Efficacy of Black Cohosh–Containing Preparations on Menopausal Symptoms: A Meta-Analysis

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This study aimed to review the evidence on the efficacy of herbal preparations containing black cohosh for the treatment of menopausal symptoms. A systematic search of three databases (PubMed, Embase, and Cochrane Library) was conducted to identify relevant literature. Two reviewers independently abstracted the data from the eligible studies. Of the 288 English language citations screened, nine randomized placebo-controlled trials were included. Among these trials, six demonstrated a significant improvement in the black cohosh group compared with the placebo group. Using data from seven trials, we calculated a combined estimate for the change in menopausal vasomotor symptoms. Preparations containing black cohosh improved these symptoms overall by 26% (95% confidence interval 11%-40%); there was, however, significant heterogeneity between these trials. Given that black cohosh is one of the most frequently used herbal medications for menopausal vasomotor symptoms in North America, more data are warranted on its effectiveness and safety.

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Menopause is defined as loss of ovarian follicular activity associated with 12 consecutive months of amenorrhea not explained by other obvious pathologic or physiological causes. The most common symptoms are vasomotor. Forty per-
Data Sources
We performed a comprehensive literature search of PubMed (1950 to January 2008), Embase (1980 to January 2008), and the Cochrane Library (1950 to January 2008) to identify all the studies on black cohosh and menopause. We used the phrases “black cohosh and menopause,” "Cimicifuga racemosa and menopause," and "Actaea racemosa and menopause" to identify the studies. In addition, we scanned the reference lists of all the identified studies and reviews for any other studies not identified by the electronic search. We included only English language studies for the present review.

Study Eligibility

The inclusion and exclusion criteria were established in advance to minimize the bias in selection of the studies for review. Studies that met the following criteria were included: the study design was an RCT, the population comprised perimenopausal/postmenopausal women, the intervention was a preparation containing black cohosh, at least one of the control groups was placebo, and at least one of the outcomes was the frequency of vasomotor symptoms. Studies that were conducted exclusively in women with a history of breast cancer were excluded. If a study had more than one published report, we included the latest published report with the maximum number of patients, although we reviewed the prior ones for study design and patient selection criteria.

Data Abstraction

Two authors (TS and MSS) independently reviewed the studies to assess inclusion criteria and abstracted data using a standardized data abstraction sheet. Abstracted data included the names of authors; the place and time of publication; the inclusion and exclusion criteria; the number of patients randomized in the intervention and the control group(s); the type and dose of black cohosh used; the type of control; the method of randomization; patient characteristics at baseline (age, body mass index, time since menopause, and smoking status); the methods of sample size calculation; statistical analyses (including handling of missing data); the measurement of the primary and secondary outcomes in the intervention and the control group(s); and the change in outcomes at follow-up. For additional information, we contacted the authors and did hear back from one of the article’s corresponding authors.¹¹

We assessed the quality of the studies based on the following criteria as proposed by Jadad: method of randomization, blinding procedure, and description of the withdrawals.¹² Each study received a score of 1 for discussion of each of these criteria and an additional point if randomization and blinding procedures were appropriate. Good quality was defined as a score of more than 3 out of 5. Both reviewers (TS and MSS) compared their results, and discrepancies were resolved by discussion with a third author (JM).

Data Analysis

The numbers of participants in the black cohosh arm (Nₜ) and the placebo arm (Nₚ) were abstracted. For each study, we calculated the change in the proportion of subjects with symptoms from baseline (dᵢ) to 12 weeks (dᵢ₋₁₂) in the black cohosh (Dₜ) and placebo (Dₚ) groups. For one study, we had information for only 16 weeks, and we included that in the analysis.) If these data were not reported in a study, they were calculated as ((dᵢ₋₁₂ − dᵢₑ)/dᵢₑ) × 100. The rate difference (Dᵢ) was then calculated as the difference between the proportions between black cohosh and the placebo groups (Dₜ − Dₚ). Additionally, we calculated the standard error (SE) of the rate difference by the following method: square root ([Dₜ(1 − Dₜ)/Nₜ] + [Dₚ(1 − Dₚ)/Nₚ]). The rate differences were combined using the general principles of fixed effects model.¹³ The weight (Wᵢ) for each study was calculated as (1/SE²). The summary measure was calculated by multiplying the weight with the rate difference (Wᵢ·Dᵢ). The pooled summary was calculated by dividing the sum of summary measures by the sum of weights (ΣWᵢ·Dᵢ/ΣWᵢ).¹⁴ Homogeneity between studies was assessed by using a chi-square statistic with a degree of freedom equal to the number of studies minus 1.¹⁵ If the studies were not found to be statistically homogeneous, then an extravariation parameter (between-studies variance) was incorporated into the analysis by using a random effects model.¹⁶ The fixed effects model takes into account the within-study variance and hence weighs the study according to the study size and precision. The random effects model, however, additionally accounts for the interstudy variation, the underlying assumption being that the studies are a random sample from a hypothetical population and that the interstudy variance can be represented by a single estimate.¹⁶

