



The Effect of Flixweed-Honey Vaginal Product on Cervicitis: a Clinical Trial

Razieh Nabimeybodi¹, Azam Meyari¹, Marzieh Vahiddastjerdi², Homa Hajimehdipoor³, Erfan Ghasemi⁴, Sodabeh Bioos⁵, Mojgan Tansaz^{1*}

¹Department of Traditional Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

²Department of Obstetrics and Gynecology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

³Traditional Medicine and Materia Medica Research Center and Department of Traditional Pharmacy, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁴Department of Biostatistics, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁵Department of Traditional Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Background and objectives: Cervicitis is a common and recurrent gynecologic disease which is usually resistant to treatments. This study was conducted to investigate the effect of Iranian traditional medicine (ITM) product, flixweed- honey, on cervicitis. **Methods:** A quasi-experimental study was conducted as a clinical trial before and after the intervention at the School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. The married women referring to the clinic aged 17-55 years with a diagnosis of cervicitis who were not pregnant and breastfeeding, without any history of cervical polyps and pelvic surgery, and non-concurrent use of herbal or other chemical medicines were included in the study. During this research, 97 patients were treated through the vaginal use of flixweed- honey for two weeks. One week after the treatment, clinical symptoms were examined. **Results:** Among 97 patients who were evaluated in this study, 72 returned for follow-up. All subjective and objective parameters including vaginal irritation, itching, discharge, bleeding and pain after coitus, tenderness, and cervical wound size and friability improved significantly in comparison to the time before taking the medication. There was no treatment; five patients (0.69%) who took the medication had vulvovaginal itching that was resolved after 3-4 days.

Conclusions: Vaginal product of flixweed- honey could be used in the treatment of clinical symptoms of cervicitis regardless of the reason causing cervicitis, without causing severe or serious side effects.

Keywords: cervicitis; *Descurainia sophia*; flixweed, honey; Iranian traditional medicine; Persian medicine

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Introduction

Cervicitis is one of the most common female genital tract infections during sexual activity with an estimated prevalence of 30-45% [1,2]. According to the available guidelines, it is diagnosed by purulent or mucopurulent discharge or bleeding upon swabbing the cervix with a

cotton swab [3]. Untreated cervicitis may lead to complications such as salpingitis, pelvic inflammatory disease, mucosal damage and adhesion, ectopic pregnancy, and infertility. Therefore, treatment of cervicitis not only resolves disease symptoms, but is also considered

* Corresponding author: tansaz_mojgan@yahoo.com

as a preventive measure for infertility [4]. There is a large body of evidence that *Mycoplasma genitalium* and *Chlamydia trachomatis* are the leading pathogenic factors causing purulent cervicitis and endometritis in women [5,6]. Doxycycline and azithromycin are the medicines used most frequently [7]. Recurrent infection is seen in 18-34% of cases with chlamydial infection [8]; moreover, drug-resistant cases have been reported to be about 16-33% in numerous studies [9-12]. Twin has reported a drug resistance rate of about 55% due to the development of mutants resistant to treatment and predicted an increasing trend [13]. In addition, in chronic cases, a course of antibiotic treatment is given like acute cervicitis. If there is no improvement after 2-3 months, surgical treatment is indicated [1]. Surgery is performed as cryotherapy, laser therapy, and electrocautery. Each one of these surgical procedures has certain side effects such as cervical stenosis [1,14].

Nowadays, the use of complementary and alternative medicine is recommended by the medical community and the World Health Organization for numerous occasions such as genital infections, because these methods are less invasive, safe, effective, and suitable [15]. Iranian Traditional Medicine (ITM), Persian medicine, is one of the richest and the oldest schools in this regard, the medical opinions of the famous Iranian philosopher and physician-Avicenna "*Ibn-e-Sina*" - were taught in European medical schools for many years [16]. The people of Iran and neighboring countries have benefited from clinical experiences based on the principles of ITM for centuries [16]. Nowadays, many drugs with natural sources have been retrieved from traditional medical systems. In ITM, plants have been used to combat various diseases and pathological conditions [17]. According to its signs and symptoms, "*Qorhah-e-Rahem*" could be considered equivalent to cervicitis in conventional medicine [18,19]. Different topical and non-topical medications have been recommended for the treatment of "*Qorhah-e-Rahem*". One of which is flixweed and honey product [19-21].

