Investigation of the role of herbal medicine, acupressure, and acupuncture in the menopausal symptoms: An evidence-based systematic review study

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ABSTRACT

Background: Menopause is an important physiological phenomenon in women's lives. Women's concern about taking the hormone treatment to ease menopausal symptoms is increasing. Over the past decade, the use of complementary and alternative medicine for the treatment of menopausal problems instead of hormone therapy has increased. **Objective:** This study aimed to investigate the role of herbal medicine, acupressure, and acupuncture in the menopausal symptoms. Methods: Data source: related articles were searched from internal scientific databases and external databases of "Web of Scopus, Cochrane, PubMed, Science Direct, Ovid, and Google scholar." Study Eligibility Criteria: The keywords such as menopause, menopausal symptoms, complementary menopausal medicine, acupuncture in menopause, herbal medicine in menopause, and acupuncture in menopause were searched in the studies from 1987 to 2019. Exclusion criteria were inadequate information in the study, lack of access to full-text articles, animal studies, and reports. At the end of the search, 145 articles out of a total of 400 articles were reviewed. Results: In various studies, different herbs such as licorice, valerian, soy, sage, ginseng, etc., were used to improve menopausal symptoms. In addition, acupuncture and acupressure were used to reduce menopausal symptoms. Conclusion: The efficacy and use of complementary and alternative medicine, along with other classical medicine care, can be a new model for improving menopausal symptoms in women. It is recommended that further clinical and review studies be conducted to develop complementary and alternative medicine.

Keywords: Acupressure and acupuncture in the menopausal symptoms, herbal medicine

Introduction

Menopause is an important physiological phenomenon in women's lives.^[1] The average age of menopause is normally 50 years. [2] The population of postmenopausal women is rising

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and by 2030, this population will reach one billion two hundred thousand people with an annual increase of 47 million new cases per year.[3] The most obvious symptom of this phenomenon is complete menstrual cessation for one year.[1] This period is accompanied by the gradual loss of reproductive activity and the transition to a new biological status. [4] Although menopause is a natural stage of life, many women experience many problems before and after it. [5,6] Women are often at the peak of their professional lives when they are at menopause. [5] Therefore, managing this stage of life is very important. [7] Menopause has

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many symptoms including vasomotor symptoms, psychological symptoms, musculoskeletal pain, osteoporosis, sleep problems, and genitourinary symptoms. [8,9] Vasomotor symptoms affect 80% of menopausal women.[10-12] Vaginal symptoms are a problem in one-third of postmenopausal women and persist for many years and sometimes begin several years after menopause. [13] About one-third of women experience sleep disorders during menopausal transition and 10% have symptoms of depression.^[14] Hormone therapy is the most effective treatment for menopausal symptoms. [15] There is strong evidence of an increased risk of hyperplasia and endometrial cancer, breast and ovarian cancer, gall bladder cancer, thromboembolism, heart disease, stroke, pulmonary embolism, and dementia following hormone replacement therapy. [16-19] In addition, 10% of women are prohibited from taking estrogen because of some diseases and hormone therapy is used in less than 20% of cases. [20] There is a growing concern among women about the use of these methods which is one of the reasons for women's lack of tendency for hormone therapy and their tendency to use nonpharmacological methods.^[21] Over the past decade, the use of complementary and alternative medicine (CAM) to treat women's problems, including menopausal problems, has increased. [22] One out of every 4 women uses complementary and nonpharmacological treatments to relieve menopausal symptoms. [23] The World Health Organization has suggested complementary and alternative medicine as ways to improve menopausal symptoms and increase the sense of well-being in women. [24] Complementary medicines used in menopause include mind-body practices (such as hypnosis, meditation, aromatherapy), natural products (such as herbs, vitamins, dietary supplements, and minerals), traditional Chinese medicine, reflexology, acupuncture, acupressure, and homeopathy. [3,25] The aim of this study was to investigate the effects of herbal medicine, acupressure, and acupuncture on menopause symptoms.

Methods

Evaluation protocol

We reviewed published articles from 1987 to 2019 on the impact of herbal therapy, acupuncture, and acupressure on menopausal symptoms based on the PRISMA flow diagram for better evaluation.^[26]

Information sources

In this review study, related articles were searched from internal scientific databases and external databases of "Web of Scopus, Cochrane, PubMed, Science Direct, EBSCO, Medline, Ovid, and Google scholar."

Eligibility criteria

The main search terms included the keywords of menopausal symptoms, complementary medicine, acupuncture, herbal therapy, and acupressure in menopause in studies from 1987 to 2019. The articles were then categorized according to the type of study and clinical applications. The study inclusion criteria were

case-control studies, review articles, cohort articles, pilot studies, and clinical trials published in English and Farsi, menstruation over the past 12 months, no medical illnesses performed during the study, and not receiving any specific treatment during the study. If there were several reports from one study, the most complete study was considered. The STROBE checklist with 22 items was used to evaluate the quality of the observation articles. The main items of the checklist were title, summary, introduction, method, findings, and discussion. Of the 22 total scores, at least 16 were considered for acceptance of the paper in the analysis. Finally, the information about each article was extracted based on the present study. The study exclusion criterion was the assessment of the quality of articles by CONSORT scale.[27] Besides, other exclusion criteria included were irrelevant research studies, inadequate data in the study, lack of access to full text of articles, editorial studies, and reports.

Study selection and data collection process

Articles were evaluated in two stages; the process of reviewing articles was that the first researcher read the articles individually and the information for each article was recorded in the table. The same reassessment was done by the second researcher. In the second step, the full text of the criterion-based articles was selected and if the researcher disagreed during the joint meeting, the final table was completed. The articles were then categorized by study type and clinical applications. Finally, information about each article was extracted based on the present study.

Results

Based on the search strategy, 400 articles were found in the first stage, 96 articles because of repeatability and 159 articles because of the lack of inclusion criteria were deleted. Then, from which 145 met the criteria for entry into the present review. Based on the findings of these studies, the various aspects of complementary medicine in menopause [Figure 1].

Evidence of the effectiveness of herbal medicine in reducing menopausal symptoms

One of the most popular and common ways to improve menopausal symptoms is the use of herbs. In the United States and the United Kingdom, 80% of postmenopausal women use herbal medicine, and 60% to 70% believe that these supplements eliminate their problems and are safe without side effects.^[28] Phytoestrogens or plant estrogens are nonsteroidal.^[29] Phytoestrogens include flavones, lignans, and coumestans. [2] The presence of phytoestrogens and phyto progesterones in the medicinal plants and the antiandrogenic effects of these plants reduce the conversion of testosterone to dihydrotestosterone and also increase the conversion of testosterone and androstenedione to estrogen in peripheral tissues which can reduce menopausal symptoms. [2] Numerous studies have shown that regular consumption of phytoestrogens in the diet of Asian women has led to a decrease in menopausal symptoms. [30] Many medicinal plants have been used to improve the symptoms of menopause [Tables 1-3]. On the other hand, in some studies, researchers found findings conflicting with other studies and acknowledged the ineffectiveness of some herbs in reducing menopausal symptoms [Table 4].