We performed a sensitivity analysis by separating the RCTs into two groups: those that used black cohosh in conjunction with other products and those that had used black cohosh alone in the intervention group.

RESULTS

Details of the literature search are shown in Figure 1. We scanned 223 abstracts initially and identified 31 potential studies for review, of which nine were not RCTs (three studies discussed the adverse effects of black cohosh,¹⁷ one was a nonrandomized study,¹⁸ one an observational study,¹⁹ one a pilot study,²⁰ and three were reviews²¹—²³). Of the remaining 22 RCTs, 13 did not meet our inclusion criteria (three included subjects with a history of breast cancer,²⁴—²⁶ one evaluated the effect of black cohosh on menstrual migraine only,²⁷ two assessed the role of black cohosh on changes in cardiovascular disease markers,²⁸—²¹ four lacked a placebo control group,²⁸—³⁰ and three were additional reports of studies already included in the current review²¹—²³). We scanned the reference lists of these articles for any RCTs not identified by the electronic search but did not identify any new studies. Thus, nine RCTs were retained for the present review and meta-analysis.

The characteristics of the sample, inclusion, and exclusion criteria of these RCTs are presented in Table 1, ordered by publication date, starting with the most recent. Of the nine RCTs, six were conducted in Europe, one in the United States, one in Israel,
and one in Korea. The mean age of women ranged between 50.5 and 59 years. All of the RCTs excluded subjects with a history of hormone-dependent cancer and/or previous use of hormones unless followed by a washout period.

The outcomes, measures, results, quality scores, and funding sources for the trials are presented in Table 2. Two trials\(^{11,13}\) did not demonstrate a significant improvement in the intensity of vasomotor symptoms in the black cohosh group when compared with the placebo group. Of these, the study by Newton et al had multiple comparison groups (multibotanical products, multibotanical with soy, conjugated equine estrogen, and placebo) and the longest follow-up period (12 months).\(^{11}\) In this trial, only the group treated with estrogens had a significant change in the frequency of vasomotor symptoms. Of the other seven trials demonstrating a significant improvement, one used a combination of black cohosh, ligans, and isoflavones;\(^{27}\) one used black cohosh in combination with *dong quai*, milk thistle, red clover, American ginseng, and chastetree berry;\(^{28}\) two used a combination of black cohosh and St John’s wort;\(^{29,30}\) and the others used black cohosh alone.\(^{31,32}\)

Some of the commonly reported side effects in the black cohosh group were gastrointestinal symptoms (0.7%-15%), musculoskeletal and connective tissue conditions (4%-9.8%), and infections and infestations (8.5%-11.9%). Breast discomfort was not seen in the intervention group in two trials,\(^{16,17}\) and in another study, the intervention and control groups reported similar proportions of breast complaints.\(^{41}\) None of the RCTs reported increased occurrence of side effects in the intervention group compared with the placebo group.

Of the nine RCTs, six received a quality score of more than 3 and were, therefore, considered good quality.\(^{11,13,18-24}\) Two of these trials\(^{11,13}\) did not demonstrate a significant improvement in vasomotor symptoms. Three RCTs received scores of 3 because appropriateness of randomization and blinding could not be determined.\(^{11,18,23}\) The trials were financed by the private funders and government research organizations.\(^{11,23}\) One study just mentioned that the intervention tablets were funded by a private funder.\(^{13}\) Three of the RCTs did not report the source of funding.\(^{17,23,31}\)

The results of seven RCTs\(^{11-16}\) were used to calculate the combined estimate of the rate difference; data for calculation of the effect size for the other two RCTs could not be obtained.\(^{41}\) The combined estimate of the rate difference for improvement of vasomotor symptoms in the black cohosh group compared with placebo using the fixed effects model was 24% (95% CI: 18%-29%). The hypothesis of homogeneity between the studies was rejected (\(P<.005\)). The combined estimate of the rate difference calculated with the random effects model was 26% (95% CI: 11%-40%; Figure 2).