Descurainia sophia (L.) Schur with the common name of flixweed belongs to Brassicaceae family. The useful part of the plant is the seed [22-24]. In folk medicine of Iran and China, *Descurainia*

sophia has laxative and antipyretic properties, it soothes inflammation in diseases like hives, measles, chicken pox, and pharyngitis [22,23,25, 26] and improves cough, asthma, edema, and diuresis [27]. Moreover, *in vitro* anti-cancer effects of *Descurainia sophia* on small cell carcinoma of the lung [28,29], colon cancer [30], and glioma [31] have been proved. It has also healing effect on wounds and injuries [23] and bedsores [22], removed uterine discharges [23], facilitated childbirth [32], and has demonstrated inhibitory effects on the growth of bacteria such as *Escherichia coli* and *staphylococcus* [26].

In ITM, honey is believed to be a healing substance removing moisture and harmful waste, and its topical impact on wound healing has been reported in numerous studies [33-35]. In addition, it is effective in the treatment of vaginal candidiasis without affecting the normal vaginal flora [36,37].

Despite all this knowledge, no documented study has evaluated the effect of flixweed-honey on cervicitis. This study was conducted to investigate the effect of the vaginal product of flixweed-honey on cervicitis.

Material and Methods

Drug preparation

In order to prepare the drug, *Descurainia sophia* seeds were purchased from a local market, Tehran and identified at the Herbarium of Traditional Medicine and Materia Medica Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran (No. 451).

The quality control tests were carried out on flixweed according to Iranian Herbal Pharmacopoeia. According to viewpoints of experts in traditional medicine, in order to prepare the product, ground *Descurainia sophia* was mixed with defoamed honey.

To prepare defoamed honey, one unit of honey and three units of water were mixed and heated until the added water was evaporated. Meanwhile, the foam on the honey was removed during heating [38]. Then, honey was mixed with plant seeds, which were ground and passed through sieve 20, with the ratio of 1:2.2. Finally it was packed in 50 g tubes.

Participants

This quasi-experimental clinical trial was conducted before and after the intervention. The

participants in the study were 72 married women aged 17-55 years of age who had admitted to Arash Women's Hospital, Tehran with complaints about cervicitis symptoms including vaginal itching, mucopurulent discharge, dysuria and urinary frequency, subabdominal pain or dyspareunia and postcoital bleeding.

After the diagnosis of cervicitis by the obstetrician, pregnant, breastfeeding women or women with history of pelvic surgery, cervical polyp, any other chronic disease related to the cervix, previous pap smear with abnormal cells and concurrent use of herbal or chemical medicines were excluded from the beginning of study. Exclusion criteria's during the study were pap smear results with abnormal cells, patients with possible side effects, patients who required other interventions and had surgery and patients who decided to leave the study with a personal request. Informed consent was obtained from all participants.

Study design

The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (license No. IR.SBMU.RAM.REC.1394.165) and was recorded in the Iranian Registry of Clinical Trials (No. IRCT2015110824951N1). The project location was the Gynecology Clinic of Arash Women's Hospital, Tehran.

After selecting eligible subjects, the purpose of the study and its stages were explained to the participants and informed consent was obtained from them. Then, a questionnaire containing questions on personal and physical characteristics and medical interventions was completed for each participants and vaginal examination was conducted by the researcher.

The results of the examination in terms of the presence of mucopurulent discharge on cervix and speculum, cervical erythema and friability, uterine tenderness and cervical motion tenderness were recorded in researcher- designed forms. If the patient had not taken the Pap smear test during the last year, a sample was taken. After a final diagnosis and the symptoms being recorded, two tubes of the prepared product along with brochures and forms of drug side effects were given to the patients. The patients were treated by the ITM product, flixweed-honey, for two weeks. They were advised to take one applicator of the drug every night. Two weeks after completing

the treatment, the patients were re-examined for response to treatment in the third week. In case of lack of recovery, the patients received conventional treatment prescribed by the gynecologist. The time to take the drug was considered at least two weeks before the menstruation and the patients were advised to come for the next visit in the third week in case of lack of menstruation. In case of menstruation, the appointment was postponed to the nearest time after it was finished. During the treatment process, a questionnaire containing possible side effects was completed by the patient.

