



# Complementary and Alternative Medicine for Menopause

Alisa Johnson, PhD<sup>1</sup>, Lynae Roberts, MA<sup>1</sup>, and Gary Elkins, PhD<sup>1</sup>

## Abstract

Menopause is associated with problematic symptoms, including hot flashes, sleep problems, mood disorders, sexual dysfunction, weight gain, and declines in cognitive functioning. Many women seek complementary and alternative medicine (CAM) for symptom management. This article critically reviews the existing literature on CAM treatments most commonly used for menopausal symptoms. Electronic searches were conducted to identify relevant, English-language literature published through March 2017. Results indicate that mind and body practices may be of benefit in reducing stress and bothersomeness of some menopausal symptoms. In particular, hypnosis is a mind-body intervention that has consistently shown to have a clinically significant effect on reducing hot flashes. Evidence is mixed in regard to the efficacy of natural products and there are some safety concerns. Health care providers should consider the evidence on CAM in providing an integrative health approach to menopausal symptom management.

## Keywords

complementary and alternative medicine, hot flashes, menopause, symptoms, review

Received October 17, 2017. Accepted for publication January 21, 2019.

Menopause occurs naturally in most women between ages 45 and 52 years and is marked by changes in hormonal status and the cessation of the menstrual cycle.<sup>1,2</sup> Approximately 1.2 billion women worldwide will be menopausal or postmenopausal by the year 2030, with 47 million new entrants each year.<sup>3</sup> More than 85% of these women will experience problematic symptoms, including hot flashes, night sweats, sleep disturbances, sexual dysfunction, mood disorders, weight gain, and cognitive declines.<sup>1,4</sup>

Vasomotor symptoms (VMS; eg, hot flashes and night sweats) are the primary symptoms of menopause. VMS affect more than 80% of women in menopause and are the menopause symptoms for which most women seek treatment.<sup>5</sup> In the United States, 40 to 50 million women suffer from VMS.<sup>6</sup> These symptoms typically last 5 to 7 years, but can persist for 15 years or more.<sup>7,8</sup> VMS are associated with sleep and mood disturbances, as well as decreased cognitive function and reduced quality of life.<sup>6</sup>

Hormone therapy has been the primary treatment for menopausal symptoms. However, because of the health risks associated with hormone therapy, many women cannot or choose not to use hormone therapy.<sup>9-11</sup> Approximately 51% of women use CAM and more than 60% perceive it be effective for menopausal symptoms.<sup>9</sup> However, the majority of women using

CAM do not discuss it with their health care providers.<sup>9</sup> Women often report feeling confused about their options and rely on the internet as their primary source of information.<sup>11,12</sup> It is imperative that physicians engage in shared decision making with women regarding treatment options, including CAM, for menopausal symptoms. This type of patient-centered integrated approach can potentially reduce the risk for under treatment and adverse events.

The purpose of this article is to critically review the most popular CAM interventions for menopausal symptoms. CAM interventions for menopause fall into 2 broad categories: mind-body practices (eg, hypnosis, cognitive behavioral therapy [CBT], relaxation, biofeedback, meditation, and aromatherapy), and natural products (eg, herbs, vitamins, minerals, and dietary supplements). In addition, there are several whole system alternative medicine approaches (eg, traditional Chinese medicine, reflexology, acupuncture, and homeopathy) that do

<sup>1</sup> Baylor University, Waco, TX, USA

## Corresponding Author:

Gary Elkins, PhD, Department of Psychology and Neuroscience, Baylor University, PO Box 97334, Waco, TX 76798-7334, USA.  
Email: gary\_elkins@baylor.edu



not fit neatly into the above categories that incorporate both mind-body practices and natural products.<sup>13</sup>

## Methods

### Literature Search

Literature sources were identified from an electronic search of the following databases: MEDLINEplus, HealthSource: Nursing/Academic, PsycINFO, PsycARTICLES, PubMed, and Cumulative Index of Nursing and Allied Health Literature and (CINAHL) and a hand search of references of relevant papers. Search terms included complementary and alternative medicine, CAM, menopause, menopausal symptoms. In addition, specific CAM treatments and menopausal symptoms were searched. The search terms were customized for each database to optimize results.

### Study Eligibility

All resulting abstracts were reviewed independently by 2 authors (AJ and LR) to determine if the articles met the inclusion criteria. The full texts of the studies meeting eligibility requirements were retrieved.

### Inclusion Criteria

This critical review included randomized controlled trials (RCTs) with a sample size of at least 10 (including randomized pilot studies), or systematic reviews, that were published in the English language, in peer-reviewed journals on or before March 31, 2017 that reported on complementary and alternative medicine for menopause symptoms. Observational, uncontrolled, nonrandomized, or case studies were not considered in this critical review.

### Interventions

Complementary and alternative medicine has been categorized as mind-body practices (eg, hypnosis, CBT, relaxation, biofeedback, meditation, aromatherapy), natural products (eg, herbs, vitamins, minerals, dietary supplements), and whole-system approaches (eg, traditional Chinese medicine, reflexology, acupuncture, homeopathy).<sup>13</sup> Trials that investigated at least one of these interventions for menopausal symptoms were included.

### Outcome Measures

Studies that included symptoms of menopause (eg, vasomotor, depression, sleep disturbance) as the primary outcome were included. The most commonly investigated menopausal symptoms are vasomotor symptoms (eg, hot flashes, hot flushes, night sweats). This is not surprising since vasomotor complaints are the primary symptoms women seek treatment for during the menopause transition.<sup>5</sup> The placebo effect has been demonstrated to reduce hot flashes on average in RCTs by 25%,<sup>14,15</sup> and previous research indicates a 50% reduction in hot flash frequency to be a clinically meaningful change.<sup>16</sup> Hot flashes can be measured through subjective reports and physiological monitoring. However, subjective and objective measures may not be reliably comparable. The method of hot flash measurement is noted where appropriate.

## Mind-Body Interventions for Menopause Symptoms

### Hypnosis

Hypnosis, a mind-body therapy that involves a deeply relaxed state of focused attention, individualized mental imagery, and suggestion,<sup>17</sup> has been investigated for menopausal symptom management. Two randomized clinical trials of 5 sessions of hypnotherapy for hot flashes among breast cancer survivors demonstrated a clinically meaningful ( $\geq 69\%$ ) reduction in hot flash severity and frequency.<sup>18,19</sup> These results are comparable to pharmacological interventions.<sup>20</sup> In an RCT of 187 women,<sup>21</sup> hypnosis was compared with an active structured attention control and found to significantly reduce subjective hot flash frequency (74%) and interference (80%), and physiologically monitored hot flashes (57%). In addition, hypnosis improved self-reported sleep quality and sexual function.<sup>21,22</sup> In a recent pilot study,<sup>23</sup> 71 women were randomized to 1 of 4 groups: venlafaxine 75 mg + hypnosis, venlafaxine 75 mg + sham hypnosis, placebo pill + hypnosis, and placebo pill + sham hypnosis. Hypnosis alone was as effective (50% reduction) as venlafaxine 75 mg alone in reducing hot flash score (frequency  $\times$  severity). The placebo group reported a 25% reduction. Hypnosis has been recommended by the North American Menopause Society, and others, for the treatment of menopausal symptoms and poses little risk.<sup>24,25</sup>

### Cognitive Behavioral Therapy

CBT is an action-oriented psychological intervention that has been used to treat hot flashes, depression, and other menopausal symptoms. CBT is a time-limited treatment that focuses on changing cognitive appraisals and behavior choices to alter symptoms. CBT may include education, motivational interviewing, relaxation, paced breathing, and other strategies to improve symptoms.<sup>26</sup> Mann et al<sup>26</sup> compared the effects of a 6-week CBT intervention to usual care (eg, standard follow-up care) among 96 female breast cancer survivors and found hot flash interference was reduced on average 52%. Women receiving usual care reported a 25% decrease in hot flash interference. Hot flash frequency was reduced by 38% in both groups, 38% indicating CBT was no better than usual care for reducing the frequency of hot flashes.<sup>26</sup> In a second RCT, 65% of women receiving a 4-week CBT intervention and 21% of a no-treatment control group, reported clinically significant improvements (eg, 2-point change on a 10-point numerical rating scale) in hot flash interference.<sup>27</sup> CBT did not demonstrate a clinically significant reduction (eg, 50%) in hot flash frequency.<sup>27</sup> Both of these trials used objective and subjective measures for hot flash frequency.<sup>26,27</sup>

In a pilot study of 39 women randomized to CBT or waitlist control, there was a statistically significant reduction in hot flash distress, but not in interference or frequency of hot flashes/night sweats, in the immediate treatment group.<sup>28</sup> The authors reported a 48% positive treatment effect for the 17 women who completed the CBT program, but it is unclear how

that effect was calculated.<sup>28</sup> In addition, there is some evidence to suggest that CBT may reduce mild depression in menopause comparable to placebo.<sup>27,29</sup> To date, no RCTs of CBT have demonstrated clinically significant improvements in hot flash frequency, but may be beneficial in reducing hot flash distress and interference and other psychological symptoms (eg, depression) associated with menopause. CBT has been recommended by the North American Menopausal Society for reducing the bothersomeness of vasomotor symptoms, but not for frequency.<sup>24</sup>

### *Biofeedback and Relaxation Training*

Biofeedback and relaxation techniques may include progressive muscle relaxation, relaxation combined with thermal control biofeedback training, paced respiration, at-home relaxation audiotapes, and applied relaxation, and have been used to treat menopausal symptoms. Biofeedback uses a device to monitor bodily functions that are normally automatic (eg, skin temperature, heart rate, or muscle tension) and provides “feedback” to the patient. Feedback and relaxation techniques (eg, guided imagery, deep breathing, and paced respiration) are then used to control stress responses. In a systematic review of psychoeducational interventions to relieve hot flashes,<sup>30</sup> reviewers identified 7 randomized trials<sup>31-37</sup> that compared relaxation with an active (eg, reading,  $\alpha$ -electroencephalography, hormone therapy) or no-treatment control. Five of the trials<sup>31,32,34-36</sup> reviewed indicated relaxation techniques (eg, paced respiration, progressive muscle relaxation) may reduce the frequency of hot flashes and improve psychological symptoms of menopause. However, the authors caution about drawing conclusions due to the low study quality and small sample sizes.<sup>30</sup> In a second systematic review and meta-analysis<sup>38</sup> of relaxation techniques for menopausal symptoms, 4 studies,<sup>31,34,39,40</sup> (2 of which<sup>31,34</sup> were included in the previous review<sup>30</sup>), were identified that compared relaxation with a control (eg, no treatment, placebo, superficial needling) for the reduction of menopausal symptoms. Researchers concluded that relaxation techniques may have a positive benefit on vasomotor symptoms and stress, yet due to low-quality evidence and inconsistent findings, relaxation techniques could not be recommended at this time.<sup>38</sup> Because of the considerable overlap in studies reviewed, effect sizes are not reported.

