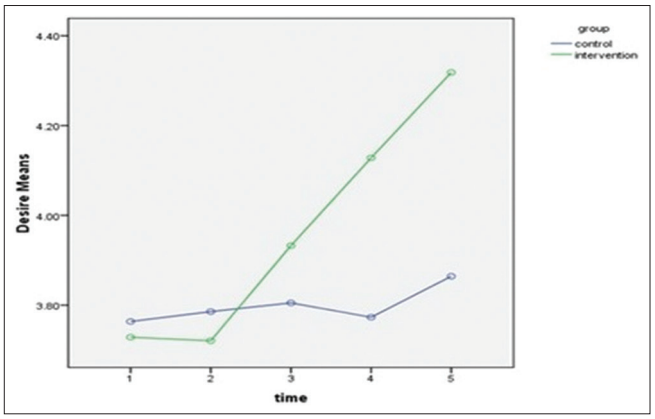

Figure 2: The comparison of the mean score of sexual desire for each measurement in the two groups of intervention and placebo in women of reproductive age

In the literature review of the effect of *V. agnus-castus* plant on sexual function, two studies were found which were conducted on postmenopausal women.[26,27] Furthermore, most studies on the effect of other medicinal plants on sexual function with a similar mechanism to the *V. agnus-castus* plant (phytoestrogen properties) were performed on postmenopausal women such as studies of Yoseefzadeh *et al*.[41] and Amiri-Pebdani *et al*.,[42] and less attention was paid to the women of reproductive age.

In a part of the present study which was a 1-month study, the results showed that after 1 month of intervention, there was no statistically significant difference between the two groups in terms of mean scores of overall sexual function and each domain ($P \geq 0.05$). Furthermore, only the orgasm score was improved in the comparison of intragroup scores ($P = 0.02$).[29] However, when consumption continued for 4 months, the effectiveness

Table 2: The comparison of mean scores of each domain of sexual function for two groups

Variable	Group	Time (0)	*P**	Time (4)	Time (8)	Time (12)	Time (16)	*P* within group**
Desire	Placebo	3.76±1.24	0.92	3.78±1.21	3.80±1.17	3.77±1.21	3.86±1.08	0.34
	Intervention	3.78±1.26		3.72±1.31	3.93±1.17	4.12±1.18	4.31±0.99	0.001
Arousal	Placebo	4.08±1.10	0.26	3.93±1.06	3.97±1.05	3.93±1.06	3.98±1.03	0.52
	Intervention	3.82±1.24		3.80±1.20	3.98±1.11	4.10±1.09	4.17±1.09	0.001
Lubrication	Placebo	4.44±1.00	0.80	4.45±0.88	4.48±0.85	4.46±0.86	4.49±0.90	0.83
	Intervention	4.48±0.94		4.48±0.88	4.61±0.85	4.72±0.79	4.76±0.80	0.001
Orgasm	Placebo	3.22±0.73	0.19	3.19±0.69	3.23±0.68	3.29±0.70	3.27±0.69	0.20
	Intervention	3.01±0.85		2.99±0.91	3.16±0.70	3.23±0.66	3.31±0.65	0.001
Satisfaction	Placebo	4.69±1.18	0.56	4.78±1.16	4.79±1.13	4.83±1.02	4.85±1.03	0.61
	Intervention	4.55±1.25		4.61±1.08	4.77±0.99	4.86±0.89	4.99±0.79	0.001
Pain	Placebo	4.44±1.26	0.76	4.45±1.26	4.53±1.27	4.64±1.24	4.74±1.17	0.001
	Intervention	4.36±1.35		4.45±1.34	4.70±1.25	4.84±1.16	4.95±1.09	0.001
The mean score of FSFI	Placebo	24.66±5.76	0.60	24.61±5.56	24.83±5.43	24.88±5.35	25.20±5.18	0.10
	Intervention	24.04±6.20		24.06±6.06	25.17±5.38	25.89±5.11	26.52±4.70	0.001

*Independent *t*-test, **One-way repeated measures ANOVA (within comparisons). ANOVA=Analysis of variance, FSFI=Female sexual function index