Acupuncture for reducing menopausal symptoms

Acupuncture is a Chinese medical intervention that involves placing small metal needles in specific areas of the body. [97] It is not yet clear how this method works but it is widely accepted

as a safe treatment.^[98] In traditional Chinese medicine, it is said that acupuncture reduces pain and cures symptoms by regulating meridian energy (Qi). On the other hand, modern Western medicine has investigated the mechanism of acupuncture based on changes in neurological, physiological, and hormonal neuronal activities.^[99] Some studies show that acupuncture increases endorphin activity. Therefore, it modulates thermoregulation in the hypothalamus and neutralizes temperature in patients with vasomotor syndrome.^[100] Acupuncture reduces hot flashes and

Scientific name of	Effective material	Mechanism of effect	Type of study	Source
the plant				
Soya (Glycine max)	Contains isoflavones, genistein, daidzein, glycine, [31] and Lecithin [32]	Reduce hot flashes. ^[31] High-dose soy lecithin (120 mg /day) increases energy, decreases diastolic blood pressure, and cardiovascular and wrist index in middle-aged women. ^[32] Soya isoflavone reduces cardiovascular disease risk index. ^[33] Soya isoflavone improves menopausal symptoms. ^[34] Soya isoflavone increases bone mineral density in postmenopausal women. ^[35]	Randomized, double-blind, placebo-controlled. [31,32] Double-blind randomized parallel. [33] Pilot study. [34] Double-blind, single-blind, placebo-controlled clinical trial. [35]	[31-35]
Vitex agnus-castus	Vitex contains phytoestrogens, proximity to opioid receptors, and the ability to increase melatonin secretion ^[36]	Reduces menopausal disorder, anxiety, and vasomotor disorder. ^[36]	Randomized, double-blind, placebo-controlled.[36]	[36]
Passion flower	Increases serotonin levels and monoamine oxidase control ^[37]	Reduces early menopausal symptoms (vasomotor symptoms, insomnia, depression, anger, headache). ^[37]	Clinical-experimental study.[37]	[37]
Hypericum perporatum	Increases serotonin levels and monoamine oxidase control ^[37]	Reduces early menopausal symptoms (vasomotor symptoms, insomnia, depression, anger, headache). ^[37]	Clinical-experimental study.[37]	[37]
Flaxseed	Rich source of ligands, omega-3 fatty acids, and fiber ^[38]	Reduce the risk of cardiovascular disease in postmenopausal women by lowering LDL-C and total cholesterol. [38] Reduce Menopausal Symptoms. [39] Reduce hot flashes. [40]	Interventional study. ^[38] Placebo-controlled randomized clinical trial. ^[39] Meta-analysis review study. ^[40]	[38-40]
Valerian	Contains phytoestrogens ^[41,42]	Reduce hot flashes. ^[41,42] Reduce symptoms of Sleep Disorders. ^[43,44]	Clinical trial, triple-blind, randomized, placebo- controlled. [41,44] Placebo-controlled randomized clinical trial. [43] Randomized, double-blind, and placebo control. [42]	[41-44]
Melissa officinalis	GABA Neurotransmitter Inhibitors ^[45]	Reduce symptoms of sleep Disorders. ^[45]	Placebo-controlled randomized clinical trial. ^[43]	[45,43]
Licorice	Contains Phytoestrogens ^[46]	Reduce hot flashes. ^[47,48]	Double-blind randomized clinical trial. ^[47] Randomized, double-blind, placebo-controlled trial. ^[48]	[46-48]
Anise	Contains Phytoestrogens ^[49]	Reduce hot flashes. ^[49]	Placebo-controlled randomized clinical trial. ^[49]	[49]
Salvia officinallisor saga	Contains Phytoestrogens, [50] Benzodiazepine GABA complex connection, receptors in the brain [51]	Reduce hot flashes. ^[51,52]	Pilot study. ^[51] Controlled clinical trial. ^[52]	[50-52]
Medicago sativa	Contains isoflavonoids And have phytoestrogenic properties ^[53]	Reduce hot flashes and night sweats. ^[52]	Controlled clinical trial. ^[52]	[52,53]

Scientific name of the plant	Effective material	Mechanism of effect	Type of study	Source
Black Cohosh	Phytoestrogenic properties. ^[54] Estrogen receptor modulators and effects of dopaminergic, serotonergic, and progestogenic and rich source of gamolenic acid (a precursor of prostaglandin E) ^[55]	Reduce sleep problems and vasomotor disorders. ^[56] Reduce the severity of hot flashes. ^[55] Reduce vasomotor symptom. ^[57]	Clinical trial, double-blind, randomized, placebo-controlled. [56,57] Randomized clinical trial. [55]	[54-57]
Evening primrose oil	Source of unsaturated fatty acids. ^[55] Source of Omega 6 Fatty Acids. ^[58] The exact mechanism of action is not well understood. ^[59]	Reduce the severity of hot flashes. ^[55,59]	Randomized clinical trial. [55] Placebo-controlled randomized clinical trial. [59]	[55,58,59]
Hop (Humulus lupulus)	Contains 8-Perenylnarangine (8-PN) is the strongest phytoestrogen known to date. ^[60]	Reduce hot flashes. ^[60] Reduce early Symptoms of menopause and hot flashes. ^[61]	Systematic review and meta- analysis. ^[60] Placebo-controlled randomized clinical trial. ^[61]	[60,61]
Ginkgo	Contains Phytoestrogenic properties. [62]	Increases libido in postmenopausal women, facilitates blood flow, affects nitric oxide systems, and has a relaxing effect on smooth muscles. ^[62] Improves memory and mental flexibility. ^[63,64]	Trial triple-blind, randomized, placebo-controlled. [62] Randomized double-blind, placebo-controlled. [63,64]	[62-64]
Wild yam	Contains DOI¹ protein for the treatment of menopausal syndrome. ^[65]	Improves the status of sex hormones, fats, and antioxidants, which may reduce the risk of breast cancer and cardiovascular disease in postmenopausal women. [66] Low impact on menopausal symptoms. [67]	Clinical trial study. ^[66] Randomized double-blind, placebo-controlled. ^[67]	[65-67]
Gin seng	Contains Phytoestrogenic properties. [68] Ginsenosides in ginseng have various biological and pharmacological activities. [69]	Improve sexual function and arousal and improve hot flashes. [70] Improve sexual function and quality of life and reduce menopausal symptoms and enhance menopausal women's health. [68] Reduce oxidative stress by increasing antioxidant enzyme activity in postmenopausal women. [69] Improvement of menopausal symptoms and reduce the risk of cardiovascular disease [71] antidepression. [72]	Review study. ^[70] Randomized, double-blind, placebo-controlled. ^[68,69,71] Clinical trial. ^[72]	[68-72]

^{1 -} Dioscorea opposita Thunb. A novel protein, designated as DOI, isolated from the Chinese yam (Dioscorea opposita Thunb), DOI is an acid - and thermo-stable protein with a distinctive N - terminal sequence

regular temperature control by increasing beta-endorphin levels and inhibiting GnRH secretion.^[101-104] The beneficial effects of acupuncture on reducing menopausal symptoms have been reported [Table 5].

Evidence of the use of acupressure in reducing menopausal symptoms

Acupressure as one of the branches of complementary and alternative medicine is a method that can be practiced by physicians, midwives, nurses, or even patients themselves.^[121] Acupressure is a noninvasive and safe technique, a form of traditional therapy skill where the fingers are used to press certain key points on the skin.^[121] Chinese believe that the human body has a network of energy channels that resemble the vascular and circulatory systems. In this network, there are 12 major pathways called meridian, several communication

pathways, and 361 acupressure points that have high directional power and affect one's health when a problem arises. [122] At the beginning of the creation of such treatment, the researchers believed that the effects were only due to their psychological effects but with further investigation and better understanding of the mechanism of the procedure, it became clear that the effects of acupressure were much greater and deeper than the purely psychological effects. [123] Acupressure balances vital energy by releasing neurotransmitters and hormones which consequently improves the early complications of menopause. [124] The effects of acupressure on menopausal symptoms have been proven [Table 6].