Three RCTs not reported in the above systematic reviews also indicate inconsistent support for relaxation techniques on menopause symptoms. In a recent RCT comparing applied relaxation with wait-list control, women receiving immediate treatment reported a 55% reduction in hot flash frequency at 12 weeks.<sup>41</sup> However, findings from a second RCT comparing paced respiration with music listening among 123 women, did not indicate clinically significant improvements in hot flash frequency for either intervention.<sup>42</sup> A third RCT comparing paced breathing with regular breathing (control) found all groups reported reductions (paced breathing 2×/day = 52%; paced breathing 1×/day = 42%; usual breathing = 46%) in hot flashes over 9 weeks.<sup>43</sup> Relaxation may provide benefit for

menopausal symptoms, yet more evidence is needed to draw conclusions.

### *Mindfulness-Based Stress Reduction*

Mindfulness-based stress reduction (MBSR) uses a variety of exercises (eg, acceptance, mindfulness meditation, and yoga) to develop awareness and acceptance of the present moment. MBSR usually involves 8 weekly group classes lasting 1.5 hours each, an all-day weekend retreat, and daily at-home practice. To our knowledge, only 1 RCT of MBSR for menopause has been conducted.<sup>44</sup> A total of 110 women were randomized to either MBSR intervention or wait-list controlled and measured on hot flash bothersomeness, hot flash intensity, quality of life, anxiety, and stress. Changes in hot flash bothersomeness and intensity failed to show clinically significant improvements. However, there was a clinically meaningful improvement (1.0) in menopause-related quality of life<sup>45</sup> and sleep quality. Perceived stress and anxiety resumed normative values in the MBSR group following treatment. MBSR is generally safe and may reduce stress and anxiety and improve sleep quality and quality of life, but does not appear to significantly reduce VMS. More research is needed to verify these effects.

### *Yoga*

Yoga originates from Hindu disciplines, but many different forms of yoga have appeared as the popularity has grown globally. Because of a branching off of many different styles, yoga practices can vary (eg, intensity level, temperature of the session, specific props used). All practices generally involve physical poses or movement sequences, conscious regulation of breathing, and mindfulness techniques to increase present awareness or positivity.<sup>46</sup>

A systematic review and meta-analysis<sup>47</sup> including 5 RCTs<sup>48-52</sup> concluded that there was moderate evidence for the short-term effects of yoga on psychological symptoms in menopause. However, there was no evidence found for the improvement of VMS, somatic, urogenital, or total menopausal symptoms and the reviewers caution that more rigorous studies are needed to support the evidence for yoga on psychological menopausal symptoms.<sup>47</sup>

Additional RCTs have been conducted that indicate yoga maybe beneficial for psychological symptoms and fatigue related to menopause. However, the evidence to support the use of yoga for other menopausal symptoms is inconsistent. Among 40 women randomized to either a 12-week yoga and meditation intervention or usual care, Cramer et al<sup>53</sup> found that yoga significantly ( $P < .05$ ) reduced menopause symptoms (Menopause Rating Scale), improved fatigue, and quality of life compared with usual care. Reed and colleagues<sup>54</sup> found that VMS, sexuality, and total scores on the Menopausal Quality of Life Questionnaire (MENQOL) were statistically significantly improved in the yoga group compared with usual activity ( $P < .05$ ). In contrast, an RCT comparing yoga with

exercise or usual activity did not show improvements in VMS frequency or bother from baseline to endpoint in the intervention groups.<sup>55</sup>

There is high variability between studies assessing the use of yoga for various ailments, which makes conclusions about efficacy difficult. These inconsistencies are mostly because of the branching off of many yoga types which vary in the level of importance given to the spiritual and physical elements of yoga.<sup>46</sup> The consensus from the compilation of research seems to be that yoga is safe and may be effective for psychological symptoms. More research is needed to determine its effects on VMS and other menopausal symptoms.

### Aromatherapy

Aromatherapy, also referred to as essential oil therapy, uses naturally extracted aromatic essences from plants to treat various physiological and psychological imbalances. The scented oils are believed to reduce anxiety and increase relaxation, which may be beneficial in easing stressful menopausal symptoms.<sup>56</sup>

Chien and colleagues<sup>56</sup> found 12 weeks of lavender inhalation to improve self-reported sleep compared with health education control. In a double-blinded 12-week clinical crossover trial of 100 women, lavender essential oil reduced hot flash frequency by 50% compared with <1% reduction in the placebo (diluted milk) control, demonstrating a clinically significant difference.<sup>57</sup> Three additional RCTs<sup>58-60</sup> of aromatherapy combined with massage, found aromatherapy massage to be more beneficial than massage alone or a control in reducing physical (eg, VMS) and psychological (eg, depression) symptoms.

The addition of aromatherapy to other CAM interventions may provide additional symptom relief. However, there is insufficient evidence to support aromatherapy as a stand-alone treatment for menopausal symptom management.

## Herbal Products, Vitamins, and Supplements

### Black Cohosh (*Cimicifuga racemosa*)

Black cohosh, is a widely studied phytopharmaceutical North American plant that has been used historically as an indigenous treatment for menopausal symptoms. The rhizome is harvested in fall and may be used in fresh or dried form. Multiple RCTs have been conducted to determine the effects of *Cimicifuga racemosa* on menopausal symptoms. In a systematic review<sup>61</sup> of 16 RCTs<sup>62-77</sup> (n = 2027) that measured the effects of oral monopreparations of *C racemosa* on menopausal symptoms, including VMS, sexual dysfunction, vulvovaginal symptoms, bone health, and quality of life, researchers concluded that there was insufficient evidence to support the use of black cohosh for menopausal symptoms at this time, but that there was sufficient evidence to warrant further investigations.<sup>61</sup> Among the studies included there was no significant difference between the intervention and placebo in the frequency of hot flashes or in menopausal symptom scores. The reviewers concluded that because of large study heterogeneity, pooling of the

results was not possible and that more high-quality RCTs were necessary before recommending *C racemosa* for menopausal symptoms.<sup>61</sup>

In an RCT comparing isopropanolic black cohosh extract in combination with ethanolic St John's wort with placebo among 301 women, scores on the Menopause Rating Scale decreased by 50% in the treatment group compared to 19% in the placebo group.<sup>78</sup> Depression also significantly decreased compared with placebo,  $P < .001$ .<sup>78</sup> In a second RCT comparing the effects of black cohosh plus St John's wort (GYNO-Plus), scores on the Kupperman Index showed significant improvements ( $p < .001$ ) in the treatment group compared with placebo.<sup>79</sup> However, it is difficult to conclude from these studies if black cohosh is beneficial in itself or only in combination with other herbs. More research is needed using standardized preparations. Side effects of black cohosh may include: gastrointestinal problems, rash, and acute hepatitis.<sup>12,17,61</sup>

### Wild Yam (*Dioscorea*)

Wild yam is a tuber that has been historically used in traditional Chinese medicine to treat multiple symptoms, including symptoms of menopause.<sup>80</sup> However, there is limited and inconsistent evidence for the effects of wild yam on menopause symptoms. In a double blind, placebo controlled, cross-over study, wild yam cream was no better than placebo in reducing menopause symptoms, or improving levels of estrogen or progesterone.<sup>81</sup> In contrast, a RCT of 50 women consuming 12 mg of *Dioscorea alata* (ie, purple yam) extract twice daily reported significant improvements (90%) in menopause symptoms (primarily psychological) compared with the placebo group (70%) as measured by the Greene Climacteric Scale.<sup>82</sup> The authors note that sexual functioning symptoms did not show the same levels of improvement.<sup>82</sup> Because of the small number of studies and insufficient information regarding long-term safety,<sup>83</sup> more research is needed in order to determine the efficacy of wild yam for menopause symptoms.