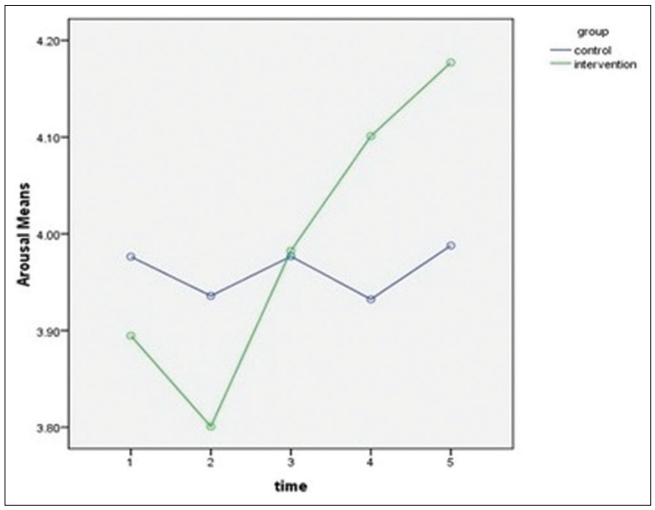

Figure 3: The comparison of the mean score of arousal for each measurement in the two groups of intervention and placebo in women of reproductive age

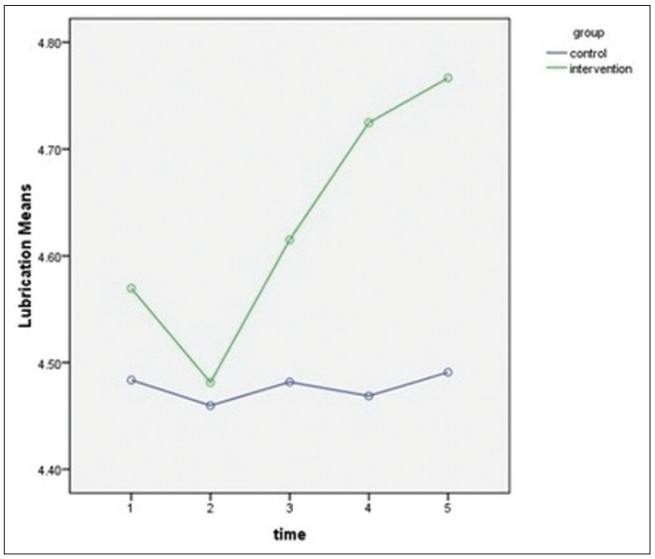

Figure 4: The comparison of the mean score of lubrication for each measurement in the two groups of intervention and placebo in women of reproductive age

of the intervention was observed on the overall score of sexual function.

Consistent with the results of the present study, the results of the study of Mirzaii-Najmabdi on perimenopause and postmenopausal women after receiving 16 weeks of *V. agnus-castus* or placebo showed that the sexual function significantly improved in the intervention group.[26] The drug form, dose, frequency of use, and inclusion criteria were not mentioned in their study. However, because of the limited information of their method and base on the existing knowledge, the improvement of sexual function in this study can be due to the effectiveness of phytoestrogens on vaginal atrophy, vasomotor symptoms, and the synergistic effect of phytoestrogens on increasing vaginal lubrication and subsequently the reduction of mental and physical problems in postmenopausal women.[43] As seen in a similar study, by resolving the problems of insomnia and hot flashes, the sexual function of postmenopausal women spontaneously improved due to the fixed underlying problems,[44] but this mechanism did not apply in women of reproductive age.

In the present study, the mean score of pain increased over time in both groups, and a significant effect was seen. Considering the scoring method of the pain domain in the questionnaire, higher pain scores meant less pain. The results of the study by Luks *et al*. also showed that after 3 months of local and inhalant consumption of *V. agnus-castus* perimenopause and postmenopause, the vaginal tone, firmness, and lubrication were increased, resulting in easier intercourse and reduced pain.[27]

Although the exact mechanism of phytoestrogens has not been established, it seems that by affecting the hypothalamic–pituitary axis, flavonoid compounds reduce the release of FSH and prolactin, modulate the