Discussion

Most menopausal women are looking for a safe alternative to hormone therapy due to its side effects. [129] Among the methods

Scientific name of the plant	Properties of plants	Mechanism of effect	Type of study	Source
kava	Contains analgesic and relaxing properties ^[73]	Reduce menopausal anxiety. ^[73]	Placebo-controlled clinical trial. ^[73]	[73]
Urtica dioica	Nettle contains many micronutrients and active ingredients such as phenols, vitamins (A, B2, B5), and minerals (calcium, potassium, magnesium, iron), and contains phytoestrogenic compounds. ^[74]	Reduce hot flashes. ^[74]	Double-blind, controlled, randomized clinical trial. ^[74]	[74]
Trigonella foehum	Contains hormone modulating activity. ^[75] Contains Phytoestrogenic properties. ^[76]	Reduce the severity of hot flashes, night sweats, and menopausal symptoms. ^[75]	Double-blind, randomized, placebo-controlled clinical trial. ^[75]	[75,76]
Hypericum perforatum	Phytoestrogenic properties. ^[77]	Reduce the severity of hot flashes. ^[77,78] Reduce sleep problems. ^[78]	Placebo-controlled randomized clinical trial. ^[77,78]	[77,78]
Red clover	Contains isoflavonoids.[79,80]	Reduce vasomotor symptoms. ^[79] Improve vaginal atrophy. ^[81] Reduce the severity of hot flashes. ^[80,82] Reduce the severity of menopausal symptoms. ^[83]	Parallel, double-blind, randomized, placebo-controlled trial. ^[79] Review and meta-analysis study. ^[80,81] Clinical trial, double-blind, randomized, placebo-controlled. ^[83] Clinical trial, randomized, placebo-controlled. ^[82]	[79-83]
Chmomile	Flavonoid compounds may have antianxiety and antidepressant properties. [84]	Reduce sleep disturbance. ^[85]	Randomized clinical trial, doubleblind. ^[85]	[84,85]
Nigella sativa	It has antioxidant activity, immune modulatory, antibacterial, blood pressure lowering, protective effects on the liver with antidiabetic effects. It also produces eicosanoid generation in leukocytes and membrane lipid peroxidation. [86] Contains hypolipidemic effects. [87]	Improve the balance between oxidants and antioxidants in the blood of postmenopausal women. [86] Improve lipid profile. [87] Improve lipid profile and blood glucose as well as hormone levels that have important effects on the pathogenesis of metabolic syndrome in menopause, have therapeutic and protective effects on menopause. [88,89]	Clinical trial. [86] Randomized clinical trial, double- blind. [87] Randomized clinical trial, placebo- controlled. [88,89]	[86-89]
Alium sativum	It has antioxidant activity, has steroid glycosides, contains vitamins B1, B2, B6, C and E; biotin, nicotinic acid; fatty acids; glycolipids; essential phospholipids and amino acids; It has antibacterial, antitumor, antiinflammatory, antithrombotic, and anticholesterol properties. [86]	Improve the balance between blood oxidants and antioxidants in postmenopausal women. ^[86]	Clinical trial. ^[86]	[86]

of complementary and alternative medicine, we can mention herbal medicine, acupuncture, and acupressure for the treatment of menopausal symptoms.^[68,119,121] Various studies have shown a high tendency of women for complementary therapies and herbal medicines. [2] In this study, 25 herbal medicines effective in menopausal symptoms were studied. The results showed that herbal therapy reduced hot flashes, increased bone mineral density, improved sleep quality, reduced vasomotor symptoms, improved metabolic disorders, reduced risk of osteoporosis and hypertension, increased libido, improved memory and mental flexibility, improved sexual function and life quality, promoted health, prevented Alzheimer's, controlled weight gain, treated hyperlipidemia, reduced psychological symptoms, improved vaginal atrophy, and generally reduced menopausal symptoms in women. Phytoestrogens are compounds found in many of the plants investigated in this study that exhibit estrogenic and in some cases antiestrogenic properties.^[130] The function of these herbal chemicals in bonding with estrogen receptors in human body cells is so similar to natural hormones that must be considered as one of the tricks of human evolution in taking advantage of nature. [131] The estrogenic power of these compounds is estimated to be one thousandth to one ten-thousandth of Estradiol but it has no adverse effects like that of synthetic estrogens. [132] Different types of phytoestrogens include isoflavones, flavonoids, coumestans, and lignans.[133] Phytoestrogens reduce the symptoms of menopause and the risk of cardiovascular disease, osteoporosis, and breast and endometrial cancers.^[134] Asian women experience fewer menopausal symptoms during menopause than Western women due to a diet high in phytoestrogens. [135] In Japan, for example, the daily amount of phytoestrogens intake is estimated as 200 mg. As a result, the rates of hormones and osteoporosis-related cancers

Ebrahimi, et al.: Herbal medicine, acupressure, and acupuncture in the menopausal symptoms

Table 4: Ineffective of plants in reducing menopausal symptoms			
Scientific name of the plant	Mechanism of effect	Type of study	Source
Soya (Glycine max)	Soya drinks have no effect on the mood of postmenopausal women. [90]	Clinical trial. ^[90]	[90]
Flaxseed	Supplementation of flaxseed has no effect on lowering cholesterol and increasing bone mineral density in postmenopausal women. [91]		[91]
Black Cohosh	According to this review study, has no clinical efficacy. [92]	Review study.[92]	[92]
Ginkgo and Ginseng	The combination of Ginkgo and Ginseng has no effect on mood and other menopausal symptoms. [93]	Clinical trial, a randomized, double-blind, placebo-controlled. ^[93]	[93]
Dong Quai	No effect on hot flashes. ^[94] No effect on vasomotor symptoms. ^[95,96]	Clinical trial, a randomized, double-blind, placebo-controlled. [94-96]	[94-96]

Table 5: The effects of acupuncture use on menopausal symptoms				
Purpose of the study	Type of study	Result	Source	
The effect of acupuncture on body and ear on sleep quality in postmenopausal women	Randomized controlled clinical trial.[105]	Improve the quality of sleep.[105]	[105]	
The effect of acupuncture on menopausal symptoms	Clinical Trial. ^[106] Randomized controlled clinical trial. ^[107] Meta-analysis study. ^[108]	Reduce menopausal symptoms.[106-108]	[106-108]	
The effect of acupuncture ratio on alprazolam on sleep quality in postmenopausal women	Randomized Clinical Trial.[109]	The effect of alprazolam was more than that of acupuncture. [109]	[109]	
The effect of acupuncture on menopausal vasomotor symptoms	Systematic review study.[110]	Reduce vasomotor symptoms.[110]	[110]	
Comparison of the effect of manual and electrical acupuncture on menopause	Randomized Clinical Trial. ^[111] Randomized clinical trial, single-blind, and controlled. ^[112]	Significant decrease in depression and anxiety symptoms in both groups.[111,112]	[111,112]	
The effect of acupuncture on symptoms of hot flashes and menopause in patients with breast cancer	Systematic review and meta-analysis. ^[99]	Reduce menopausal symptoms and no effect on hot flashes. ^[99]	[99]	
The effect of acupuncture on the treatment of dry eye disease in postmenopausal women	Randomized clinical trial. ^[113]	Improve dry eye.[113]	[113]	
The effect of laser acupuncture on postmenopausal metabolic syndrome	Randomized controlled clinical trial.[114]	Improve metabolic syndrome.[114]	[114]	
Comparison of the effect of acupuncture and acetazolam on sleep quality in postmenopausal women	Randomized clinical trial.[115]	Acupuncture has better effect on menopausal insomnia than acetazolam. ^[115]	[115]	
Comparison of the effect of acupuncture and diazepam on severity of irritability in postmenopausal women	Clinical trial.[116]	The effect of acupuncture on reducing irritability is more than diazepam (2.5 mg). [116]	[116]	
The effect of acupuncture on hot flashes in postmenopausal women	Randomized clinical trial. ^[25]	Reduce hot flashes. ^[25]	[25]	
The effect of acupuncture on hot flashes, menopausal complications, and sleep quality of postmenopausal women	Meta-analysis. ^[117]	Improves hot flashes, reduces menopausal symptoms, and enhances quality of life. ^[117]	[117]	
The effect of acupuncture on mood and quality of sleep	Randomized, 2-group clinical study.[118]	Improves sleep quality and menopausal symptoms.[118]	[118]	
The effect of acupuncture on vasomotor symptoms and quality of life in postmenopausal women	Randomized clinical trial.[119]	Reduce vasomotor symptoms and improve quality of life. [119]	[119]	
The effect of acupuncture on hot flashes and quality of life in postmenopausal women	This study involved a multicenter, pragmatic, randomized, controlled trial with two parallel arms. ^[120]	Reduces hot flashes and enhances quality of life. [120]	[120]	

and hot flashes in Japanese women are lower than the women in other parts of the world. [132] Herbs such as valerian, black cohosh, chamomile, *Hypericum perforatum*, licorice, anise, soya, red clover, *Vitex-agnus castus*, [136] and sage [133] are phytoestrogenic and have been recommended for the treatment of menopausal

symptoms. Although most studies indicated the positive effects of therapeutic herbal interventions on menopausal symptoms, a number of studies showed that some herbs had no effect on menopausal symptoms. [90-96] The reason for these discrepancies may be due to differences in sampling methods, low sample