### Dong Quai (*Angelica sinensis*)

Dong quai is a traditional Chinese herb that is most often used in combination with other herbs to treat female reproductive problems.<sup>84</sup> It is extracted from the root *Angelica sinensis* and administered in herbal preparations. In an RCT investigating the effects of Dong quai on vaginal cells, endometrial thickness, and menopausal symptoms among 71 women, Dong quai was not superior to placebo for the reduction of menopausal symptoms (including VMS) and did not show any estrogenic effects in endometrial tissues or vaginal cells.<sup>85</sup> In an RCT comparing a combined preparation of *A sinensis* and *Matricaria chamomilla* (ie, Climex), to placebo among 55 women reporting hot flashes and refusing hormone therapy, the herbal preparation demonstrated clinically significant improvement in the frequency and intensity of hot flashes (90%-96%) compared with placebo (15%-20%) over the 3-month trial.<sup>86</sup> In a double-blind, placebo-controlled RCT, *A sinensis* was

combined with other herbs (ie, black cohosh, milk thistle, red clover, American ginseng, chaste-tree berry; Phyto-Female Complex), and tested among 50 healthy women. At 12 weeks, participants receiving the herbal preparation reported a 73% decrease in hot flushes and a 69% decrease in night sweats, compared with 38% and 29% improvement in the placebo group, respectively.<sup>87</sup> The treatment group also reported greater improvements in sleep quality.<sup>87</sup> However, it is difficult to determine the effects of *A sinensis* from these 2 trials due to the use of combined preparations. Dong quai may be effective only in combination with other herbs. In addition, important safety concerns exist regarding *A sinensis*, including interactions with other medications and herbs, photosensitization, anticoagulation, and possible carcinogenicity.<sup>24,88</sup> Further investigations into the efficacy and safety of Dong quai are needed.

### **Maca (*Lepidium meyenii*)**

Maca, a plant native to South America, of the brassica family has been used for centuries in Andean cultures as a treatment for anemia, infertility, and female hormone balance. A recent systematic review<sup>89</sup> found 4 RCTs<sup>90-92</sup> (2 were contained in 1 publication,<sup>91</sup> [n = 202], testing the effects of maca in healthy women during various stages of menopause. Three studies used pregelatinized maca,<sup>91,92</sup> and 1 study used dried maca.<sup>90</sup> All studies employed a placebo control for comparison. Each of these trials indicated favorable effects of maca on menopausal symptoms as measured by the Greene Climacteric Scale and the Kupperman Index compared with placebo. However, the reviewers concluded that despite initial evidence for the benefits of maca, findings were limited by the small number of trials and lack of safety information. More data are needed to determine the efficacy and safety of maca for menopausal symptoms.

### **Pollen Extract**

Pollen extract, made from flower pollen and sold under the brand names Serelys, Femal, Femalen, and Relizen, has not been sufficiently tested to determine efficacy or safety. One small RCT of pollen extracts for menopause symptoms was identified.<sup>93</sup> Fifty-four women randomized to either Femal or placebo completed the 12-week trial. Menopause symptoms were measured using the Menopause Rating Scale and diaries. Women taking Femal reported a 22% (Menopause Rating Scale) and 27% (diary) reduction in hot flashes at 12 weeks. The placebo group reported a 4% increase in frequency of hot flashes at 12 weeks. Though there were superior improvements for the active treatment group in all symptom categories (eg, VMS, tiredness, dizziness, mood, quality of life), these improvements did not reach clinical significance.<sup>93</sup> An animal study of Femal has indicated that the extract does not act estrogenically and could be a safe alternative to hormone therapy.<sup>94</sup> However, more studies are needed to clarify the effectiveness of pollen extract for menopausal symptoms.

### **Evening Primrose Oil (*Oenothera biennis*)**

Evening primrose oil (EPO), the oil from the seed of the evening primrose plant, contains essential omega-6 fatty acids and has been used to treat multiple inflammatory diseases and women's health conditions. In an RCT comparing the effects of EPO to placebo on VMS, Chenoy et al<sup>95</sup> reported that 4 g/d of EPO for 6 months was no better than placebo for reducing hot flushing. There were no significant improvements demonstrated in either group.<sup>95</sup> In a recent RCT comparing 500 mg of EPO daily to placebo on VMS, hot flash frequency was reduced by 39% (EPO) and 32% (placebo) after 6 weeks. Hot flash severity and duration decreased by 42% (EPO) and 32% (placebo) and 19% (EPO) and 18% (placebo), respectively. While the differences between EPO and placebo were statistically significant, improvements in the treatment group were not clinically meaningful.<sup>96</sup> Two RCTs<sup>97</sup> have been conducted to investigate the effects of EPO on bone mineral density loss in premenopause and post menopause. Both groups of participants (pre- and postmenopause) were randomized to receive EPO (4.0 g) in combination with marine fish oil (440 mg) and calcium (1.0 g) (ie, Efacal) compared with calcium (1.0 g) alone. All participants, irrespective of treatment or menopause phase, showed significant increases (1%) in bone mineral density. The supplement Efacal was not significantly better than calcium alone for increasing bone mineral density.<sup>97</sup> There is not enough evidence to support the use of EPO for menopausal symptoms at this time.

### **Phytoestrogens**

Phytoestrogens are nonsteroidal plant-derived compounds commonly sourced from soy and red clover (*isoflavones*), flaxseed (*lignans*), and hops (*Humulus lupulus*). Phytoestrogens are thought to act estrogenically or anti-estrogenically in humans.<sup>98,99</sup> Soy and red clover contain large amounts of the isoflavones genistein and daidzein that may produce estrogen like effects. Hops contain the phytoestrogen 8-prenylnaringenin (8-PN), which is thought to be a more potent phytoestrogen than soy isoflavone.<sup>100,101</sup> In a systematic review and meta-analysis<sup>102</sup> of phytoestrogens for VMS among peri- and postmenopausal women, researchers identified 43 RCTs, including one unpublished trial, that tested the effectiveness of dietary soy,<sup>103-115</sup> soy extracts<sup>116-126</sup> (Bicca et al., unpublished data), red clover extracts,<sup>127-134</sup> genistein extracts,<sup>135-138</sup> natural S-Equol,<sup>139</sup> flaxseed,<sup>109,140</sup> *Rheum rhabdiponticum* extract,<sup>141</sup> and hop extract,<sup>142</sup> for at least 12 weeks.<sup>102</sup> The majority of studies were too heterogeneous to be combined in the meta-analysis. Of the 43 RCTs, 5 trials investigating the effects of red clover extract (Promensil) on VMS<sup>127,131-134</sup> were pooled for the meta-analysis. Results indicated that red clover extract did not significantly improve VMS symptoms compared to placebo. The authors of this review concluded that the evidence was did not support the use of

phytoestrogens to reduce the frequency or severity of VMS at the time, but did recommend further investigation of genistein for menopausal symptoms.<sup>102</sup>

In a recent RCT (not included in the previous review<sup>102</sup>), women administered dried red clover leaves (40 mg) for 12 weeks reported significant improvements in menopausal symptoms (10-point mean reduction on the Menopause Rating Scale), compared with placebo.<sup>143</sup> Other RCTs of phytoestrogens show mixed results. In an RCT of 102 women receiving 12 months of isoflavones compared with placebo, there were no significant reductions in hot flashes over the course of the study.<sup>144</sup> Participants in both groups (isoflavones and placebo) reported increases in hot flashes.<sup>144</sup> In addition, Van Patten et al<sup>145</sup> found that 12 weeks of isoflavones (90 mg) did not show clinically meaningful improvements in hot flash frequency. Among the 64 breast cancer survivors receiving isoflavones, there was a 25% reduction in hot flash frequency compared with the 33% reduction reported in the placebo group (n = 59).<sup>145</sup> Two RCTs investigating the effects of isoflavones to placebo did not demonstrate isoflavones to be superior to placebo in reducing scores on the Kupperman Index.<sup>146,147</sup> In contrast, an RCT comparing the effects of isoflavones to placebo among 51 women did demonstrate a clinically meaningful reduction of hot flashes (57%) after 6 months of treatment (60 mg) compared with placebo (18%).<sup>148</sup> Phytoestrogens appear to be safe for 12 months of continuous use,<sup>102</sup> yet the evidence to support efficacy is inconsistent. Therefore, more RCTs using standardized methods that will allow for study comparison are needed in order to draw definitive conclusions regarding the use of phytoestrogens for menopausal symptoms.

### Vitamin E

Vitamin E is a fat-soluble vitamin thought to act as an antioxidant in the body. There are anecdotal accounts of the benefits of vitamin E for menopausal symptoms. However, few RCTs have been conducted to investigate the use of vitamin E for menopause symptom reduction. In a crossover trial of 120 women receiving 800 IU of vitamin E followed (4 weeks) by placebo (4 weeks) or vice versa,<sup>149</sup> participants reported a decrease of 1 hot flash per day with vitamin E. The authors concluded this was not a clinically meaningful difference.<sup>149</sup> In a similar randomized crossover trial, 50 women taking 400 IU of vitamin E followed by placebo or vice versa for 4 weeks each, participants showed a reduction of about 2 hot flashes per day and reduced hot flash severity with vitamin E.<sup>150</sup> In an RCT comparing the effects of gabapentin to vitamin E among 115 women for VMS reduction, hot flush frequency and score decreased by 10.02% and 7.28%, respectively in the vitamin E group.<sup>151</sup> At this time there is an insufficient amount of empirical evidence to conclude the effectiveness of vitamin E supplementation for menopausal symptoms.

## Whole System Alternative Medicine Approaches

### Reflexology

Reflexology is a specific type of massage performed on the feet and hands that is believed to stimulate corresponding glands and organs. The principle behind reflexology states that there are reflex points on the hands and feet that correspond to certain body zones, and when pressure is applied to these points, disease-causing energy blockages are eliminated from the corresponding body zone.