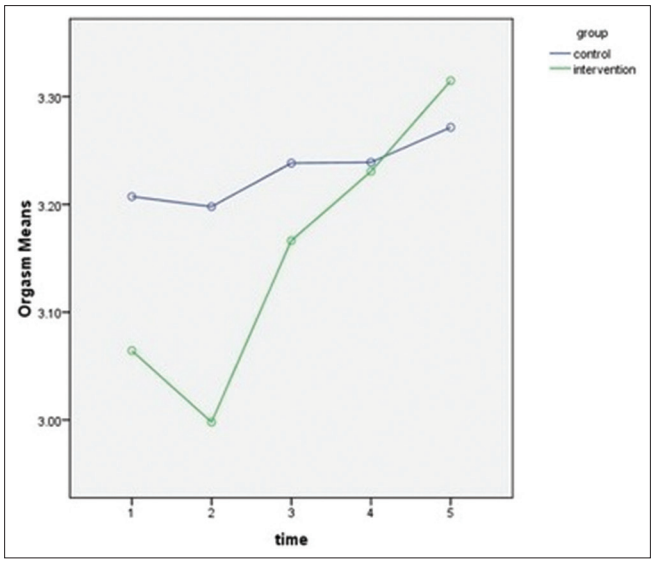

Figure 5: The comparison of the mean score of orgasm for each measurement in the two groups of intervention and placebo in women of reproductive age

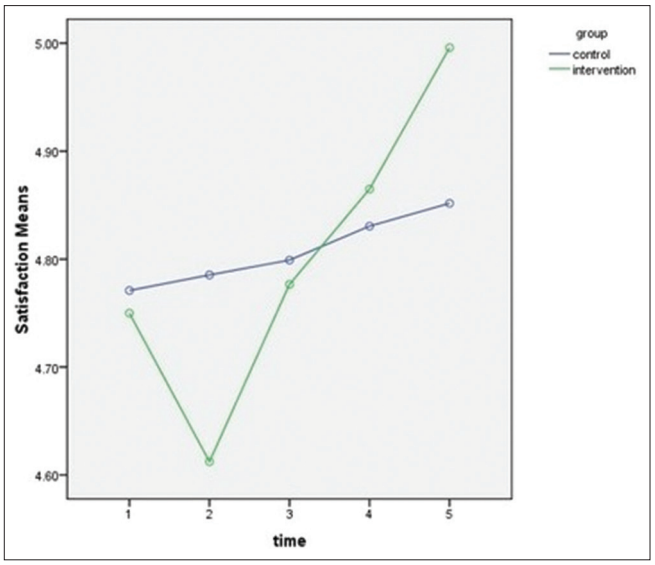

Figure 6: The comparison of the mean score of satisfaction for each measurement in the two groups of intervention and placebo in women of reproductive age

Table 3: The mixed model for comparing sexual function domains and overall score between two groups of intervention and placebo

Variable	Estimate	Df	*T*	*P*
FSFI	−3.88	112.22	−3.95	0.001
Desire	−0.24	110.83	−1.06	0.29
Arousal	−0.21	109.20	−1.11	0.27
Lubrication	0.03	105.86	0.23	0.81
Orgasm	−0.30	109.03	−1.77	0.07
Satisfaction	0.01	109.12	0.08	0.93
Pain	−0.44	107.83	−1.96	0.05

FSFI=Female sexual function index

release of LH from the pituitary gland, and consequently increase total estrogen and progesterone levels and decrease prolactin.[45,46] The dopaminergic effect of *V. agnus-castus* as an effective neurotransmitter on the sexual response can improve sexual function and long-term use of *V. agnus-castus* with stabilization of this condition can be effective.[32,33]

The reported side effects of *V. agnus-castus* are mild, recurrent, and reversible. In <2% of consumers, some symptoms such as digestion problems, pruritus, fatigue, headache, dry mouth, tachycardia, nausea, and vomiting were reported.[47] The results of the present study also showed that *V. agnus-castus* was well-tolerated. This was in line with the results of other studies on the *V. agnus-castus* that have been performed on gynecological diseases. Considering that this plant is widely used in gynecology, this finding also confirmed that this plant is safe for women.[10-12,48]

One of the strengths of this study was the administration of *V. agnus-castus* for 4 months, which is the recommended duration of administration for phytoestrogen plants. Furthermore, since the first line of treatment in women with sexual dysfunction is counseling and follow-up of patients, at the beginning of the study, both groups received the same training and they were referred to the relevant specialist if the problem persisted at the end of the intervention.

Based on the results of the present study, for alternative therapies, similar studies must be conducted in women of reproductive age to obtain sufficient evidence for the use of *V. agnus-castus*. However, the first line of treatment in the improvement and treatment of sexual dysfunction in women includes education and counseling,[39] and a proper sexual function in women is affected by various factors such as pleasant sexual experience, sexual skills, quality of the interpersonal and emotional relationship of couples and the authors could not have a completely biological point of view about sexual issues. Therefore, during treatment, efforts should be made to improve the physical and mental health of women and also the relationship between couples along with the alternative therapies.[39,49,50] Improvement and treatment of sexual dysfunction require multidimensional physical-psychological, social, and spiritual interventions.[6,49] Therefore, although the results showed an improvement in sexual function during 4 months of the study, it is anticipated that for continued effectiveness, multidimensional therapies must be designed and implemented in conjunction with such alternative therapies.