Table 6: The effects of acupressure use on menopausal symptoms			
Purpose of the study	Type of study	Result	Source
The effect of acupressure on early menopausal complications	Blind random clinical trial and placebo- controlled. [121]	Reduce menopause complications. ^[121]	[121]
The effect of acupressure on sleep quality in postmenopausal women	Single-blind randomized clinical trial. [125] Double-blind randomized clinical trial. [126]	Improve sleep quality.[125,126]	[125,126]
The effect of acupressure on hot flashes in postmenopausal women	Clinical trial. ^[25] Randomized clinical trial through purposive sampling. ^[127]	Improve hot flashes and menopausal symptoms. ^[25,127]	[25,127]
The relationship of subjective sleep quality and cardiac autonomic nervous system in postmenopausal women with insomnia under auricular acupressure	A pretest/posttest study.[128]	Increases the parasympathetic activity of the heart and decreases the sympathetic activity of the heart which can improve sleep quality. ^[128]	[128]

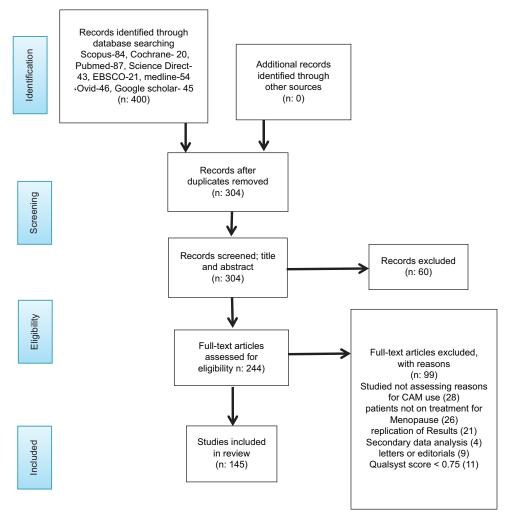


Figure 1: Flowchart of the inclusion of studies in the review[26]

numbers, concealment, incomplete data usage, and prescribing procedures. Although medicinal herbs have fewer side effects than drug therapy,^[74] they may also have some side effects. Reports indicate that Black cohosh side effects are rare, mild, and reversible. Gastrointestinal problem is the most common side effect of this plant.^[137] Headache, dizziness, and vomiting may occur in high doses.^[138,139] Allergic skin reactions, skin problems, and neurological symptoms have also been reported in the use of kava.^[140] Kava may interfere with other anxiolytics;

there is a reported case of Kava interfering with alprazolam.^[141] Kava was associated with liver damage and removed from the market of Canada and several countries in Europe.^[142] On the other hand, long-term use of ginseng may lead to hypertension, edema, diarrhea, skin rashes, insomnia, depression, and amenorrhea.^[141] It also causes nervousness, dizziness, and uterine bleeding and some effects on liver enzymes.^[69] A case of suspected drug interference of Dong quai with Warfarin has also been reported.^[141] The use of *Hypericum perporatum* has been

associated with gastrointestinal complications and headaches. Vitex agnus-castus consumption has also been associated with headaches and dizziness.[143] Another branch of complementary and alternative medicine is acupuncture. [99] Acupuncture is used to treat menopausal symptoms as a complementary and alternative therapy without serious side effects.[113] We examined 18 acupuncture studies. Studies showed that acupuncture improved sleep quality, decreased vasomotor symptoms, reduced symptoms of depression and anxiety, improved dry eye and sleep disturbances, improved metabolic syndrome, reduced irritability and hot flashes, enhanced quality of life, and reduced menopausal symptoms. In one study, the effect of acupuncture compared with alprazolam on sleep quality in postmenopausal women was investigated and the results showed a greater effect of alprazolam.[109] In another study, the effect of acupuncture compared with diazepam on the irritability of postmenopausal women was investigated in which the results indicated a greater effect of acupuncture than diazepam tablets.^[116] Acupressure is another branch of complementary and alternative medicine. [128] In this study, 6 clinical trials were studied. The results showed that acupressure improved sleep quality, hot flashes, and reduced menopausal complications in postmenopausal women. The function of acupressure is unknown but studies have shown that by pushing acupressure points, myelinated nerve fibers are activated and send messages to the spinal cord. This activates three neural centers of the spinal cord, middle brain, and hypothalamic-pituitary axis. [144] In the case of hot flashes, for example, it has been hypothesized that an increase in endorphin hormone during acupressure modulates hypothalamic temperature regulation. Peptide levels, associated with the calcitonin gene, a potent vasodilator released during flushing, decrease during acupressure therapy. In addition, in some studies, this treatment may increase the level of plasma hormones such as estradiol during and after acupressure therapy. [144] Limitations of this study included focusing on published articles in English and limited studies of complementary medicine including herbal therapy in the world, except in some countries. In addition, due to the interventional nature of herbal medicine, acupuncture, and acupressure, the risk of bias might occur in the studies and affect the results of the studies. Further studies should be conducted with careful blinding methods to provide further evidence of the effectiveness of these interventions. To better understand the impact of complementary medicine interventions on menopausal symptoms, more systematic review studies and meta-analyzes should be performed for clinical trial evaluations.

Conclusion

There are many complementary medicine methods to improve menopausal symptoms and it is difficult to determine which method has more beneficial therapeutic benefits. Hence, patients interested in complementary medicine treatments should talk to their healthcare providers about the value and potential implications of it. Some herbal medicines have some side effects. Therefore, they should be used with caution. However, many herbs are either without side effects or have very minor side effects; thus, some herbal medicines that have been proven to be effective can be used to improve menopausal symptoms. Acupuncture and acupressure are also beneficial treatments with no side effects to improve menopausal symptoms.

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Conflicts of interest

There are no conflicts of interest.

References

- 1. Nappi RE, Kokot-Kierepa M. Women's voices in the menopause: Results from an international survey on vaginal atrophy. Maturitas 2010;67:233-8.
- Kargozar R, Azizi H, Salari R. A review of effective herbal medicines in controlling menopausal symptoms. Electron Physician 2017;9:5826-33.
- Johnson A, Roberts L, Elkins G. Complementary and Alternative Medicine for Menopause. Journal of evidencebased integrative medicine. 2019;24(1):2515690x19829380.
- Pérez JAM, Garcia FC, Palacios S, Pérez M. Epidemiology of risk factors and symptoms associated with menopause in Spanish women. Maturitas 2009;62:30-6.
- Russo R, Corosu R. The clinical use of a preparation based on phyto-oestrogens in the treatment of menopausal disorders. Acta Biomed 2003;74:137-43.
- Woods NF, Mitchell ES. Symptoms during the perimenopause: Prevalence, severity, trajectory, and significance in women's lives. Am J Med 2005;118:14-24.
- MacLennan AH. Evidence-based review of therapies at the menopause. Int J Evid Based Healthc 2009;7:112-23.
- 8. Oddens B, Boulet MJ, Lehert P, Visser AP. Has the climacteric been medicalised? A study on the use of medication for climacteric complaints in four countries. Maturitas 1993;171-81.
- 9. Pan H-A, Wu M-H, Hsu C-C, Yao B-L, Huang K-E. The perception of menopause among women in Taiwan. Maturitas 2002;41:269-74.
- 10. Gartoulla P, Bell RJ, Worsley R, Davis SR. Moderate-severely bothersome vasomotor symptoms are associated with lowered psychological general wellbeing in women at midlife. Maturitas 2015;81:487-92.
- 11. Duffy O, Iversen L, Hannaford PC. The impact and management of symptoms experienced at midlife: A community-based study of women in northeast Scotland. Br J Obstet Gynaecol 2012;119:554-64.
- 12. Ayers B, Hunter M. Health-related quality of life of women with menopausal hot flushes and night sweats. Climacteric 2013;16:235-9.
- 13. Avis NE, Brockwell S, Randolph JF Jr, Shen S, Cain VS, Ory M, *et al.* Longitudinal changes in sexual functioning as women transition through menopause: Results from the study of women's health across thenation (SWAN). Menopause (New York, NY) 2009;16:442-52.
- 14. Xu Q, Lang CP, Rooney N. A systematic review of the longitudinal relationships between subjective sleep disturbance and menopausal stage. Maturitas 2014;79:401-12.