In order to assess the effect of the product on cervicitis clinical symptoms, the symptoms of discharge, itching, irritation, pain during intercourse and post intercourse bleeding were asked from the patients on a scale of 0-10 before and after taking the drug according to visual analogue scale. The scores 0 and 10 were defined as for discharge, no complaint about discharge and daily use of pad; for itching, as no itching and itching disturbing daily activities and sleep; for irritation, as no irritation and irritation disrupting daily activities and sleep; for post intercourse bleeding, as no bleeding and severe bleeding requiring the use of pads, and for pain during intercourse, as no pain and the pain disrupting daily activities and sleep. By asking the patients about these symptoms, the severity of each was determined and graded based on the following points:

Grade Zero: no discharge, irritation, itching and pain during intercourse or post intercourse bleeding

Grade 1: A score of 1-3 for each one of the symptoms of discharge, irritation, itching, pain during intercourse and post intercourse bleeding

Grade 2: A score of 4-6 for each one of the symptoms of discharge, irritation, itching, pain during intercourse, and post intercourse bleeding

Grade 3: A score of 7-10 for of each one of the symptoms of discharge, irritation, itching, pain during intercourse, and post intercourse bleeding

Moreover, the signs of friability were specified as the presence or absence of friability, tenderness or lack of tenderness, tenderness on cervix palpation, and cervical motion tenderness.

The size and depth of the wound were classified based on the gynecologist's diagnosis by visual examination and the locations of the scars were marked on the following shapes before and after

the treatment that were designed by the research team (figure 1):

Grade Zero: lack of scar

Grade 1: Small wounds (about 1×1)

Grade 2: moderate wounds (about 2×2)

Grade 3: large wounds (about 3×3)

Clinical response to the product was categorized based on the following criteria:

Cure: Elimination of all the clinical signs and symptoms

Improvement: Elimination or reduction of the severity of the clinical signs and symptoms

Failure: No change or worsening of previous clinical symptoms or development of new clinical symptoms.

Statistical analysis

After data collection, SPSS software version 19 was used to analyze the data. In this study, central tendency and dispersion, rate, percentage, and frequency tables and graphs were used to describe the collected data. Quantitative variables were described by mean and standard deviation and qualitative variables were described through percentage. In order to compare the quantitative variables before and after intervention, paired *t-test* was used if the data were distributed normally. Wilcoxon *t-test* was used if the data distribution was not normal. The Kolmogorov-Smirnov test was used to assess data normality. The chi-square was applied to compare qualitative variables.

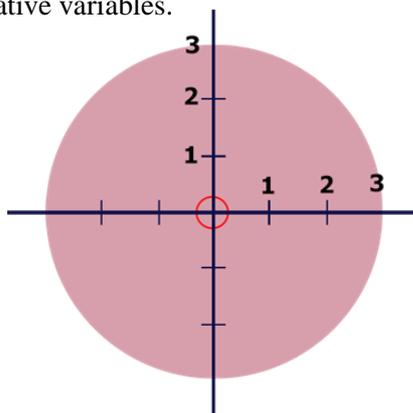


Figure 1. Range of cervical wound before the treatment

Results and Discussion

As shown in figure 2, from 115 patients who were referred to the clinic, 15 were excluded due to lack of inclusion criteria and 3 due to pregnancy. Therefore, 97 patients were included, of whom 25 patients did not return for the final

visit. Hence, 72 patients were enrolled in the study and their data were collected.

Participants in the study were 21-46 years of age with a mean age of 30.24 ± 4.7 years. To be more specific, 51.5% of the participants were 21-30 years of age, 45.8% were 31-40 years of age, and only 2.7% were over the age of 41. All of the participants were married and 25% suffered from infertility. Prenatal care (16.67%) and infertility (15.28%) were the leading causes of referral. Fifty-four patients (75%) had inflammatory changes in the Pap smear and in spite of referring two patients for colposcopy, no malignant changes were observed. Other personal characteristics and complaints of the participants have been displayed in table 1. Sixty-nine subjects (95.82%) in the study had discharge, 38 (52.77%) had irritation, 32 subjects (55.55%) had itching, 45 subjects (62.5%) experienced pain during intercourse, and 15 subjects (20.83%) had post intercourse bleeding. After taking the product, all the mentioned symptoms in the history were cured (22 patient, *i.e.* 30.5%) or improved significantly (50 patients, *i.e.* 69.5%), (table 2).