Limitation and recommendation

Limitations of the present study included the shame of raising sexual issues as well as the inability to express sexual problems was effective in how the women in the

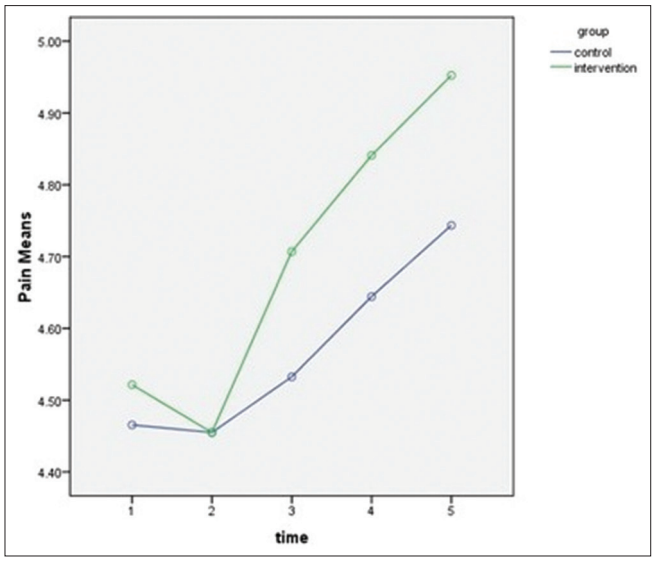

Figure 7: The comparison of the mean score of pain for each measurement in the two groups of intervention and placebo in women of reproductive age

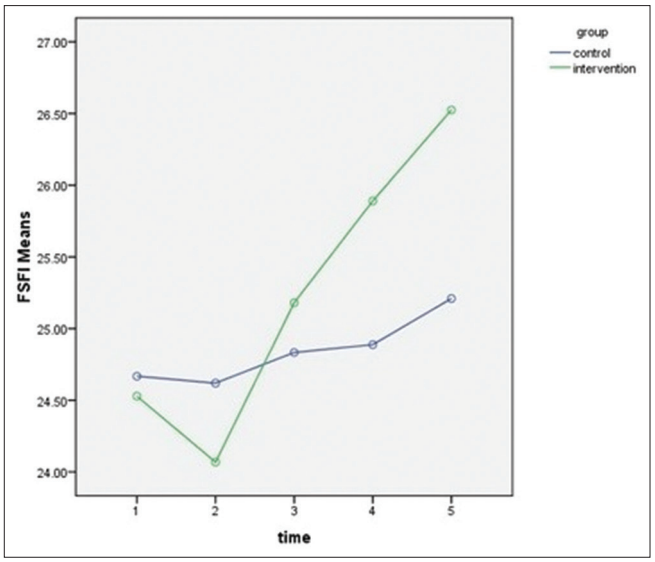

Figure 8: The comparison of the mean score of FSFI for each measurement in the two groups of intervention and placebo in women of reproductive age

study responded. By providing a private and intimate environment, the authors tried to reduce the effect of this problem. One of the most important limitations of the present study was the lack of similar studies to determine the drug dose and the duration of the effective intervention without complications. Therefore, in order to observe the safe dose, this drug dose was selected based on the studies of the *V. agnus-castus* on sexual applications of gynecological diseases, and the duration of the study was selected to be 16 weeks based on the recommendations of traditional medicine studies.

Further studies with a larger sample size are needed to be performed. Its prescription in the clinic should be assessed based on the results of the current study and larger studies.

Conclusion

In the present study, the results showed that scores of the intervention group increased over time in all domains of sexual desire, arousal, lubrication, orgasm, satisfaction, and pain, and the overall score of female sexual function significantly increased. On the other hand, in the placebo group, the mean score of the pain and the overall score of female sexual function was statistically significantly increased. In the study of the effect of the intervention type between the two groups in terms of the sexual domains, the overall score of female sexual function in the intervention group was higher than the placebo group during 16 weeks and a statistically significant difference was observed between the two groups. *V. agnus-castus* was more effective than placebo in improving sexual dysfunction.

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Conflicts of interest

There are no conflicts of interest.

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