- 15. Davis SR, Panjari M, Robinson PJ, Fradkin P, Bell RJ. Menopausal symptoms in breast cancer survivors nearly 6 years after diagnosis. Menopause 2014:21:1075-81.
- 16. Rees M. The need to improve compliance to HRT. Br J Obstet Gynaecol 1997;104:1-3.
- 17. Guttuso T Jr, Kurlan R, McDermott MP, Kieburtz K. Gabapentin's effects on hot flashes in postmenopausal women: A randomized controlled trial. Obstet Gynecol 2003;101:337-45.
- 18. Elkind-Hirsch K. Cooling off hot flashes: Uncoupling of the circadian pattern of core body temperature and hot flash frequency in breast cancer survivors. Menopause 2004;11:369-71.
- 19. Fernandez E, Gallus S, Bosetti C, Franceschi S, Negri E, La Vecchia C. Hormone replacement therapy and cancer risk: A systematic analysis from a network of case-control studies. Int J Cancer 2003;105:408-12.
- 20. Lindh-Åstrand L, Hoffmann M, Hammar M, Spetz Holm A-C. Hot flushes, hormone therapy and alternative treatments: 30 years of experience from Sweden. Climacteric 2015;18:53-62.
- 21. Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy: Annual trends and response to recent evidence. JAMA 2004;291:47-53.
- 22. Borrelli F, Ernst E. Alternative and complementary therapies for the menopause. Maturitas 2010;66:333-43.
- 23. Gentry-Maharaj A, Karpinskyj C, Glazer C, Burnell M, Bailey K, Apostolidou S, *et al.* Prevalence and predictors of complementary and alternative medicine/non-pharmacological interventions use for menopausal symptoms within the UK Collaborative Trial of Ovarian Cancer Screening. Climacteric 2017;20:240-7.
- 24. Gollschewski S, Kitto S, Anderson D, Lyons-Wall P. Women's perceptions and beliefs about the use of complementary and alternative medicines during menopause. Complement Ther Med 2008;16:163-8.
- 25. Zhou J, Qu F, Sang X, Wang X, Nan R. Acupuncture and auricular acupressure in relieving menopausal hot flashes of bilaterally ovariectomized Chinese women: A randomized controlled trial. Evid Based Complement Alternat Med 2011;2011:713274.
- 26. Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009;6:e1000097.
- 27. Sepehrirad M, Bahrami H, Noras M. The role of complementary medicine in control of premenstrual syndrome evidence based (Regular Review Study). Iran J Obstet Gynecol Infertil 2016;19:11-22.
- 28. Geller SE, Studee L. Contemporary alternatives to plant estrogens for menopause. Maturitas 2006;55:S3-13.
- 29. Ciotta L, Stracquadanio M, Pagano I, Andò A, Valenti O, Roccasalva L. [Clinical effects of treatment with phytoestrogens in postmenopausal women]. Minerva Ginecol 2012;64:15-22.
- Adlercreutz H, Hämäläinen E, Gorbach S, Goldin B. Dietary phyto-oestrogens and the menopause in Japan. Lancet 1992;339:1233.
- 31. Imhof M, Gocan A, Imhof M, Schmidt M. Soy germ extract alleviates menopausal hot flushes: Placebo-controlled double-blind trial. Eur J Clin Nutr 2018;72:961-70.
- 32. Hirose A, Terauchi M, Osaka Y, Akiyoshi M, Kato K, Miyasaka N. Effect of soy lecithin on fatigue and menopausal

- symptoms in middle-aged women: A randomized, double-blind, placebo-controlled study. Nutr J 2018;17:4.
- Sathyapalan T, Aye M, Rigby AS, Thatcher NJ, Dargham SR, Kilpatrick ES, et al. Soy isoflavones improve cardiovascular disease risk markers in women during the early menopause. Nutrition, metabolism, and cardiovascular diseases. Nutr Metab Cardiovasc Dis 2018;28:691-7.
- 34. Ahsan M, Mallick AK. The effect of soy isoflavones on the menopause rating scale scoring in perimenopausal and postmenopausal women: A pilot study. J Clin Diagn Res 2017;11:FC13-6.
- 35. Levis S, Strickman-Stein N, Ganjei-Azar P, Xu P, Doerge DR, Krischer J. Soy isoflavones in the prevention of menopausal bone loss and menopausal symptoms: A randomized, double-blind trial. JAMA Intern Med 2011;171:1363-9.
- 36. Naseri R, Farnia V, Yazdchi K, Alikhani M, Basanj B, Salemi S. Comparison of Vitex agnus-castus extracts with placebo in reducing menopausal symptoms: A randomized double-blind study. Korean J Fam Med 2019;40:362-7.
- 37. Fahami F, Asali Z, Aslani A, Fathizadeh N. A comparative study on the effects of Hypericum perforatum and passion flower on the menopausal symptoms of women referring to Isfahan city health care centers. Iran J Nurs Midwifery Res 2010;15:202-7.
- 38. Patade A, Devareddy L, Lucas EA, Korlagunta K, Daggy BP, Arjmandi BH. Flaxseed reduces total and LDL cholesterol concentrations in Native American postmenopausal women. J Womens Health 2008;17:355-66.
- 39. Colli MC, Bracht A, Soares AA, de Oliveira AL, Boer CG, de Souza CG, *et al.* Evaluation of the efficacy of flaxseed meal and flaxseed extract in reducing menopausal symptoms. J Med Food 2012;15:840-5.
- 40. Ghazanfarpour M, Sadeghi R, Latifnejad Roudsari R, Khadivzadeh T, Khorsand I, Afiat M, *et al.* Effects of flaxseed and Hypericum perforatum on hot flash, vaginal atrophy and estrogen-dependent cancers in menopausal women: A systematic review and meta-analysis. Avicenna J Phytomed 2016;6:273-83.
- 41. Jenabi E, Shobeiri F, Hazavehei SMM, Roshanaei G. The effect of Valerian on the severity and frequency of hot flashes: A triple-blind randomized clinical trial. Women Health 2018;58:297-304.
- 42. Mirabi P, Mojab F. The effects of Valerian root on hot flashes in menopausal women. Iran J Pharm Res 2013;12:217-22.
- 43. Taavoni S, Nazem Ekbatani N, Haghani H. Valerian/lemon balm use for sleep disorders during menopause. Complement Ther Clin Pract 2013;19:193-6.
- 44. Taavoni S, Ekbatani N, Kashaniyan M, Haghani H. Effect of valerian on sleep quality in postmenopausal women: A randomized placebo-controlled clinical trial. Menopause 2011;18:951-5.
- 45. Awad R, Muhammad A, Durst T, Trudeau VL, Arnason JT. Bioassay-guided fractionation of lemon balm (Melissa officinalis L.) using an *in vitro* measure of GABA transaminase activity. Phytother Res 2009;23:1075-81.
- 46. Hajirahimkhan A, Simmler C, Yuan Y, Anderson JR, Chen SN, Nikolic D, et al. Evaluation of estrogenic activity of licorice species in comparison with hops used in botanicals for menopausal symptoms. PLoS One 2013;8:e67947.
- 47. Menati L, Khaleghinezhad K, Tadayon M, Siahpoosh A. Evaluation of contextual and demographic factors on licorice effects on reducing hot flashes in postmenopause women. Health Care Women Int 2014;35:87-99.