Only 2 RCTs have examined the use of reflexology for menopausal symptoms. Both studies compared reflexology with a nonspecific foot massage control. Williamson and colleagues<sup>152</sup> found no significant differences between nonspecific foot massage and reflexology on symptoms of anxiety, depression, and VMS. However, in a more recent RCT of 120 women randomized to reflexology or nonspecific foot massage control, VMS, and sexual dysfunction symptoms (MENQOL) were significantly improved among women receiving foot reflexology compared to control ( $P < .001$ ).<sup>153</sup> Hot flash frequency reduced by 56% after 12 twice-weekly reflexology sessions.<sup>153</sup>

Because of the small number of RCTs and inconsistent findings, more research is needed to determine the efficacy of reflexology for menopausal symptoms.

### Homeopathy

Homeopathic practitioners (homeopaths) subscribe to the principle that "like cures like." Patients are given dilutions of natural substances that would be harmful to a person in ideal health. Some commonly used preparations include sepia (from cuttlefish ink), lachesis (from venom of the South American Bushmaster), and pulsatilla (from a flower of the same name).<sup>154</sup> Individualized formulas are prepared to treat presenting symptoms.<sup>155</sup>

One study (n = 223)<sup>156</sup> found homeopathy may be beneficial in reducing distress in climacteric years. However, a review of homeopathic approaches for menopause showed no convincing evidence for the efficacy of homeopathy in menopause.<sup>155</sup> The National Health Interview Survey<sup>157</sup> found that almost 5 million adults and children used homeopathy for various reasons in the previous year, so this is a therapy that needs to be evaluated further for efficacy and safety.

### Acupuncture

Acupuncture techniques come from traditional Chinese medicine and involve insertion of small needles into the skin at certain points on the body, which are called acupoints. The foundation of acupuncture is a belief that diseases and symptoms occur because of disruptions in an individual's qi, or life force energy.

There have been several RCTs of traditional acupuncture for various menopausal symptoms, some of which are noted in the

section on traditional Chinese medicine because of their combination with additional modalities. Four trials found no significant difference between acupuncture and placebo of superficially placed needles or needling at non-acupoints.<sup>158-161</sup> One study found that an acupuncture plus auricular acupressure intervention was not significantly better than a hormone replacement control at improving hot flash severity.<sup>162</sup> Six trials showed that acupuncture could improve vasomotor, sleep, or somatic symptoms more significantly than placebo.<sup>40,163-167</sup>

An additional acupuncture technique that has been studied for use in menopause is electroacupuncture, which includes the passing of a small electrical current between acupuncture needles. Three trials assessed the use of electroacupuncture. One study found significant improvements in mood only.<sup>168</sup> Two studies found no significant difference from placebo.<sup>169,170</sup>

More research with precise methods is needed to uncover the true efficacy and the mechanisms behind the benefit some participants receive from acupuncture.

### *Traditional Chinese and East Asian Medicine*

Traditional Chinese medicine can include the use of herbs, self-massage, acupuncture, diet, or meditative exercise (eg, Tai Chi). What ties these modalities together is the ancient technique and tenets of *qi* (life force energy) and yin and yang (harmony between opposite forces) behind their use.

A trial using a Chinese herbal medicine formula found that compared to placebo control, herbal treatment significantly improved hot flash frequency. However, hot flash reduction was larger in a third hormone replacement group.<sup>171</sup> Two trials reported no significant difference between hormone replacement therapy and Chinese herbs in reducing self-report VMS, anxiety,<sup>172</sup> and depression.<sup>173</sup> Another study using Japanese traditional medicine found greater improvement in VMS and psychological symptoms for a Paroxetine control than with herbal treatment.<sup>174</sup>

Grady and colleagues<sup>175</sup> found that an herbal extract was significantly more effective than placebo at improving VMS frequency, VMS severity, and sexual functioning. Wiklund et al<sup>176</sup> reported significant improvement in depression or QOL over placebo, but no difference for VMS. Other trials reported that Chinese herbs were significantly more effective than placebo at improving self-report menopause symptom improvement,<sup>177,178</sup> tension, and insomnia,<sup>82</sup> but no improvement of self-report hot flashes specifically.<sup>178</sup>

One RCT used acupuncture paired with traditional Chinese medicine (diet therapy and Tuina self-massage) and found that this combination significantly improved hot flash frequency, irritability, and sleep problems from baseline to endpoint and significantly greater than a waitlist control.<sup>179</sup> Several RCTs found no significant difference between Chinese medicinal herbs and placebo in hot flash severity, hot flash frequency, sleep quality, or menopause related quality of life.<sup>85,180-183</sup>

While there is some evidence that traditional Chinese medicine can be effective in relieving menopausal symptoms, there

are mixed findings overall. In addition, the heterogeneity among studies makes drawing conclusions difficult. As is the case for many other CAM modalities, it is inherently difficult to conduct controlled research of a treatment that is focused on individualization and techniques based on ancient beliefs. Patterns explaining which modalities work best for which symptoms remain unclear.

### **Author Perspectives**

Existing research indicates that mind-body interventions such as relaxation, mindfulness, and CBT therapy can reduce stress and bothersomeness associated with menopausal symptoms. Hypnosis intervention for hot flashes has been shown to result in a clinically significant reduction (ie, 50% or more) in hot flashes and associated symptoms. However, hypnosis for hot flashes is not widely available, thus limiting accessibility. Mind-body interventions have few negative side effects and seem to provide safe treatment options worthy of consideration. The effects and safety of herbal preparations is difficult to ascertain due to large variations in the RCTs that have been conducted. Investigations of standardized herbal preparations may provide a path for better understanding their effects and safety. There are no herbal treatments that have demonstrated consistent clinically meaningful benefits for menopausal symptoms. This lack of consistent evidence may not be due to the ineffectiveness of the treatments, rather it may indicate the need for more rigorously conducted RCTs regarding each of these modalities on menopausal symptoms. Some CAM interventions show promise (eg, aromatherapy, acupuncture, reflexology), but lack empirical support due to the limited number of studies. Health care decisions regarding CAM therapies for menopausal symptoms can be informed by existing scientific evidence for effectiveness and safety.

There are limitations to this critical review and need to be taken into account. Though we chose to include many CAM modalities and populations (eg, various stages of menopause, cancer and natural menopause), we acknowledge that this is not an exhaustive review of all CAM options. In addition, the broad scope and study design (eg, critical review) may make drawing conclusions difficult, but it does provide the reader with a good indication of the most promising interventions and areas where more research is needed. Because the study was not a systematic review, we were unable to include effect sizes for each intervention. We did report clinical significance where available. Finally, only studies published in English were included, which may have limited the number of studies reviewed. However, this review provides an overview of the available evidence and areas of need regarding multiple CAM interventions for menopause.

### **Recommendations for Future Research**

More high-quality RCTs are needed for each CAM intervention. Among herbal products (eg, black cohosh, phytoestrogens), RCTs of standardized preparations given in consistent

methods would allow for more systematic reviews and meta-analyses of these interventions. Hypnosis is a mind-body intervention that has been shown to reduce the frequency and bothersomeness of menopausal symptoms. Future research is needed to determine optimal delivery of effective self-hypnosis training in order to achieve wider dissemination. In addition, the use of standardized protocols for other CAM interventions (eg, yoga, acupuncture) would allow for the pooling of results for meta-analyses. Researchers should consider potential mechanisms action in regard to improvements in VMS and other menopausal symptoms. Higher quality studies with larger populations are needed to determine efficacy and safety among all reviewed CAM interventions for menopausal symptoms.

## Conclusions

CAM interventions for menopause, including mind-body practices, herbal products, and other whole system alternative medicine approaches are commonly used to treat menopausal symptoms. Not all CAM interventions are efficacious and safe. It is important for women to be informed about the risks and benefits of CAM for menopausal symptoms. Women view health care providers as the most reliable sources of information on CAM interventions, but seldom seek their guidance in choosing CAM.<sup>11</sup>

Mind and body practices including hypnosis and CBT have been demonstrated to be safe for treating some of the most common and problematic symptoms of menopause (eg, vasomotor, sexual dysfunction, sleep regulation). Other mind and body practices (biofeedback, MBSR, relaxation techniques) may reduce stress and improve quality of life for women transitioning through menopause, but have not shown efficacy for specific menopausal symptoms. Hypnosis has consistent evidence for clinically significant reduction of hot flashes. However, trained practitioners are not widely available, thus limiting its use.

Herbal products are frequently used. However, there is no consistent evidence to support their efficacy and safety. There is the added concern that when used in combination with other medications, some herbal products could pose serious health risks. Vitamins and minerals may be important for women who are at risk for deficiencies, but do not seem to reduce menopausal symptoms. Physician-initiated discussions of CAM with women transitioning through menopause will help to promote an integrative model of care that will ensure the highest level of patient care.

## Author Contributions

AJ and LR conducted the literature search and data extraction. AJ wrote the first draft of the manuscript. AJ, LR, and GE contributed to the writing of the manuscript. AJ, ER, and GE agree with manuscript results and conclusions. AJ, ER, and GE made critical revisions and approved the final version. All authors reviewed and approved the final manuscript.

## Declaration of Conflicting Interests

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

## Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

## Ethical Approval

Ethical approval was not required for this article.