Five trials\(^{11-15}\) had used black cohosh in combination with other products; the combined estimate of these trials using the random effects model was 41% (95% CI: 20%-62%). The combined estimate of the two RCTs\(^{16,17}\) that used a combination of black cohosh and St John’s wort in the intervention group was 33% (95% CI: 24%-42%); the results of these two studies were homogeneous and the fixed effects model was used. Two RCTs\(^{18,30}\) had used only black cohosh in the intervention group; the combined estimate using a fixed effects model was 11% (95% CI: 1%-20%), as these RCTs were homogeneous.

**COMMENT**

We report a systematic review of nine placebo-controlled RCTs of preparations containing black cohosh in healthy perimenopausal women between the ages of 40 and 60 years. We were able to perform a meta-analysis with data from seven of these trials. Overall, black cohosh–containing preparations were found to be efficacious in reducing the symptoms of menopause in comparison to placebo, although the trials were significantly heterogeneous. Notably, the trial with the longest follow-up (12 months) and the highest dose of black cohosh (160 mg) did not demonstrate significant improvement in the black cohosh group compared with the placebo group.\(^{11}\) Black cohosh in combination with other multibotanicals and St John’s wort appeared to be more efficacious in treating menopausal symptoms compared with black cohosh alone. Side effects in the black cohosh group were similar to those in the placebo group.

We excluded three RCTs conducted on breast cancer.
<table>
<thead>
<tr>
<th>Study No.</th>
<th>Author, Place, Year</th>
<th>Inclusion/Exclusion Criteria</th>
<th>Intervention/(Number of Participants Randomized)</th>
<th>Comparison Group/(Number of Participants Randomized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Chung et al, Korea, (2007)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Inclusion: - Perimenopausal women (specific age not discussed) - Women with typical climacteric symptoms Exclusion: - Patients with history of breast cancer</td>
<td>Black cohosh and St John’s wort (264 mg tablet; 0.0364 ml of extract from <em>Cimicifuga racemosa</em>) (n=47)</td>
<td>Placebo preparation (n=42)</td>
</tr>
<tr>
<td>2</td>
<td>Rotem et al, Israel, (2007)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Inclusion: - Pre- and postmenopausal women aged 45-65 years - Amenorrhea for at least 6 months - Elevated follicle-stimulating hormone level (&gt;30 μg/mL) - Hot flushes and/or night sweats at least 3x/d Exclusion: - Women with a history of any cancer were excluded from the study&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Black cohosh (<em>Cimicifuga racemosa</em>) 100 mg, <em>dong quai</em> root extract 75 mg, milk thistle herb extract 75 mg, red clover flower extract 50 mg, American ginseng 59 mg, chastetree berry fruit extract 50 mg (n=19)</td>
<td>Placebo capsules outwardly identical to the study preparation (n=16)</td>
</tr>
<tr>
<td>3</td>
<td>Sammartino et al, Italy (2006)&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Inclusion: - Last menses at least 6 months before inclusion and no more than 24 months - Minimum number of 7 moderate-to-severe hot flushes (including night sweats) per 24-hour period Exclusion: - Neoplastic, metabolic, and infectious diseases - Past or concomitant use of estrogen/progesterone replacement therapy or other drugs used to treat climacteric symptoms</td>
<td><em>Cimicifuga racemosa</em> (50 mg) with isoflavones and lignans (n=40)</td>
<td>Calcium supplements (n=40)</td>
</tr>
<tr>
<td>4</td>
<td>Uebelhack et al, Germany (2006)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Inclusion: - Women aged 45 to 60 years - Menopausal Rating Scale of 0.4 or more in at least 3 items Exclusion: - Did not specifically mention exclusion of breast cancer cases</td>
<td>Black cohosh and St John’s wort (22.5-41.25 mg of rootstock of black cohosh) (n=151)</td>
<td>Placebo preparation (n=150)</td>
</tr>
<tr>
<td>5</td>
<td>Newton et al, United States (2006)&lt;sup&gt;5&lt;/sup&gt;</td>
<td>Inclusion: - Women aged 45 to 55 years - Two or more vasomotor symptoms per day Exclusion: - History of breast cancer - Contraindication(s) to hormone therapy</td>
<td>Black cohosh 160 mg daily (n=80)</td>
<td>4 groups: 1) Multibotanical groups: black cohosh, alfalfa, boron, chastetree, <em>dong quai</em>, false unicorn, licorice, oats, pomegranate, Siberian ginseng (n=76) 2) Multibotanical and soy counselling (n=79) 3) 0.625 mg of conjugated equine estrogen for women with uterus and 2.5 mg of medroxyprogesterone acetate 4) Placebo (n=84)</td>
</tr>
<tr>
<td>6</td>
<td>Verhoeven et al, Netherlands (2005)&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Inclusion: - Women aged 45 to 65 years - Amenorrheic for at least 6 months Exclusion: - History of hormone-dependent cancer - Women on hormone therapy required a washout period of at least 6 months</td>
<td>100 mg of black cohosh extract (Additionally: 125 mg soy extract, 1500 mg primrose oil, 1.25 μg vitamin D, 200 mg calcium, and 10 IU vitamin E) (n=60)</td>
<td>Placebo preparation (2000 mg olive oil) (n=64)</td>
</tr>
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</table>
Table 1, continued