- Nahidi F, Zare E, Mojab F, Alavi-Majd H. Effects of licorice on relief and recurrence of menopausal hot flashes. Iran J Pharm Res 2012:11:541-8.
- 49. Nahidi F, Kariman N, Simbar M, Mojab F. The study on the effects of pimpinella anisum on relief and recurrence of menopausal hot flashes. Iran J Pharm Res 2012;11:1079-85.
- 50. Rahte S, Evans R, Eugster PJ, Marcourt L, Wolfender J-L, Kortenkamp A, *et al.* Salvia officinalis for hot flushes: Towards determination of mechanism of activity and active principles. Planta Med 2013;79:753-60.
- 51. Vandecasteele K, Ost P, Oosterlinck W, Fonteyne V, De Neve W, De Meerleer G. Evaluation of the efficacy and safety of Salvia officinalis in controlling hot flashes in prostate cancer patients treated with androgen deprivation. Phytother Res 2012;26:208-13.
- 52. De VL, Lanzetta D, Cazzavacca R, Morgante G. Treatment of neurovegetative menopausal symptoms with a phytotherapeutic agent. Minerva Ginecol 1998;50:207-11.
- 53. Adaay MH, Al-Dujaily SS, Khazzal FK. Effect of aqueous extract of Medicago sativa and Salvia officinalis mixture on hormonal, ovarian and uterine parameters in mature female mice. J Mater Environ Sci 2013;4:424-33.
- 54. Miao LY, Chu TTH, Li P, Jiang Y, Li HJ. Cimicifuga heracleifolia is therapeutically similar to black cohosh in relieving menopausal symptoms: Evidence from pharmacological and metabolomics studies. Chin J Nat Med 2019;17:435-45.
- 55. Mehrpooya M, Rabiee S, Larki-Harchegani A, Fallahian AM, Moradi A, Ataei S, *et al.* A comparative study on the effect of "black cohosh" and "evening primrose oil" on menopausal hot flashes. J Educ Health Promot 2018;7:36.
- 56. Jiang K, Jin Y, Huang L, Feng S, Hou X, Du B, *et al.* Black cohosh improves objective sleep in postmenopausal women with sleep disturbance. Climacteric 2015;18:559-67.
- 57. Shahnazi M, Nahaee J, Mohammad-Alizadeh-Charandabi S, Bayatipayan S. Effect of black cohosh (cimicifuga racemosa) on vasomotor symptoms in postmenopausal women: A randomized clinical trial. J Caring Sci 2013;2:105-13.
- 58. Bayles B, Usatine R. Evening primrose oil. Am Fam Physician 2009;80:1405-8.
- 59. Farzaneh F, Fatehi S, Sohrabi MR, Alizadeh K. The effect of oral evening primrose oil on menopausal hot flashes: A randomized clinical trial. Arch Gynecol Obstet 2013;288:1075-9.
- Abdi F, Kazemi F, Ramezani Tehrani F, Roozbeh N. Protocol for systematic review and meta-analysis: Hop (Humulus lupulus L.) for menopausal vasomotor symptoms. BMJ Open 2016;6:e010734.
- 61. A g h a m i r i V, M i r g h a f o u r v a n d M, Mohammad-Alizadeh-Charandabi S, Nazemiyeh H. The effect of Hop (Humulus lupulus L.) on early menopausal symptoms and hot flashes: A randomized placebo-controlled trial. Complement Ther Clin Pract 2016;23:130-5.
- 62. Pebdani MA, Taavoni S, Seyedfatemi N, Haghani H. Triple-blind, placebo-controlled trial of Ginkgo biloba extract on sexual desire in postmenopausal women in Tehran. Iran J Nurs Midwifery Res 2014;19:262-5.
- 63. Elsabagh S, Hartley DE, File SE. Limited cognitive benefits in Stage+2 postmenopausal women after 6 weeks of treatment with Ginkgo biloba. J Psychopharmacol (Oxford, England) 2005;19:173-81.
- 64. Hartley DE, Heinze L, Elsabagh S, File SE. Effects on

- cognition and mood in postmenopausal women of 1-week treatment with Ginkgo biloba. Pharmacol Biochem Behav 2003;75:711-20.
- 65. Wong KL, Lai YM, Li KW, Lee KF, Ng TB, Cheung HP, *et al.* A novel, stable, estradiol-stimulating, osteogenic yam protein with potential for the treatment of menopausal syndrome. Sci Rep 2015;5:10179.
- 66. Wu WH, Liu LY, Chung CJ, Jou HJ, Wang TA. Estrogenic effect of yam ingestion in healthy postmenopausal women. J Am Coll Nutr 2005;24:235-43.
- 67. Komesaroff P, Black C, Cable V, Sudhir K. Effects of wild yam extract on menopausal symptoms, lipids and sex hormones in healthy menopausal women. Climacteric 2001;4:144-50.
- 68. Ghorbani Z, Mirghafourvand M, Charandabi SM, Javadzadeh Y. The effect of ginseng on sexual dysfunction in menopausal women: A double-blind, randomized, controlled trial. Complement Ther Med 2019;45:57-64.
- 69. Seo SK, Hong Y, Yun BH, Chon SJ, Jung YS, Park JH, *et al.* Antioxidative effects of Korean red ginseng in postmenopausal women: A double-blind randomized controlled trial. J Ethnopharmacol 2014;154:753-7.
- 70. Lee HW, Choi J, Lee Y, Kil KJ, Lee MS. Ginseng for managing menopausal woman's health: A systematic review of double-blind, randomized, placebo-controlled trials. Medicine (Baltimore) 2016;95:e4914.
- 71. Kim SY, Seo SK, Choi YM, Jeon YE, Lim KJ, Cho S, *et al.* Effects of red ginseng supplementation on menopausal symptoms and cardiovascular risk factors in postmenopausal women: A double-blind randomized controlled trial. Menopause 2012;19:461-6.
- 72. Yamada N, Araki H, Yoshimura H. Identification of antidepressant-like ingredients in ginseng root (Panax ginseng C.A. Meyer) using a menopausal depressive-like state in female mice: Participation of 5-HT2A receptors. Psychopharmacology 2011;216:589-99.
- 73. De Leo V, La Marca A, Morgante G, Lanzetta D, Florio P, Petraglia F. Evaluation of combining kava extract with hormone replacement therapy in the treatment of postmenopausal anxiety. Maturitas 2001;39:185-8.
- 74. Kargozar R, Salari R, Jarahi L, Yousefi M, Pourhoseini SA, Sahebkar-Khorasani M, *et al.* Urtica dioica in comparison with placebo and acupuncture: A new possibility for menopausal hot flashes: A randomized clinical trial. Complement Ther Med 2019;44:166-73.
- 75. Steels E, Steele ML, Harold M, Coulson S. Efficacy of a proprietary trigonella foenum-graecum L. de-husked seed extract in reducing menopausal symptoms in otherwise healthy women: A double-blind, randomized, placebo-controlled study. Phytother Res 2017;31:1316-22.
- 76. Anjaneyulu K, Bhat KM, Srinivasa SR, Devkar RA, Henry T. Beneficial role of hydro-alcoholic seed extract of trigonella foenum graecum on bone structure and strength in menopause induced osteopenia. Ethiop J Health Sci 2018;28:787-94.
- 77. Abdali K, Khajehei M, Tabatabaee HR. Effect of St John's wort on severity, frequency, and duration of hot flashes in premenopausal, perimenopausal and postmenopausal women: A randomized, double-blind, placebo-controlled study. Menopause 2010;17:326-31.
- 78. Al-Akoum M, Maunsell E, Verreault R, Provencher L, Otis H, Dodin S. Effects of Hypericum perforatum (St. John's wort) on hot flashes and quality of life in perimenopausal women: A randomized pilot trial. Menopause 2009;16:307-14.