The results of the examination showed that all participants had shown some degrees of cervical ulcer, 60 of them (83.33%) had cervical motion tenderness in the examination and 44 participants (61.11%) had bleeding after the swab test. After intervention, 25 participants (34.72%) were cured completely and the rest showed marked improvement (tables 3, 4). No cases of treatment failure were observed in terms of signs and symptoms. Five patients (0.69%) developed vulvovaginal itching that was severe in one case and mild in four cases. It disappeared after 3-4 days. No other complications were reported.

The present study showed that after two weeks of vaginal use of Flixweed- honey by women with cervicitis, the symptoms decreased significantly one week after the treatment; all patients were cured or showed improvement without treatment failure. The side effect of this product, vulvovaginal itching, occurred in less than 1% of the cases and no other complications were reported by the participants.

Descurainia Sophia belongs to Brassicaceae family. Although there is no evidence about effectiveness of this plant on gynecological infections, some antimicrobial properties of *Descurainia Sophia* have been evaluated and approved in different studies.

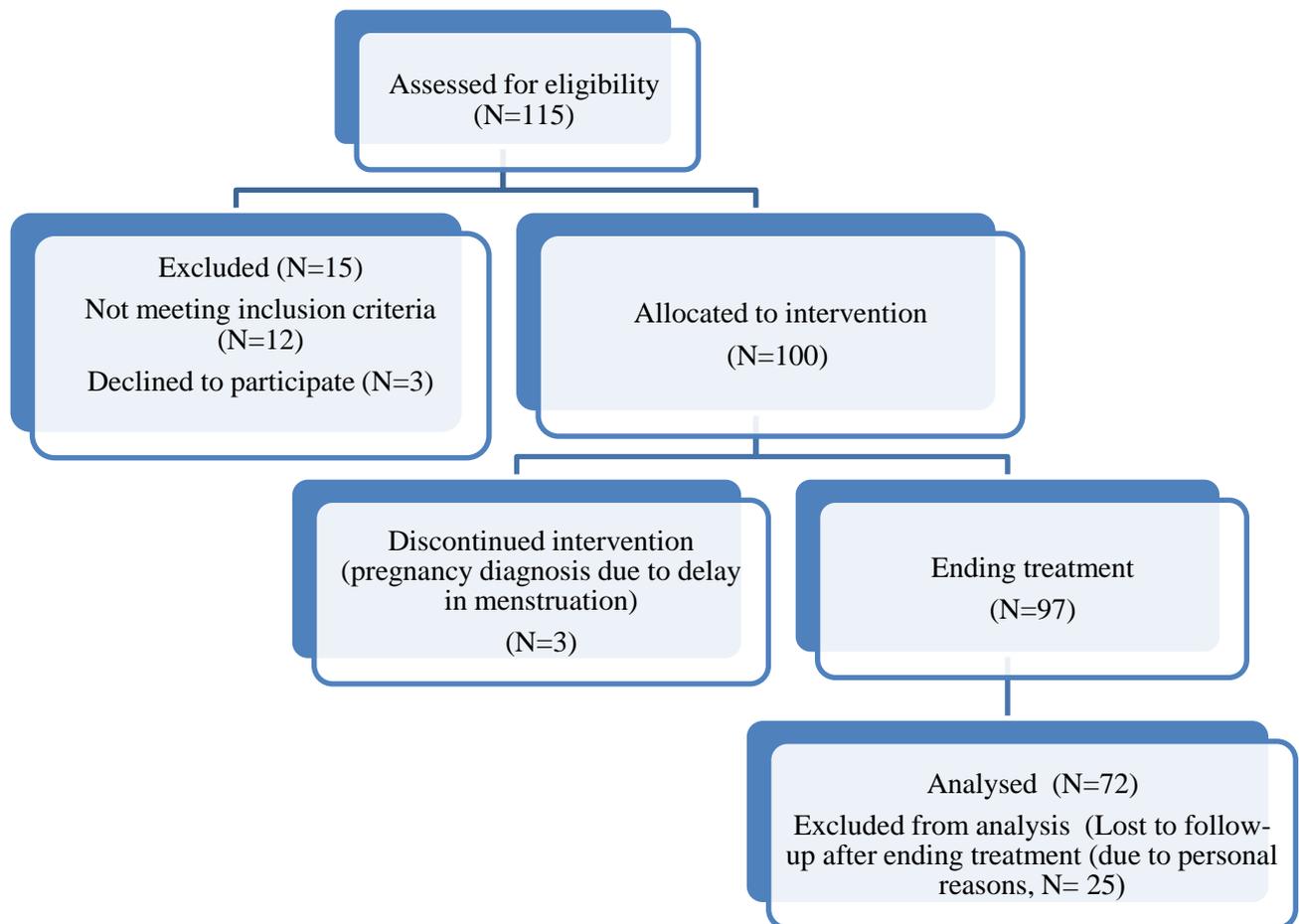


Figure 2. Study flowchart

Ethanol extract of plant has been able to inhibit the growth of *Streptococcus pyogenes* in the culture medium [39]. Allyl isothiocyanate reported from this family, has been effective on *salmonella Montevideo*, certain strains of *E.coli* and *listeria monocytogenes*. Antibacterial effect of 6-(methylsulfinyl) hexyl isothiocyanate on *E.coli* and *Staphylococcus aureus* has been also identified [26]. The antioxidant properties due to the phenolic components [40], anti-inflammatory properties due to flavonoids [29] have been also confirmed. Furthermore, several clinical trials have shown the antibacterial and antifungal properties of honey, which is consistent with our finding. For example, Fazel *et al.* conducted a randomized controlled trial (RCT) to compare the effectiveness of honey and clotrimazole on *Candida vaginitis*. The results revealed a statically significant improvement in users of