<table>
<thead>
<tr>
<th>Study No.</th>
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<th>Inclusion/Exclusion Criteria</th>
<th>Intervention/(Number of Participants Randomized)</th>
<th>Comparison Group/(Number of Participants Randomized)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Frei-Kleiner et al, Switzerland (2005)</td>
<td>Inclusion: - Women aged 45 to 60 years - ≥ 3 hot flushes per day - ≥ 1 normal functioning ovary Exclusion: - History of breast cancer or endometrial cancer - Use of hormonal replacement therapy within the last month</td>
<td>Black cohosh (<em>Cimicifuga racemosa</em>) average of 42 mg of crude drug (n=84)</td>
<td>Identical placebo capsule (n=45)</td>
</tr>
<tr>
<td>8</td>
<td>Osmers et al, Germany (2005)</td>
<td>Inclusion: - At least 45 years of age - Postmenopausal women (interval of &gt; 12 months since last regular menstruation) Exclusion: - BMI &gt; 28 kg/m², later &gt; 35 kg/m² - Cancer, no concomitant hormone replacement therapy</td>
<td><em>Cimicifuga racemosa</em> 40 mg of the root stock daily (n=153)</td>
<td>Identical-looking placebo (n=151)</td>
</tr>
<tr>
<td>9</td>
<td>Wutke et al, Czech Republic (2003)</td>
<td>Inclusion: - Women aged 40 to 60 years - Postmenopausal (BMI &lt; 30 kg/m²) Exclusion: - Suspected/existence of estrogen-dependent mammary and/or endometrial cancer - Any contraindication(s) for estrogens or progestins</td>
<td><em>Actaea racemosa</em> 20 mg of the herbal drug</td>
<td>2 groups</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NA, but n=20 for the final analysis</td>
<td>1) Conjugated estrogen: 0.3 mg NA, but n=22 for final analysis</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2) Placebo: identical-looking placebo NA, but n=20 for final analysis</td>
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</table>

*BMI indicates body mass index; NA, not available.
†Information provided by the study’s corresponding author.

patients who may take prescription medications that influence the severity of hot flushes (e.g., tamoxifen). One of these studies randomized 136 breast cancer survivors in two groups: one received tamoxifen and the other received *Cimicifuga racemosa*. Patients in the combination group had significantly fewer hot flushes than those in tamoxifen group after 6 months. The second trial randomized 85 women into two groups stratified by tamoxifen use: one group was given black cohosh, and the other group was treated with placebo. They found that although hot flushes decreased in both the placebo and intervention groups, the difference between these groups was not significant. The third trial used a double-blind randomized crossover clinical trial with two 4-week periods: 132 patient were randomized to black cohosh or placebo; 75% of their population used tamoxifen, raloxifene, or aromatize inhibitors. They did not find significant reduction of hot flushes in the black cohosh group compared to the placebo group.

Strengths of the present systematic review are the inclusion of only randomized double-blind placebo-controlled trials of black cohosh, with a total of nine published trials, the largest number to date. The importance of including a placebo control group is underscored by the 25% to 30% reduction in the severity or frequency of hot flushes within 4 weeks of placebo treatment. In addition, a Cochrane review has shown that placebo alone may cause a reduction in vasomotor symptoms of up to 50%.