- 79. Lambert MNT, Thorup AC, Hansen ESS, Jeppesen PB. Combined Red Clover isoflavones and probiotics potently reduce menopausal vasomotor symptoms. PLoS One 2017;12:e0176590.
- 80. Ghazanfarpour M, Sadeghi R, Latifnejad Roudsari R, Mirzaii Najmabadi K, Mousavi Bazaz M, Abdolahian S, *et al.* Effects of red clover on hot flash and circulating hormone concentrations in menopausal women: A systematic review and meta-analysis. Avicenna J Phytomed 2015;5:498-511.
- 81. Ghazanfarpour M, Sadeghi R, Roudsari RL, Khorsand I, Khadivzadeh T, Muoio B. Red clover for treatment of hot flashes and menopausal symptoms: A systematic review and meta-analysis. J Obstet Gynaecol 2016;36:301-11.
- 82. van de Weijer PH, Barentsen R. Isoflavones from red clover (Promensil[®]) significantly reduce menopausal hot flush symptoms compared with placebo. Maturitas 2002;42:187-93.
- 83. Shakeri F, Taavoni S, Goushegir A, Haghani H. Effectiveness of red clover in alleviating menopausal symptoms: A 12-week randomized, controlled trial. Climacteric 2015;18:568-73.
- 84. Mao JJ, Xie SX, Keefe JR, Soeller I, Li QS, Amsterdam JD. Long-term chamomile (Matricaria chamomilla L.) treatment for generalized anxiety disorder: A randomized clinical trial. Phytomedicine 2016;23:1735-42.
- Abbasinia H, Alizadeh Z, Vakilian K, Ranjbaran M. Effect of chamomile extract on sleep disorder in menopausal women. Iran J Obstet Gynecol Infertil 2016;19:1-7.
- 86. Mostafa RM, Moustafa YM, Mirghani Z, AlKusayer GM, Moustafa KM. Antioxidant effect of garlic (Allium sativum) and black seeds (Nigella sativa) in healthy postmenopausal women. SAGE Open Med. 2013;1(1):2050312113517501.
- 87. Ibrahim RM, Hamdan NS, Mahmud R, Imam MU, Saini SM, Rashid SN, *et al.* A randomised controlled trial on hypolipidemic effects of Nigella Sativa seeds powder in menopausal women. J Transl Med 2014;12:82.
- 88. Latiff LA, Parhizkar S, Dollah MA, Hassan ST. Alternative supplement for enhancement of reproductive health and metabolic profile among perimenopausal women: A novel role of Nigella sativa. Iran J Basic Med Sci 2014;17:980-5.
- Ibrahim RM, Hamdan NS, Ismail M, Saini SM, Abd Rashid SN, Abd Latiff L, et al. Protective effects of nigella sativa on metabolic syndrome in menopausal women. Adv Pharm Bull 2014;4:29-33.
- Simpson EE, Furlong ON, Parr HJ, Hodge SJ, Slevin MM, McSorley EM, et al. The effect of a randomized 12-week soy drink intervention on everyday mood in postmenopausal women. Menopause 2019;26:867-73.
- 91. Dodin S, Lemay A, Jacques H, Légaré F, Forest J-C, Mâsse B. The effects of flaxseed dietary supplement on lipid profile, bone mineral density, and symptoms in menopausal women: A randomized, double-blind, wheat germ placebo-controlled clinical trial. J Clin Endocrinol Metab 2005;90:1390-7.
- 92. Leach MJ, Moore V. Black cohosh (Cimicifuga spp.) for menopausal symptoms. Cochrane Database Syst Rev 2012:CD007244.doi:10.1002/14651858.CD007244.pub2.
- 93. Hartley D, Elsabagh S, File S. Gincosan (a combination of Ginkgo biloba and Panax ginseng): The effects on mood and cognition of 6 and 12 weeks' treatment in post-menopausal women. Nutr Neurosci 2004;7:325-33.
- Al-Bareeq RJ, Ray AA, Nott L, Pautler SE, Razvi H. Dong Quai (angelica sinensis) in the treatment of hot flashes

- for men on androgen deprivation therapy: Results of a randomized double-blind placebo controlled trial. Can Urol Assoc I 2010:4:49-53.
- 95. Hirata JD, Swiersz LM, Zell B, Small R, Ettinger B. Does dong quai have estrogenic effects in postmenopausal women? A double-blind, placebo-controlled trial. Fertil Steril 1997;68:981-6.
- 96. Haines CJ, Lam PM, Chung TK, Cheng KF, Leung PC. A randomized, double-blind, placebo-controlled study of the effect of a Chinese herbal medicine preparation (Dang Gui Buxue Tang) on menopausal symptoms in Hong Kong Chinese women. Climacteric 2008;11:244-51.
- 97. Ee CC, Thuraisingam S, Pirotta MV, French SD, Xue CC, Teede HJ. Expectancy after the first treatment and response to acupuncture for menopausal hot flashes. PLoS One 2017;12:e0186966.
- 98. Selva Olid A, Martinez Zapata MJ, Sola I, Stojanovic Z, Uriona Tuma SM, Bonfill Cosp X. Efficacy and safety of needle acupuncture for treating gynecologic and obstetric disorders: An overview. Med Acupunct 2013;25:386-97.
- Chien T-J, Hsu C-H, Liu C-Y, Fang C-J. Effect of acupuncture on hot flush and menopause symptoms in breast cancer-A systematic review and meta-analysis. PLoS One 2017;12:e0180918.
- 100. Filshie J, Bolton T, Browne D, Ashley S. Acupuncture and self acupuncture for long-term treatment of vasomotor symptoms in cancer patients--audit and treatment algorithm. Acupunct Med 2005;23:171-80.
- 101. Andersson S, Lundeberg T. Acupuncture—from empiricism to science: Functional background to acupuncture effects in pain and disease pain and disease. Med Hypotheses 1995;45:271-81.
- 102. Han J-S. Acupuncture and endorphins. Neurosci Lett 2004;361:258-61.
- 103. Shoupe D, Lobo RA. Endogenous opioids in the menopause. Seminars in Reproductive Endocrinology 1987;5:199-20.
- 104. Tepper R, Neri A, Kaufman H, Schoenfeld A, Ovadia J. Menopausal hot flushes and plasma beta-endorphins. Obstet Gynecol 1987;70:150-2.
- 105. Zhang S, Jia SH, Yang LJ, Jin ZG. [Clinical trials of treatment of woman menopause insomnia due to disharmony between heart and kidney by body and auricular acupuncture]. Zhen Ci Yan Jiu 2019;44:516-9.
- 106. Palma F, Fontanesi F, Facchinetti F, Cagnacci A. Acupuncture or phy (F) itoestrogens vs. (E) strogen plus progestin on menopausal symptoms. A randomized study. Gynecol Endocrinol 2019;35:995-8.
- 107. Lund KS, Siersma V, Brodersen J, Waldorff FB. Efficacy of a standardised acupuncture approach for women with bothersome menopausal symptoms: A pragmatic randomised study in primary care (the ACOM study). BMJ Open 2019;9:e023637.
- 108. Li W, Luo Y, Fu W, Lei R. Acupuncture may improve quality of life in menopausal women: A meta-analysis of randomized controlled trials. Complement Med Res 2018;25:183-90.
- 109. Li O, Wang F. Acupuncture at back-shu points of five zang, Geshu (BL 17) and Shenmen (HT 7) for the treatment of menopausal insomnia. Zhongguo zhen jiu= Chinese acupuncture & moxibustion 2018;38:4672-93.
- 110. Befus D, Coeytaux RR, Goldstein KM, McDuffie JR, Shepherd-Banigan M, Goode AP, *et al.* Management of menopause symptoms with acupuncture: An umbrella