honey compared to clotrimazole [36]. Tabatabaee Chehr *et al.* found that although there was no significant difference in the treatment of *Candida vaginitis* between the vaginal use of honey wax and vaginal clotrimazole, the recurrence of clinical symptoms was significantly lower in the group that used honey wax [41]. Banaeian *et al.* also reported that despite the *in vitro* effect of honey on *Candida*, it was ineffective on the normal vaginal flora (lactobacilli) [37]. Also the studies conducted by Al-Waili, Dunford, and Biglari showed the effect of honey on the healing of surgical scar wounds, leg wounds, and wounds resulting from spinal cord injury [33-35], which are in concord with our findings. The results of this study are comparable with other studies that investigated the effect of another herbal medicine drugs on cervicitis.

Table 1. Demographic characteristics of participants

Demographic characteristic		frequency	Percentage
Education	Able to read and write	3	4.17%
	High school	14	19.44%
	university	55	76.39%
Socioeconomic status	Low	3	4.17%
	Average	67	93.06%
	High	2	2.78%
Gynecology data			
Number of pregnancies	zero	30	41.67%
	1 or 2	21	29.17%
	3 and more	21	29.17%
Abortion	-	6	8.34%
Infertility	-	18	25%
Number of sexual partners	Zero	0	0
	1	72	100%
	2 and more	0	0
Past medical history of infections	Vaginitis	65	90%
	Cervicitis	42	58%
Treatment	No treatment or unaware of treatment	22	30.55%
	Drug treatment	50	69.45%
	Cervix freezing	10	13.89%
	No cervix freezing	62	86.11%
Method of contraception	No contraception	17	23.61%
	Condoms	20	27.78%
	IUD	0	0
	Other	35	48.61%
Cause of referral	Preconception care	12	16.67%
	Discharge or irritation and itching	12	16.67%
	Infertility	11	15.28%
	Wound	8	11.11%
	Polycystic ovary syndrome	6	8.33%
	Periodic examinations	6	8.33%
	Spotting	4	5.55%
	Recurrent spontaneous abortion	2	2.78%
	Other	9	12.5%
	Pap smear result	normal	18
Mild inflammation		28	38.89%
Moderate inflammation		21	29.17%
Severe inflammation		5	6.94%