Limitations of the meta-analysis are the small number of trials and their heterogeneity. Heterogeneity between the studies may be due to multiple factors, including differences in design, the population under study, the treatments given, and the measures of menopausal symptoms. The dose and formulation of black cohosh were different in these RCTs; this may weaken the findings but it reflects the market availability of the medication. Although we chose only placebo-controlled RCTs in our meta-analysis, trials were conducted in different regions of the world using different doses of black cohosh, and assessment of vasomotor symptoms employed using different scales (e.g., Menopausal Rating Scale, Kupperman Index). Although these scales measure a similar underlying construct, symptoms are not rated in the same manner; this may have contributed to the heterogeneity.

Other potential study limitations are the exclusion of studies that were not published or not written in English (due to practical considerations). There is a tendency to not publish smaller studies that have a negative result or results closer to null effect, and excluding these unpublished studies may lead to publication bias. The decision was made to exclude unpublished reports because such studies are not always peer-reviewed, and the results may change between the time that research is presented at conferences and formally published. Further, though we did
### TABLE 2 Outcome, Quality Score, and Funding Sources for Studies Included in the Review

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Principal Outcome</th>
<th>Measurement of the Outcome</th>
<th>Significance</th>
<th>Quality Score</th>
<th>Funding Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Kupperman Index</td>
<td>Intervention group: Baseline: 26.46±10.64 4 weeks: 12.46±6.96 12 weeks: 6.37±4.16 Change: 20.09±4.16 Control group: Baseline: 25.38±10.16 4 weeks: 19.63±11.09 12 weeks: 17.14±11.61 Change: 8.24±7.57</td>
<td>.002&lt;sup&gt;†&lt;/sup&gt; &lt;.001&lt;sup&gt;†&lt;/sup&gt; &lt;.001&lt;sup&gt;†&lt;/sup&gt;</td>
<td>3</td>
<td>Private funding</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt;</td>
<td>Number of hot flushes</td>
<td>Intervention group: Baseline: 5.57±2.57 (mean number of hot flushes) 4 weeks: 4.2±3 (percentage change from baseline) 12 weeks: 73±5 (percentage change from baseline) Control group: Baseline: 5.06±2.98 (mean number of hot flushes) 4 weeks: 18±4 (percentage change from baseline) 12 weeks: 38±5 (percentage change from baseline)</td>
<td>.026&lt;sup&gt;†&lt;/sup&gt;</td>
<td>3</td>
<td>The intervention capsules were donated by a private company</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt;</td>
<td>Kupperman Index</td>
<td>Intervention group: Baseline: 3.0 (2.4 to 3.6) 12 weeks: 8 (6 to 10) Control group: Baseline: 3.1 (2.6 to 3.6) 12 weeks: 2.6 (2.3 to 2.9)</td>
<td>&lt;.05&lt;sup&gt;†&lt;/sup&gt;</td>
<td>5</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Menopausal Rating Scale</td>
<td>Intervention group (change from baseline): 8 weeks: 0.1±0.13 16 weeks: 0.2±0.13 Control group (change from baseline): 8 weeks: 0.0±0.13 16 weeks: 0.0±0.12</td>
<td>&lt;.001&lt;sup&gt;†&lt;/sup&gt; &lt;.001&lt;sup&gt;†&lt;/sup&gt;</td>
<td>4</td>
<td>Private funding</td>
</tr>
<tr>
<td>5&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Mean change in intensity of vasomotor symptoms</td>
<td>Black cohosh vs placebo 3 months: -0.96 (-2.03 to 0.11) 6 months: -0.48 (-1.63 to 0.66) 12 months: -0.80 (-1.30 to 0.93) All: -0.54 (-1.47 to 0.38) MBA vs placebo 3 months: 0.41 (-0.67 to 1.50) 6 months: 0.80 (-0.36 to 1.96) 12 months: 0.09 (-1.03 to 1.20) All: 0.43 (-0.50 to 1.37) MBAS vs placebo 3 months: -0.53 (-1.60 to 0.54) 6 months: 0.32 (-0.83 to 1.47) 12 months: 0.49 (-0.62 to 1.60) All: 0.09 (-0.83 to 1.02) CEE vs placebo 3 months: -4.55 (-6.51 to -2.59) 6 months: -3.86 (-5.73 to -2.00) 12 months: -3.76 (-5.76 to -1.76) All: -4.06 (-5.93 to -2.19)</td>
<td>&lt;.001&lt;sup&gt;†&lt;/sup&gt;</td>
<td>5</td>
<td>Government funding</td>
</tr>
</tbody>
</table>
### TABLE 2, continued