## References

1. Sussman M, Trocio J, Best C, et al. Prevalence of menopausal symptoms among mid-life women: findings from electronic medical records. *BMC Women's Health*. 2015;15:58.
2. Treloar AE. Menstrual cyclicality and the pre-menopause. *Maturitas* 1981;3:249-264.
3. Hill K. The demography of menopause. *Maturitas*. 1996;23:113-127.
4. Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med*. 2005;118(suppl 12B):14-24.
5. Thurston RC, Joffe H. Vasomotor symptoms and menopause: findings from the Study of Women's Health across the nation. *Obstet Gynecol Clin North Am*. 2011;38:489-501.
6. Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. *Health Qual Life Outcomes*. 2005;3:47.
7. Dennerstein L, Lehert P, Burger HG, Guthrie JR. New findings from non-linear longitudinal modeling of menopausal hormone changes. *Hum Reprod Update*. 2007;13:551-557.
8. The North American Menopause Society. *Menopause Practice: A Clinician's Guide*. 5th ed. Mayfield Heights, OH: North American Menopause Society; 2014.
9. Posadzki P, Lee MS, Moon TW, Choi TY, Park TY, Ernst E. Prevalence of complementary and alternative medicine (CAM) use by menopausal women: a systematic review of surveys. *Maturitas*. 2013;75:34-43.
10. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. 2002;288:321-333.
11. Ma J, Drieling R, Stafford RS. US women desire greater professional guidance on hormone and alternative therapies for menopause symptom management. *Menopause*. 2006;13:506-516.
12. Ernst E, Posadzki P. Alternative therapies for the management of menopausal symptoms. In: Panay N, Briggs P, Kovacs G, eds. *Managing the Menopause: 21st Century Solutions*. Cambridge, England: Cambridge University Press; 2015:157-162.
13. National Center for Complementary and Integrative Health. Complementary, alternative, or integrative health: what's in name? <https://nccih.nih.gov/health/integrative-health>. Accessed June 1 2017.
14. Barton DL, LaVasseur BI, Sloan JA, et al. Phase III, placebo-controlled trial of three doses of citalopram for the treatment of



- hot flashes: NCCTG trial N05C9. *J Clin Oncol.* 2010;28:3278-3283.
15. Sloan JA, Loprinzi CL, Novotny PJ, Barton DL, Lavoie BI, Windschitl H. Methodologic lessons learned from hot flash studies. *J Clin Oncol.* 2001;19:4280-4290.
  16. Freeman EW, Guthrie KA, Caan B, et al. Efficacy of escitalopram for hot flashes in healthy menopausal women: a randomized controlled trial. *JAMA.* 2011;305:267-274.
  17. Elkins GR. *Relief From Hot Flashes: The Natural, Drug Free Program to Reduce Hot Flashes, Improve Sleep, and Ease Stress.* New York, NY: Demos HEALTH; 2014.
  18. Elkins G, Marcus J, Stearns V, Hasan Rajab M. Pilot evaluation of hypnosis for the treatment of hot flashes in breast cancer survivors. *Psychooncology.* 2007;16:487-492.
  19. Elkins G, Marcus J, Stearns V, et al. Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. *J Clin Oncol.* 2008;26:5022-5026.
  20. Fisher WI, Johnson AK, Elkins GE, et al. Risk factors, pathophysiology, and treatment of hot flashes in cancer. *CA Cancer J Clin.* 2013;63:167-192.
  21. Elkins GE, Fisher WI, Johnson AK, Carpenter JS, Keith TZ. Clinical hypnosis in the treatment of post-menopausal hot flashes: a randomized controlled trial. *Menopause.* 2013;20:291-298.
  22. Johnson AK, Johnson AJ, Barton D, Elkins GE. Hypnotic relaxation therapy and sexual function in postmenopausal women: results of a randomized controlled clinical trial. *Int J Clin Exp Hypn.* 2016;64:213-224.
  23. Barton DL, Schroeder KCF, Banerjee T, Wolf S, Keith TZ, Elkins GE. Efficacy of a biobehavioral intervention for hot flashes: a randomized controlled pilot study. *Menopause.* 2017;24:774-782.
  24. Nonhormonal management of menopause-associated vasomotor symptoms: 2015 position statement of the North American Menopause Society. *Menopause.* 2015;22:1155-1174.
  25. Goldstein KM, Shepherd-Banigan M, Coeytaux RR, et al. Use of mindfulness, meditation and relaxation to treat vasomotor symptoms. *Climacteric.* 2017;20:178-182.
  26. Mann E, Smith M, Hellier J, et al. Cognitive behavioural treatment for women who have menopausal symptoms after breast cancer treatment (MENOS 1): a randomised controlled trial. *Lancet.* 2012;380:309-318.
  27. Ayers B, Smith M, Hellier J, Mann E, Hunter M. Effectiveness of group and self-help cognitive behavior therapy in reducing problematic menopausal hot flashes and night sweats (MENOS 2): a randomized controlled trial. *Menopause.* 2012;19:749-759.
  28. Keefer L, Blanchard EB. A behavioral group treatment program for menopausal hot flashes: results of a pilot study. *Appl Psychophysiol Biofeedback.* 2005;30:21-30.
  29. Khoshbooi R, Hassan SA, Hamzah MSG, Baba MB. Effectiveness of group cognitive behavioral therapy on depression among Iranian women around menopause. *Aust J Basic Appl Sci.* 2011;5:991-995.
  30. Tremblay A, Sheeran L, Aranda SK. Psychoeducational interventions to alleviate hot flashes: a systematic review. *Menopause.* 2008;15:193-202.
  31. Freedman RR, Woodward S. Behavioral treatment of menopausal hot flashes: evaluation by ambulatory monitoring. *Am J Obstet Gynecol.* 1992;167:436-439.
  32. Freedman R, Woodward S, Brown B, Javaid J, Pandey G. Biochemical and thermoregulatory effects of behavioral treatment for menopausal hot flashes. *Menopause.* 1995;2:211-218.
  33. Fenlon D. Relaxation therapy as an intervention for hot flashes in women with breast cancer. *Eur J Oncol Nurs.* 1999;3:223-231.
  34. Nedstrand E, Wijma K, Wyon Y, Hammar M. Applied relaxation and oral estradiol treatment of vasomotor symptoms in postmenopausal women. *Maturitas.* 2005;51:154-162.
  35. Germaine LM, Freedman RR. Behavioral treatment of menopausal hot flashes: evaluation by objective methods. *J Consult Clin Psychol.* 1984;52:1072-1079.
  36. Nedstrand A, Wijma K, Wyon Y, Hammar M. Vasomotor symptoms decrease in women with breast cancer randomized to treatment with applied relaxation or electro-acupuncture: a preliminary study. *Climacteric.* 2005;8:243-250.
  37. Irvin JH, Domar AD, Clark C, Zuttermeister PC, Friedman R. The effects of relaxation response training on menopausal symptoms. *J Psychosom Obstet Gynecol.* 1996;17:202-207.
  38. Saensak S, Vutyavanich T, Somboonporn W, Srisurapanont M. Relaxation for perimenopausal and postmenopausal symptoms. *Cochrane Database Syst Rev.* 2014;(7):CD008582.
  39. Fenlon DR, Corner JL, Haviland JS. A randomized controlled trial of relaxation training to reduce hot flashes in women with primary breast cancer. *J Pain Symptom Manage.* 2008;35:397-405.
  40. Zaborowska E, Brynhildsen J, Damberg S, et al. Effects of acupuncture, applied relaxation, estrogens and placebo on hot flashes in postmenopausal women: an analysis of two prospective, parallel, randomised studies. *Climacteric.* 2007;10:38-45.
  41. Lindh-Astrand L, Nedstrand E. Effects of applied relaxation on vasomotor symptoms in postmenopausal women: a randomized controlled trial. *Menopause.* 2013;20:401-408.
  42. Huang AJ, Phillips S, Schembri M, Vittinghoff E, Grady D. Device-guided slow-paced respiration for menopausal hot flashes: a randomized controlled trial. *Obstet Gynecol.* 2015;125:1130-1138.
  43. Sood R, Sood A, Wolf SL, et al. Paced breathing compared with usual breathing for hot flashes. *Menopause.* 2013;20:179-184.
  44. Carmody JE, Crawford S, Salmoirago-Blotcher E, Leung K, Churchill L, Olendzki N. Mindfulness training for coping with hot flashes: results of a randomized trial. *Menopause.* 2011;18:611-620.
  45. Lewis JE, Hilditch JR, Wong CJ. Further psychometric property development of the Menopause-Specific Quality of Life questionnaire and development of a modified version, MENQOL-Intervention questionnaire. *Maturitas.* 2005;50:209-221.
  46. Feuerstein G. *The Yoga Tradition: Its History, Literature, Philosophy, and Practice.* 3rd ed. Prescott, AZ: Hohm Press; 2001.
  47. Cramer H, Lauche R, Langhorst J, Dobos G. Effectiveness of yoga for menopausal symptoms: a systematic review and meta-analysis of randomized controlled trials. *Evid Based Complement Alternat Med.* 2012;2012:863905.