- systematic review and meta-analysis. J Altern Complement Med (New York, NY) 2018;24:314-23.
- 111. Wen C, Liu Y, Pan X, Mao Z, Zhou L, Zhang H. [Manual acupuncture versus electroacupuncture for menopausal syndrome: A randomized controlled trial]. Zhongguo Zhen Jiu 2017;37:491-5.
- 112. Sandberg M, Wijma K, Wyon Y, Nedstrand E, Hammar M. Effects of electro-acupuncture on psychological distress in postmenopausal women. Complement Ther Med 2002:10:161-9.
- 113. Liu Q, Liu J, Ren C, Cai W, Wei Q, Song Y, *et al.* Proteomic analysis of tears following acupuncture treatment for menopausal dry eye disease by two-dimensional nano-liquid chromatography coupled with tandem mass spectrometry. Int J Nanomedicine 2017;12:1663-71.
- 114. El-Mekawy HS, ElDeeb AM, Ghareib HO. Effect of laser acupuncture combined with a diet-exercise intervention on metabolic syndrome in post-menopausal women. J Adv Res 2015;6:757-63.
- 115. Lu C, Yang XJ, Hu J. [Efficacy comparison between acupuncture smoothing-liver and regulating-spleen method and regulating Governor Vessel method for menopausal insomnia]. Zhongguo Zhen Jiu 2014;34:759-62.
- 116. Kou ST. [Efficacy comparison of menopausal irritability between acupuncture and medication: A randomized controlled trial]. Zhongguo Zhen Jiu 2014;34:455-8.
- 117. Chiu H-Y, Pan C-H, Shyu Y-K, Han B-C, Tsai P-S. Effects of acupuncture on menopause-related symptoms and quality of life in women in natural menopause: A meta-analysis of randomized controlled trials. Menopause 2015;22:234-44.
- 118. Cohen SM, Rousseau ME, Carey BL. Can acupuncture ease the symptoms of menopause? Holist Nurs Pract 2003;17:295-9.
- 119. Avis NE, Coeytaux RR, Isom S, Prevette K, Morgan T. Acupuncture in menopause (AIM) study: A pragmatic, randomized controlled trial. Menopause 2016;23:626-37.
- 120. Borud EK, Alraek T, White A, Fonnebo V, Eggen AE, Hammar M, *et al.* The acupuncture on hot flushes among menopausal women (ACUFLASH) study, A randomized controlled trial. Menopause 2009;16:484-93.
- 121. Armand M, Ozgoli G, Giti RH, Majd HA. Effect of Acupressure on early complications of menopause in women referring to selected health care centers. Iran J Nurs Midwifery Res 2017;22:237-42.
- 122. Schacht E. Rationale for treatment of involutional osteoporosis in women and for prevention and treatment of corticosteroid-induced osteoporosis with alfacalcidol. Calcif Tissue Int 1999:65:317-27.
- 123. Askari F, Basiri MK, Basiri MM, Torabi S, Gholamfarkhani S, Mohareri M, *et al.* Age of natural menopause and the comparison of incidence of its early complications in menopause transition stages in women from Gonabad city. OFOGH-E-DANESH 2012;17:42-8.
- 124. Tsay SL, Chen HL, Chen SC, Lin HR, Lin KC. Effects of reflexotherapy on acute postoperative pain and anxiety among patients with digestive cancer. Cancer Nurs 2008;31:109-15.
- 125. Ahmadinezhad M, Kargar M, Vizeshfar F, Hadianfard MJ. Comparison of the effect of acupressure and pilates-based exercises on sleep quality of postmenopausal women: A Randomized controlled trial. Iran J Nurs Midwifery Res 2017;22:140-6.
- 126. Abedian Z, Eskandari L, Abdi H, Ebrahimzadeh S. The effect

- of acupressure on sleep quality in menopausal women: A randomized control trial. Iran Med Sci 2015:40:328-34.
- 127. Jokar A, Zynali F, Akbarzade M, Zare N. Comparison of the effects of acupressure at Yong Quan (KI-1) and hegu (LI-4) acupoints on hot flashes in menopaus: Clinical trial. J Zanjan Univ Med Sci Health Serv 2017;25:1-10.
- 128. Kung Y-Y, Yang CCH, Chiu J-H, Kuo TBJ. The relationship of subjective sleep quality and cardiac autonomic nervous system in postmenopausal women with insomnia under auricular acupressure. Menopause 2011;18:638-45.
- 129. Taylor M. Botanicals: Medicines and menopause. Clin Obstet Gynecol 2002;44:853-63.
- 130. Breinholt V, Hossaini A, Svendsen GW, Brouwer C, Nielsen S. Estrogenic activity of flavonoids in mice. The importance of estrogen receptor distribution, metabolism and bioavailability. Food Chem Toxicol 2000;38:555-64.
- 131. Tamaya T. Phytoestrogens and reproductive biology. Reprod Med Biol 2005;4:225-9.
- 132. Hakimi S, Mohammad Alizadeh S, Delazar A, Abbasalizadeh F, Bamdad Mogaddam R, Siiahi M, *et al.* Probable effects of fenugreek seed on hot flash in menopausal women. J Med Plants 2006;3:9-14.
- 133. Abdallah Izaz, Khattab HA, Sawiress FA, El-Banna RA. Effect of Salvia Officinalis L.(Sage) herbs on osteoporotic changes in aged non-cycling female rats. Med J Cairo Univ 2010;78:1.
- 134. Lobo R. Treatment of the Post Menopausal Women. 2nd *ed*. Philadelphia: Williams and Wilkings. 2007; p. 315-28.
- 135. Pachman DR, Jones JM, Loprinzi CL. Management of menopause-associated vasomotor symptoms: Current treatment options, challenges and future directions. Int J Womens Health 2010;2:123-35.
- 136. Allahtavakoli M, Honari N, Pourabolli I, Kazemi Arababadi M, Ghafarian H, Roohbakhsh A, *et al.* Vitex agnus castus extract improves learning and memory and increases the transcription of estrogen receptor alpha in hippocampus of ovariectomized rats. Basic Clin Neurosci 2015;6:185-92.
- 137. Huntley A, Ernst E. A systematic review of the safety of black cohosh. Menopause 2003;10:58-64.
- 138. Chenoy R, Hussain S, Tayob Y, O'Brien P, Moss M, Morse P. Effect of oral gamolenic acid from evening primrose oil on menopausal flushing. Bmj 1994;308:501-3.
- 139. Nasr A, Nafeh H. Influence of black cohosh (Cimicifuga racemosa) use by postmenopausal women on total hepatic perfusion and liver functions. Fertil Steril 2009;92:1780-2.
- 140. Stevinson C, Huntley A, Ernst E. A systematic review of the safety of kava extract in the treatment of anxiety. Drug Saf 2002;25:251-61.
- 141. Huntley AL, Ernst E. A systematic review of herbal medicinal products for the treatment of menopausal symptoms. Menopause 2003;10:465-76.
- 142. Wooltorton E. Brief safety updates: Acetaminophen, ASA and kava. CMAJ 2002;167:1034.
- 143. Ghazanfarpour M, Sadeghi R, Roudsari RL, Khadivzadeh T. Effects of flaxseed and Hypericum perforatum on hot flash, vaginal atrophy and estrogen-dependent cancers in menopausal women: A systematic review and meta-analysis. Avicenna J Phytomed 2016;6:273-83.
- 144. Etemadrezaei F, Shariati Sarabi J, Hateffard M, Soltanifar A, Rahmani S. Frequency of osteoporosis and osteopenia in post-menopausal women in Mashhad City, between 1389-1390. Med J Mashhad Univ Med Sci 2014;56:369-75.