<table>
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<tr>
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<th>Funding Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>6&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Modified Kupemian Index Scale, change at 12 weeks compared with baseline</td>
<td>Intervention group: Baseline: 28.1±5.7</td>
<td>-26 (-33 to -18)</td>
<td>Control: Baseline: 27.9±5.8</td>
<td>4</td>
</tr>
<tr>
<td>7&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Hot flashes, weekly weighted scores, Kupperman Index</td>
<td>Intervention group: 12 weeks Baseline: 20.7±8.9</td>
<td>Percentage change from baseline</td>
<td>Controls: Baseline: 22.5±8.2</td>
<td>4</td>
</tr>
<tr>
<td>8&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Menopausal Rating Score I (MRS)</td>
<td>Beta coefficient of the regression model (including interaction terms, medically relevant model) 12 weeks Treatment: -0.0788 (-0.120 to -0.0374) MRS at baseline: -0.301 (-0.395 to -0.207) Duration treatment: .00387 (.000801 to .000694)</td>
<td>&lt;.001§</td>
<td>5</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>9&lt;sup&gt;st&lt;/sup&gt;</td>
<td>Validated Menstrual Rating Score (MRS)</td>
<td>Intervention group: 12 weeks Change from baseline: -1.8 (-1.7 to -2.0) Controls: 12 weeks Change from baseline for CE: -1.78 (-1.7 to -1.9) Change in baseline for placebo group: 1.5 (-1.35 to -1.6)</td>
<td>.0506§</td>
<td>3</td>
<td>Government funding</td>
</tr>
</tbody>
</table>

*MBA indicates multibotanical groups; MBAS, multibotanical groups with soy and counseling; CEE, conjugated equine estrogen; CE, conjugated estrogen.

†P value is the comparison between intervention and control group.

‡P value for change.

§P value for coefficient.

scan the references of the reviewed studies, we may have missed other articles not captured by these three databases. It also has been shown that fewer CAM trials with positive outcomes are published in high-impact mainstream medical journals, and medical journals in the United States are less likely to report positive outcomes of CAM trials than are European journals. This, potentially, may have resulted in some publication bias in our meta-analysis.

Overall, our results are consistent with those of previous reviews that suggested a benefit of black cohosh in reducing the frequency of vasomotor symptoms. The present study advances the literature on the efficacy of black cohosh in reducing the vasomotor symptoms in menopause because we have included more RCTs and performed a quantitative meta-analysis of these trials.

Additionally, our finding that St John's wort, an herbal...
antidepressant, in combination with black cohosh may increase the efficacy of black cohosh has not been reported in previous systematic reviews. This finding should be interpreted cautiously, however, as it was based on only two RCTs. A recent Cochrane review concluded that St John’s wort is superior to placebo for the treatment of major depression and has similar effectiveness to standard antidepressants but with fewer side effects. Further clinical controlled trials to assess the role of St John’s wort and black cohosh vs each herbal medication alone may also be warranted to tease apart the independent contribution of each to the reduction of vasomotor symptoms.

Although an essay discussing the effectiveness of Cimicifuga was published in Germany as early as 1960, clinical trials were not conducted until 1982. Despite the paucity of quality evidence to date, black cohosh is considered by some to be one of the three most effective CAM products used by perimenopausal women. The mechanism of action of black cohosh in the reduction of menopausal symptoms is controversial. Whereas some studies suggest that black cohosh has estrogenic properties on vaginal cytology and bone markers, others found no effect on vaginal cytology or on gynecologically relevant hormones. Other authors suggest that black cohosh has antiestrogenic properties and augments the effects of tamoxifen in vivo as well as in vitro. Though the exact mechanism is not known, it is suggested that the combined effects of essential fatty acids, vitamins, minerals, betacarotenes, and other chemical components may play a role in the observed physiological effects of black cohosh. Since the publication of the Women’s Health Initiative study in 2002, the use of hormone replacement therapy has drastically decreased. Fear of breast cancer, stroke, and myocardial infarct associated with HRT has led many menopausal women experiencing vasomotor symptoms to seek nonhormonal treatment.

We did not find significant differences in side effects in the black cohosh and placebo groups. However, two previous reviews reported serious side effects including hepatic side effects (hepatotoxicity, hepatic failure, and hepatic enzyme elevation) and cardiovascular side effects (arrhythmias and bleeding and coagulation disorders). Given that black cohosh is one of the most frequently used herbal medications for vasomotor symptoms in North America and Europe, more research about its effectiveness and safety is warranted.

Acknowledgment
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REFERENCES