48. Afonso RF, Hachul H, Kozasa EH, et al. Yoga decreases insomnia in postmenopausal women: a randomized clinical trial. *Menopause*. 2012;19:186-193.
49. Carson JW, Carson KM, Porter LS, Keefe FJ, Seewaldt VL. Yoga of Awareness program for menopausal symptoms in breast cancer survivors: results from a randomized trial. *Support Care Cancer* 2009;17:1301-1309.
50. Chattha R, Raghuram N, Venkatram P, Hongasandra NR. Treating the climacteric symptoms in Indian women with an integrated approach to yoga therapy: a randomized control study. *Menopause*. 2008;15:862-870.
51. Elavsky S, McAuley E. Physical activity and mental health outcomes during menopause: a randomized controlled trial. *Ann Behav Med*. 2007;33:132-142.
52. Joshi S, Khandwe R, Bapat D, Deshmukh U. Effect of yoga on menopausal symptoms. *Menopause Int*. 2011;17:78-81.
53. Cramer H, Rabsilber S, Lauche R, Kümmel S, Dobos G. Yoga and meditation for menopausal symptoms in breast cancer survivors—a randomized controlled trial. *Cancer*. 2015;121:2175-2184.
54. Reed SD, Guthrie KA, Newton KM, et al. Menopausal quality of life: RCT of yoga, exercise, and omega-3 supplements. *Am J Obstet Gynecol*. 2014;210:244.e1-e11.
55. Newton KM, Reed SD, Guthrie KA, et al. Efficacy of yoga for vasomotor symptoms: a randomized controlled trial. *Menopause*. 2014;21:339-346.
56. Chien LW, Cheng SL, Liu CF. The effect of lavender aromatherapy on autonomic nervous system in midlife women with insomnia. *Evid Based Complement Alternat Med*. 2012;2012:740813.
57. Kazemzadeh R, Nikjou R, Rostamnegad M, Norouzi H. Effect of lavender aromatherapy on menopause hot flushing: a crossover randomized clinical trial. *J Chin Med Assoc*. 2016;79:489-492.
58. Darsareh F, Taavoni S, Joolae S, Haghani H. Effect of aromatherapy massage on menopausal symptoms: a randomized placebo-controlled clinical trial. *Menopause*. 2012;19:995-999.
59. Lotfipour-Rafsanjani SM, Vaziri-Nejad R, Ismailzadeh S, et al. Comparison of the efficacy of massage and aromatherapy massage with geranium on depression in postmenopausal women: a clinical trial. *Zahedan J Res Med Sci*. 2015;17(4):29-33.
60. Taavoni S, Darsareh F, Joolae S, Haghani H. The effect of aromatherapy massage on the psychological symptoms of postmenopausal Iranian women. *Complement Ther Med*. 2013;21:158-163.
61. Leach M, Moore V. Black cohosh (*Cimicifuga* spp) for menopausal symptoms. *Cochrane Database Syst Rev*. 2012;(9):CD007244.
62. Amsterdam JD, Yao Y, Mao JJ, Soeller I, Rockwell K, Shults J. Randomised, double-blind, placebo-controlled trial of *Cimicifuga racemosa* (black cohosh) in women with anxiety disorder due to menopause. *J Clin Psychopharmacol*. 2009;29:478-483.
63. Bai W, Henneicke-von Zepelin HH, Wang S, et al. Efficacy and tolerability of a medicinal product containing an isopropanolic black cohosh extract in Chinese women with menopausal symptoms: a randomized, double blind, parallel-controlled study versus tibolone. *Maturitas*. 2007;58:31-41.
64. Bebenek M, Kemmler W, von Stengel S, Engelke K, Kalender WA. Effect of exercise and *Cimicifuga racemosa* (CR BNO 1055) on bone mineral density, 10-year coronary heart disease risk, and menopausal complaints: the randomized controlled Training and Cimicifuga Racemose Erlangen (TRACE) study. *Menopause* 2010;17:791-800.
65. Carlisle A, Jessup JV. *Effect of Black Cohosh on Biochemical Markers of Bone Remodeling in Postmenopausal Women* [dissertation]. Gainesville, FL: University of Florida; 2008.
66. Frei-Kleiner S, Schaffner W, Rahlfs VW, Bodmer CH, Birkhauser M. *Cimicifuga racemosa* dried ethanolic extract in menopausal disorders: a double-blind placebo-controlled clinical trial. *Maturitas*. 2005;51:397-404.
67. Geller SE, Shulman LP, van Breemen RB, et al. Safety and efficacy of black cohosh and red clover for the management of vasomotor symptoms: a randomized controlled trial. *Menopause*. 2009;16:1156-1166.
68. Jacobson JS, Troxel AB, Evans J, et al. Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer. *J Clin Oncol*. 2001;19:2739-2745.
69. Kronenberg F, Warren M, Coleton M, Jin Z, McMahon DJ, Sauerli W. Effect of black cohosh extract on hot flashes and other menopausal symptoms. Poster presented at: 20th Annual Meeting of the North American Menopause Society; September 30–October 3, 2009; San Diego, CA.
70. Lehmann-Willenbrock WE, Riedel HH. Clinical and endocrinologic examinations about therapy of climacteric symptoms following hysterectomy with remaining ovaries. *Zentralbl Gynakol*. 1988;110:611-618.
71. Nappi RE, Malavasi B, Brundu B, Facchinetti F. Efficacy of *Cimicifuga racemosa* on climacteric complaints: a randomized study versus low-dose transdermal estradiol. *Gynecol Endocrinol*. 2005;20:30-35.
72. Newton KM, Reed SD, LaCroix AZ, Grothaus LC, Ehrlich K, Guiltinan J. Treatment of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo: a randomized trial. *Ann Intern Med*. 2006;145:869-879.
73. Oktem M, Eroglu D, Karahan HB, Taskintuna N, Kuscü E, Zeyneloglu HB. Black cohosh and fluoxetine in the treatment of postmenopausal symptoms: a prospective, randomized trial. *Adv Ther*. 2007;24:448-461.
74. Osmer R, Friede M, Liske E, et al. Efficacy and safety of isopropanolic black cohosh extract for climacteric symptoms. *Obstet Gynecol*. 2005;105(5 pt 1):1074-1083.
75. Pockaj BA, Gallagher JG, Loprinzi CL, et al. Phase III double-blind, randomized, placebo-controlled crossover trial of black cohosh in the management of hot flashes: NCCTG Trial N01CC1. *J Clin Oncol*. 2006;24:2836-2841.
76. Stoll W. Phytopharmakon influences atrophic vaginal epithelium: double blind study: cimicifuga vs. estrogenic substances. *Therapeutikum*. 1987;1:23-31.
77. Wuttke W, Gorkow C, Seidlová-Wuttke D. Effects of black cohosh (*Cimicifuga racemosa*) on bone turnover, vaginal mucosa, and various blood parameters in postmenopausal women: a double-blind, placebo-controlled, and conjugated estrogens-controlled study. *Menopause*. 2006;13:185-196.
78. Uebelhack R, Blohmer JU, Graubaum HJ, Busch R, Gruenwald J, Wernecke KD. Black cohosh and St. John's wort for climacteric

- complaints: a randomized trial. *Obstet Gynecol.* 2006;107(2 pt 1): 247-255.
79. Chung DJ, Kim H Y, Park KH, et al. Black cohosh and St. John's wort (GYNO-Plus) for climacteric symptoms. *Yonsei Med J.* 2007;48:289-294.
80. Liu SY, Wang JY, Shyu YT, Song LM. Studies on yams (*Dioscorea* spp.) in Taiwan. *J Chin Med.* 1995;6:111-126.
81. Komesaroff PA, Black CV, Cable V, Sudhir K. Effects of wild yam extract on menopausal symptoms, lipids and sex hormones in healthy menopausal women. *Climacteric.* 2001;4:144-150.
82. Hsu CC, Kuo HC, Chang SY, Wu TC, Huang KE. The assessment of efficacy of *Dioscorea alata* for menopausal symptom treatment in Taiwanese women. *Climacteric.* 2011;14:132-139.
83. Wojcikowski K, Wohlmuth H, Johnson DW, Gobe G. *Dioscorea villosa* (wild yam) induces chronic kidney injury via pro-fibrotic pathways. *Food Chem Toxicol.* 2008;46:3122-3131.
84. Chang HM, But PPH. *Pharmacology and Applications of Chinese Materia Medica.* Vol 1 (Yao S-C, Wang L-L, Yeung SCS, translators). Singapore: World Scientific; 1986:489-505.
85. 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: 981-986.
86. Kupfersztain C, Rotem C, Fagot R, Kaplan B. The immediate effect of natural plant extract, *Angelica sinensis* and *Matricaria chamomilla* (Climex) for the treatment of hot flushes during menopause. A preliminary report. *Clin Exp Obstet Gynecol.* 2003;30:203-206.
87. Rotem C, Kaplan B. Phyto-female complex for the relief of hot flushes, night sweats and quality of sleep: randomized, controlled, double-blind pilot study. *Gynecol Endocrinol.* 2007;23:117-122.
88. Fugh-Berman A. Herb-drug interactions. *Lancet.* 2000;355: 134-138.
89. Lee MS, Shin BC, Yang EJ, Lim HJ, Ernst E. Maca (*Lepidium meyenii*) for treatment of menopausal symptoms: a systematic review. *Maturitas.* 2011;70:227-233.
90. Brooks NA, Wilcox G, Walker KZ, Ashton JF, Cox MB, Stojanovska L. Beneficial effects of *Lepidium meyenii* (maca) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content. *Menopause.* 2008;15:1157-1162.
91. Meissner HO, Mscisz A, Reich-Bilinska H, et al. Hormone-balancing effect of pre-gelatinized organic maca (*Lepidium peruvianum* chacon): (ii) physiological and symptomatic responses of early-postmenopausal women to standardized doses of maca in double blind, randomized, placebo-controlled, multi-centre clinical study. *Int J Biomed Sci.* 2006;2:360-374.
92. Meissner HO, Reich-Bilinska H, Mscisz A, Kedzia B. Therapeutic effects of pre-gelatinized organic maca (*Lepidium peruvianum* chacon) used as a non-hormonal alternative to HRT in perimenopausal women—clinical pilot study. *Int J Biomed Sci.* 2006;2: 143-159.
93. Winther K, Rein E, Hedman C. Femal, a herbal remedy made from pollen extracts, reduces hot flushes and improves quality of life in menopausal women: a randomized, placebo-controlled, parallel study. *Climacteric.* 2005;8:162-170.
94. Hellstrom AC, Muntzing J. The pollen extract Femal—a nonestrogenic alternative to hormone therapy in women with menopausal symptoms. *Menopause.* 2012;19:825-829.
95. Chenoy R, Hussain S, Tayob Y, O'Brien PM, Moss MY, Morse PF. Effect of oral gamma-linolenic acid from evening primrose oil on menopausal flushing. *BMJ.* 1994;308:501-503.
96. 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;288:1075-1079.
97. Bassey EJ, Littlewood JJ, Rothwell MC, Pye DW. Lack of effect of supplementation with essential fatty acids on bone mineral density in healthy pre- and postmenopausal women: two randomized controlled trials of Efacal v. calcium alone. *Br J Nutr.* 2000;83:629-635.
98. Kronenberg F, Fugh-Berman A. Complementary and alternative medicine for menopausal symptoms: a review of randomized, controlled trials. *Ann Intern Med.* 2002;137:805-813.
99. Borrelli F, Ernst E. Alternative and complementary therapies for menopause. *Maturitas.* 2010;6:333-343.
100. Depypere HT, Comhaire FH. Herbal preparations for the menopause: beyond isoflavones and black cohosh. *Maturitas.* 2014; 77:191-194.
101. Overk CR, Yao P, Chadwick LR, et al. Comparison of the in vitro estrogenic activities of compounds from hops (*Humulus lupulus*) and red clover (*Trifolium pratense*). *J Agric Food Chem.* 2005;53:6246-6253.
102. Lethaby A, Marjoribanks J, Kronenberg F, Roberts H, Eden J, Brown J. Phytoestrogens for menopausal vasomotor symptoms. *Cochrane Database Syst Rev.* 2013;(12):CD001395.
103. Albertazzi P, Pansini F, Bonaccorsi G, Zanotti L, Forini E, De Aloysio D. The effect of dietary soy supplementation on hot flushes. *Obstet Gynecol.* 1998;91:6-11.
104. Balk JL, Whiteside DA, Naus G, DeFerrari E, Roberts JM. A pilot study of the effects of phytoestrogen supplementation on the postmenopausal endometrium. *J Soc Gynecol Invest.* 2002; 9:238-242.
105. Brzezinski A, Adlercreutz H, Shaoul R, et al. Short-term effects of phytoestrogen-rich diet on postmenopausal women. *Menopause.* 1997;4:89-94.
106. Burke GL, Legault C, Anthony M, et al. Soy protein and isoflavone effects on vasomotor symptoms in peri- and postmenopausal women: the Soy Estrogen Alternative Study. *Menopause* 2003;10:147-153.
107. Carmigiani LO, Pedro AO, Cost-Paiva LH, Pinto-Neto AM. The effect of dietary soy supplementation compared to estrogen and placebo on menopausal symptoms: a randomized controlled trial. *Maturitas.* 2010;67:262-269.
108. Cheng G, Wilczek B, Warner M, Gustafsson JA, Landgren BL. Isoflavone treatment for acute menopausal symptoms. *Menopause* 2007;14(3 pt 1):468-473.
109. Dalais FS, Rice GE, Wahlqvist ML, et al. Effects of dietary phytoestrogens in postmenopausal women. *Climacteric.* 1998; 1:124-129.
110. Hanachi P, Golkho S. Assessment of soy phytoestrogens and exercise on lipid profiles and menopause symptoms in menopausal women. *J Biol Sci.* 2008;8:789-793.