Table 2. The rate of symptoms before and after intervention*

parameter	Before intervention		After intervention		p value
	Mean	SD	Mean	SD	
Irritation	2.72	2.97	0.58	0.98	<0.001
Itching	2.77	2.90	0.54	0.91	<0.001
Discharge	5.84	2.29	1.34	1.53	<0.001
Pain after intercourse	3.63	3.18	1.22	1.57	<0.001
Post intercourse bleeding	0.81	1.81	0.15	0.59	0.001

*using paired samples statistics test

Table 3. The rate of sings & examination before and after intervention*

Parameter	Before intervention	After intervention	p value
Fragility in contact with swab*	59.7%	2.7%	0.001
Tenderness**	81.94% 47.22% in touching 34.72% in motion	2.7% 2.7% in touching 0 in motion	0.001
Mean of Wound size***	2.00±0.84	0.58±0.72	<0.001
Mean of Wound depth***	1.78±0.89	0.41±0.57	<0.001

*using McNemar's test; p=0.001, considered strongly significant

**using symmetry test; p=0.001, considered strongly significant

***using Paired Samples Statistics

Table 4. The effect of flixweed-honey product on cervicitis

parameters	cure	Improvement	failure
Subjective	30.5%	69.5%	0
objective	34.72%	65.28%	0

Ranjana *et al.* used V-Gel plant combination for the topical treatment of cervicitis and vaginitis. The clinical symptoms of the disease were resolved by 60% after two weeks. The compounds used in this herbal product included *Berberis aristata*, *Vitex negundo* leaves, *Lawsonia* (Henna), *Elettaria cardamomum*, *Cedrous deodara* oil, oil of *Tajetes erectus* leaves, *Rosa centifolia* flowers, *Boerhaavia diffusa*, *Anthrums sowa* fruit, *Nelumbonucifera* (sacred lotus), which have anti-inflammatory properties [42]. Also a study conducted by Hashemi *et al.* showed that oral use of the herbal compound of Safoof Mundi (*Sphaeranthus indicus* Linn) along with topical use of Henna cream (a combination of Henna (*Lawsonia inermis*) and *Plumbiodidum*) for 9 weeks led to a significant improvement in cervicitis [43]. In another study carried out by Swati Mohite *et al.* cervix inflammation and other clinical symptoms of cervicitis improved significantly following the oral use of Dashamoolarishta-a well-known polyherbal formulation in *Ayurveda* that consisted of root extracts of various plants such as *Dashamoola* viz. *Aegle marmelos*, *Premna integrifolia*, *Desmodium gangeticum*, *Oroxylum indicum* and used for different ailments especially inflammation -for 90 days [44]. Tabassum Latafat *et al.* also reported about the healing effect of an ITM herbal combination

called Marham Dakhelion on chronic cervicitis and cervical erosion in a population of 100 people was 80% during three weeks [45].

The herbal products in the above studies composed of several plants, but in our study only honey and flaxseed were used giving similar effect; so, this product could be prepared more easily. The duration of treatment by herbal remedies in the above studies, except for the study conducted by Ranjani, were more than two weeks and a lower response rate were observed as compared to our study.

The present study showed noticeable improvement and cure of flixweed-honey vaginal product on cervicitis without important complication compared with conventional therapies that have mainly gastrointestinal side effects [7]. Also inexpensive and more available compounds in comparison with common drugs are considerable. However, this research has some limitations. Since this study was an open study without any control group, especially in subjective parameters, future studies should focus on the control groups to omit the bias of observer and participants. Also drug resistance, relapse of disease and microbial inclusion were not evaluated. Further studies to investigate the disease recurrence as well as microbial resistance to this product are suggested to be conducted.

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Author contributions

Razieh Nabimeybodi was the main study investigator and conceived study conception and design. Azam Meyari contributed to write the manuscript. Marzieh Vahiddastjerdi was one of the thesis's supervisors and contributed to the collect the data. Homa Hajimehdipoor participated in the preparation of product and revised the manuscript. Erfan Ghasemi participated in the data analysis and interpretation. Soodabeh Bioos contributed to collect the data.

Mojgan Tansaz was one of the thesis's supervisors, developed the theory and critically revised the manuscript.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the content of the paper.

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Abbreviations

ITM: Iranian traditional medicine