111. Knight DC, Howes JB, Eden JA, Howes LG. Effects on menopausal symptoms and acceptability of isoflavone-containing soy powder dietary supplementation. *Climacteric*. 2001;4:13-18.
112. Kotsopoulos D, Dalais FS, Liang YL, McGrath BP, Teede HJ. The effects of soy protein containing phytoestrogens on menopausal symptoms in postmenopausal women. *Climacteric*. 2000;3:161-167.
113. Lewis JE, Nickell LA, Thompson LU, Szalai JP, Kiss A, Hilditch JR. A randomized controlled trial of the effect of dietary soy and flaxseed muffins on quality of life and hot flashes during menopause. *Menopause*. 2006;13:631-642.
114. Radhakrishnan G, Agarwal N, Vaid N. Evaluation of isoflavone rich soy protein supplementation for postmenopausal therapy. *Pak J Nutr*. 2009;8:1009-1017.
115. St Germain A, Peterson CT, Robinson JG, Alekel DL. Isoflavone-rich or isoflavone-poor soy protein does not reduce menopausal symptoms during 24 weeks of treatment. *Menopause*. 2001;8:17-26.
116. Campagnoli C, Abbá C, Ambroggio S, Peris C, Perona M, Sanseverino P. Polyunsaturated fatty acids (PUFAs) might reduce hot flashes: an indication from two controlled trials on soy isoflavones alone and with a PUFA supplement. *Maturitas*. 2005;51:127-134.
117. Faure ED, Chantre P, Mares P. Effects of a standardized soy extract on hot flashes: a multicenter, double-blind, randomized placebo-controlled study. *Menopause*. 2002;9:329-334.
118. Han KK, Soares JM Jr, Haidar MA, de Lima GR, Baracat EC. Benefits of soy isoflavone therapeutic regimen on menopausal symptoms. *Obstet Gynecol*. 2002;99:389-394.
119. Jou HJ, Wu SC, Chang F, Ling PY, Chu KS, Wu WH. Effect of intestinal production of equol on menopausal symptoms in women treated with soy isoflavones. *Int J Gynaecol Obstet*. 2008;102:44-49.
120. Kaari C, Haidar MA, Júnior JM, et al. Randomized clinical trial comparing conjugated equine estrogens and isoflavones in postmenopausal women: a pilot study. *Maturitas*. 2006;53:49-58.
121. Khaodhlar L, Ricciotti HA, Li L, et al. Daidzein-rich isoflavone-aglycones are effective in reducing hot flashes in menopausal women. *Menopause*. 2008;15:125-132.
122. Levis S, Strickman-Stein N, Ganjei-Azar P, Xu P, Doerge D, Krischer J. Soy isoflavones in the prevention of menopausal bone loss and menopausal symptoms: a randomized, double-blind trial. *Arch Intern Med*. 2011;171:1363-1368.
123. Nahas EA, Nahas-Neto J, Orsatti FL, Carvalho EP, Oliveira ML, Dias R. Efficacy and safety of a soy isoflavone extract in postmenopausal women: a randomized double-blind, and placebo-controlled study. *Maturitas*. 2007;58:249-258.
124. Penotti M, Fabio E, Modena AB, Rinaldi M, Omodei U, Viganó P. Effect of soy-derived isoflavones on hot flashes, endometrial thickness and the pulsatility index of the uterine and cerebral arteries. *Fertil Steril*. 2003;79:1112-1117.
125. Upmalis DH, Lobo R, Bradley L, Warren M, Cone FL, Lamia CA. Vasomotor symptom relief by soy isoflavone extract tablets in postmenopausal women: a multicenter double-blind randomized placebo-controlled study. *Menopause*. 2000;7:236-242.
126. Ye YB, Wang ZL, Zhuo SY, et al. Soy germ isoflavones improve menopausal symptoms but have no effect on blood lipids in early postmenopausal Chinese women: a randomized placebo-controlled trial. *Menopause*. 2012;19:791-798.
127. Baber RJ, Templeman C, Morton T, Kelly GE, West L. Randomized placebo-controlled trial of an isoflavone supplement and menopausal symptoms in women. *Climacteric*. 1999;2:85-92.
128. del Giorno C, Maggio da Fonseca A, Bagnoli VR, Serrano de Assis J, Soares JM Jr, Baracat EC. Effects of *Trifolium pratense* on climacteric and sexual symptoms in postmenopausal women. *Rev Assoc Med Bras (1992)*. 2010;56:558-562.
129. Hidalgo LA, Chedraui PA, Morocho N, Ross S, Miguel GS. The effect of red clover isoflavones on menopausal symptoms, lipids and vaginal cytology in menopausal women: a randomized, double-blind, placebo-controlled study. *Gynecol Endocrinol*. 2005;21:257-264.
130. Imhof M, Gocan A, Reithmayer F, et al. Effects of a red clover extract (MF11RCE) on endometrium and sex hormones in postmenopausal women. *Maturitas*. 2006;55:76-81.
131. Jeri A. The use of an isoflavone supplement to relieve hot flashes. *Female Pat*. 2002;27:47-49.
132. Knight DC, Howes JB, Eden JA. The effect of Promensil, an isoflavone extract, on menopausal symptoms. *Climacteric*. 1999;2:79-84.
133. Tice JA, Ettinger B, Ensrud K, Wallace R, Blackwell T, Cummings SR. Phytoestrogen supplements for the treatment of hot flashes: the isoflavone clover extract (ICE) study: a randomized controlled trial. *JAMA*. 2003;290:207-214.
134. van de Weijer PH, Barentsen R. Isoflavones from red clover (Promensil) significantly reduce menopausal hot flush symptoms compared with placebo. *Maturitas*. 2002;42:187-193.
135. Crisafulli A, Marini H, Bitto A, et al. Effects of genistein on hot flashes in early postmenopausal women: a randomized, double-blind EPT- and placebo-controlled study. *Menopause*. 2004;11:400-404.
136. D'Anna R, Cannata M, Atteritano M, et al. Effects of the phytoestrogen genistein on hot flashes, endometrium, and vaginal epithelium in postmenopausal women: a 1-year randomized, double-blind, placebo-controlled study. *Menopause* 2007;14:648-655.
137. Evans M, Ellito JG, Sharma P, Berman R, Guthrie N. The effect of synthetic genistein on menopause symptom management in healthy postmenopausal women: a multi-center, randomized, placebo-controlled study. *Maturitas*. 2011;68:189-196.
138. Ferrari A. Soy extract phytoestrogens with high dose of isoflavones for menopausal symptoms. *J Obstet Gynaecol Res*. 2009;35:1083-1090.
139. Aso T, Uchiyama S, Matsumura Y, et al. A natural S-Equol supplement alleviates hot flashes and other menopausal symptoms in equol nonproducing postmenopausal Japanese women. *J Womens Health (Larchmt)*. 2012;21:92-100.
140. Colli MC, Bracht A, Soares AA, et al. Evaluation of the efficacy of flaxseed meal and flaxseed extract in reducing menopausal symptoms. *J Med Food*. 2012;15:840-845.
141. Heger M, Ventskovskiy BM, Borzenko I, et al. Efficacy and safety of a special extract of *Rheum rhaponticum* (ERr 731) in

- perimenopausal women with climacteric complaints: a 12-week randomized double-blind, placebo-controlled trial. *Menopause*. 2006;13:744-759.
142. Heyerick A, Vervarcke S, Depypere H, Bracke M, De Keuleleire D. A first prospective, randomized, double-blind, placebo-controlled study on the use of a standardized hop extract to alleviate menopausal discomforts. *Maturitas*. 2006;54:164-175.
143. Shakeri F, Taavoni S, Goushegir A, Haghani H. Effectiveness of red clover in alleviating menopausal symptoms: a 12-week randomized, controlled trial. *Climacteric*. 2015;18:568-573.
144. Atkinson C, Warren RM, Sala E, et al. Red-clover-derived isoflavones and mammographic breast density: a double-blind, randomized, placebo-controlled trial [ISRCTN42940165]. *Breast Cancer Res*. 2004;6:R170-R179.
145. Van Patten CL, Olivotto IA, Chambers GK, et al. Effect of soy phytoestrogens on hot flashes in postmenopausal women with breast cancer: a randomized, controlled clinical trial. *J Clin Oncol*. 2002;20:1449-1455.
146. Cancellieri F, De Leo V, Genazzani AD, et al. Efficacy on menopausal neurovegetative symptoms and some plasma lipids blood levels of an herbal product containing isoflavones and other plant extracts. *Maturitas*. 2007;56:249-256.
147. Riesco E, Choquette S, Audet M, Tessier D, Dionne IJ. Effect of exercise combined with phytoestrogens on quality of life in postmenopausal women. *Climacteric*. 2011;14:573-580.
148. Petri Nahas E, Nahás Neto J, De Luca L, Traiman P, Pontes A, Dalben I. Benefits of soy germ isoflavones in postmenopausal women with contraindication for conventional hormone replacement therapy. *Maturitas*. 2004;48:372-380.
149. Barton DL, Loprinzi CL, Quella SK, et al. Prospective evaluation of vitamin E for hot flashes in breast cancer survivors. *J Clin Oncol*. 1998;16:495-500.
150. Ziaei S, Kazemnejad A, Zareai M. The effect of vitamin E on hot flashes in menopausal women. *Gynecol Obstet Invest*. 2007;64:204-207.
151. Biglia N, Sgandurra P, Peano E, et al. Non-hormonal treatment of hot flushes in breast cancer survivors: gabapentin vs vitamin E. *Climacteric*. 2009;12:310-318.
152. Williamson J, White A, Hart A, Ernst E. Randomised controlled trial of reflexology for menopausal symptoms. *BJOG*. 2002;109:1050-1055.
153. Gozuyesil E, Baser M. The effect of foot reflexology applied to women aged between 40 and 60 on vasomotor complaints and quality of life. *Complement Ther Clin Pract*. 2016;24:78-85.
154. MacEoin B. *Homeopathy for Women*. London, England: Hodder & Stroughton; 1996.
155. Thompson EA. Alternative and complementary therapies for the menopause: a homeopathic approach. *Maturitas*. 2010;66:350-354.
156. Nayak C, Singh V, Singh K, et al. Management of distress during climacteric years by homeopathic therapy. *J Altern Complement Med*. 2011;17:137-1042.
157. Barnes PM, Bloom B, Nahin R. Complementary and alternative medicine use among adults and children: United States, 2007. *Natl Health Stat Report*. 2008;(12):1-23.
158. Avis NE, Legault C, Coeytaux RR, et al. A randomized, controlled pilot study of acupuncture treatment for menopausal hot flashes. *Menopause*. 2008;15:1070-1078.
159. Kim DI, Roh JJ, Choi MS, et al. A clinical trial to assess the efficacy of acupuncture on hot flashes in postmenopausal women. *Korean J Orient Med*. 2007;28:74-85.
160. Vincent A, Barton DL, Mandrekar JN, et al. Acupuncture for hot flashes: a randomized, sham-controlled clinical study. *Menopause*. 2007;14:45-52.
161. Kim DI, Jeong JC, Kim KH, et al. Acupuncture for hot flushes in perimenopausal and postmenopausal women: a randomised, sham-controlled trial. *Acupunct Med*. 2011;29:249-256.
162. 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.
163. Borud EK, Alraek T, White A, et al. The Acupuncture on Hot Flashes Among Menopausal Women (ACUFLASH) study, a randomized controlled trial. *Menopause*. 2009;16:484-493.
164. Kim KH, Kang KW, Kim DI, et al. Effects of acupuncture on hot flashes in perimenopausal and postmenopausal women—a multicenter randomized clinical trial. *Menopause*. 2010;17:269-280.
165. Cohen SM, Rousseau ME, Carey BL. Can acupuncture ease the symptoms of menopause? *Holistic Nurs Pract*. 2003;17:295-299.
166. Huang MI, Nir Y, Chen B, Schnyer R, Manber R. A randomized controlled pilot study of acupuncture for postmenopausal hot flashes: effect on nocturnal hot flashes and sleep quality. *Fertil Steril*. 2006;86:700-710.
167. Nir Y, Huang MI, Schnyer R, Chen B, Manber R. Acupuncture for postmenopausal hot flashes. *Maturitas*. 2007;56:383-395.
168. Sandberg M, Wijma K, Wyon Y, Nedstrand E, Hammar M. Effects of electro-acupuncture on psychological distress in postmenopausal women. *Complement Ther Med*. 2002;10:161-169.
169. Wyon Y, Lindgren R, Lundeberg T, Hammar M. Effects of acupuncture on climacteric vasomotor symptoms, quality of life and urinary excretion of neuropeptides among postmenopausal women. *Menopause*. 1995;2:3-12.
170. Wyon Y, Wijma K, Nedstrand E, Hammar M. A comparison of acupuncture and oral estradiol treatment of vasomotor symptoms in postmenopausal women. *Climacteric*. 2004;7:153-164.
171. Kwee SH, Tan HH, Marsman A, Wauters C. The effect of Chinese herbal medicines (CHM) on menopausal symptoms compared to hormone replacement therapy (HRT) and placebo. *Maturitas*. 2007;58:83-90.
172. Chen LC, Tsao YT, Yen KY, Chen YF, Chou MH, Lin MF. A pilot study comparing the clinical effects of Jia-Wey Shiao-Yau San, a traditional Chinese herbal prescription, and a continuous combined hormone replacement therapy in postmenopausal women with climacteric symptoms. *Maturitas*. 2003;44:55-62.
173. Qu F, Cai X, Gu Y, et al. Chinese medicinal herbs in relieving perimenopausal depression: a randomized, controlled trial. *J Altern Complement Med*. 2009;15:93-100.
174. Yasui T, Yamada M, Uemura H, et al. Changes in circulating cytokine levels in midlife women with psychological symptoms

- with selective serotonin reuptake inhibitor and Japanese traditional medicine. *Maturitas*. 2009;62:146-152.
175. Grady D, Sawaya GF, Johnson KC, et al. MF101, a selective estrogen receptor beta modulator for the treatment of menopausal hot flashes: a phase II clinical trial. *Menopause*. 2009;16:458-465.
176. Wiklund I, Mattson L, Lindgreen R, Limoni C. Effect of a standardized ginseng extract on quality of life and physiological parameters in symptomatic postmenopausal women: a double-blind, placebo-controlled trial. Swedish Alternative Medicine Group. *Int J Clin Pharmacol Res*. 1999;19:89-99.
177. Chang A, Kwak BY, Yi K, Kim JS. The effect of herbal extract (EstroG-100) on pre-, peri-and post-menopausal women: a randomized double-blind, placebo-controlled study. *Phytother Res*. 2012;26:510-516.
178. Kim SY, Seo SK, Choi YM, 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;19:461-466.
179. Baccetti S, Da Frè M, Becorpi A, et al. Acupuncture and traditional Chinese medicine for hot flushes in menopause: a randomized trial. *J Altern Complement Med*. 2014;20:550-557.
180. Davis SR, Briganti EM, Chen RQ, Dalais FS, Bailey M, Burger HG. The effects of Chinese medicinal herbs on postmenopausal vasomotor symptoms of Australian women. A randomised controlled trial. *Med J Aust*. 2001;174:68-71.
181. 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;11:244-251.
182. van der Sluijs CP, Bensoussan A, Chang S, Baber R. A randomized placebo-controlled trial on the effectiveness of an herbal formula to alleviate menopausal vasomotor symptoms. *Menopause*. 2009;16:336-344.
183. Woo J, Lau E, Ho SC, et al. Comparison of *Pueraria lobata* with hormone replacement therapy in treating the adverse health consequences of menopause. *Menopause*. 2003;10:352-361.