Review Article

Exploring the Efficacy and Safety of Black Cohosh (*Cimicifuga racemosa*) in Menopausal Symptom Management

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ABSTRACT

Black cohosh (*Cimicifuga racemosa*) is a perennial plant used to treat menopause. This plant is known to have a serotonergic rather than estrogenic impact. It has been recommended to treat vasomotor symptoms associated with breast cancer patients. It also relieves symptoms such as night sweats and hot flashes, commonly called vasorelaxation. The variability in the study's results, doses, and assessment methods requires more rigorous research to establish its efficacy and safety. Standardized trials are needed to provide more precise information on the benefits and limitations of menopause treatment, informing women seeking alternatives to hormone therapy. Black cohosh has shown the potential to reduce the frequency and intensity of vasomotor symptoms in breast cancer patients undergoing tamoxifen treatment. In addition to its effectiveness in alleviating night sweats and hot flashes, the vasorelaxation properties contribute to its overall positive impact on menopausal symptoms. Due to discrepancies, varying dosages, and assessment techniques, further comprehensive studies are essential to determine the optimal dosage, long-term safety, and overall efficacy. Only through standardized trials can women make informed decisions about black cohosh as a viable alternative to hormone therapy during menopause.

KEYWORDS: *Black cohosh, efficacy, menopausal symptoms, safety, symptom management*

INTRODUCTION

Structure and function change throughout menopause, leading to the development of biological mechanisms.[1] In up to 85% of women, menopausal estrogen insufficiency is associated with vasomotor, pelvic, and psychiatric symptoms such as hot flashes, dry vagina, and reduced bone.[2] Typically, between the ages of 45 and 52 years, women inevitably go through menopause and hormonal changes, and the absence of menstruation is its defining characteristic.[3] In most cases, menopause begins in women at 42 years of age.[4] Perimenopause is a transition period that begins several years before menstruation and is marked by the cessation of more significant functions. Hot flashes, nocturnal sweats, and psychosomatic symptoms are all part of acute menopausal syndrome, which is classified on a scale of 1–4, including depressive symptoms, attention-deficient disorder, pain in the bones and joints, migraines, arrhythmias, and para-anesthesia.[1,4] The best treatment is hormone therapy. The use of hormone treatment has declined in recent decades. The Women's Health Initiative found that hormone therapy is associated with a higher risk of breast cancer and cardiovascular disease.[5] Menopausal symptoms are known to have a significant and detrimental impact on quality of life (QOL) during menopause.[6] *Cimicifuga racemosa*, another name for *Actaea racemosa*, is indigenous to North America and is the source of the common herbal remedy black cohosh. It is said to have estrogenic properties and is generally used to treat menopausal symptoms.[7] Triterpene glycosides, phenolic acids, flavonoids, volatile oils,

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tannins, and other substances are all present in black cohosh rhizomes.[2,8] Black cohosh, a natural substance with similar estrogen effects and endocrine regulation function, has been especially well-liked. *A. racemosa* black cohosh, an isopropyl alcohol extract, can reduce menopausal symptoms while causing minimal side effects.[9] Black cohosh may affect the frequency of hot flashes if it increases estrogen levels and reduces luteinizing hormone (LH) pulsatile release. However, there were no discernible differences between the LH pulse frequency before and after chronic black cohosh administration. Black cohosh reduced the number of cells going through apoptosis, decreased mitochondrial swelling, and restored the shape of acinar cells.[8,9] This review evaluates the clinical effectiveness and safety of black cohosh in treating menopausal symptoms.

Review

Methods

To perform a comprehensive literature search, we used the PubMed and Google Scholar databases. We searched for articles published between 2006 and 2023, using the next search (black cohosh) OR (black cohosh) OR (*Cimicifuga racemosa*) OR (*Cimicifuga racemosa*) OR (*Actaea racemosa*) OR (*Actaea racemosa*) OR (black cohosh safety) OR (black cohosh efficacy) OR (black cohosh uses) OR (Black Cohosh Uses). We applied the following inclusion criteria for the final review: (1) original research articles, (2) English language, (3) peer-reviewed, (4) relevant to a review on menopause and the use of black cohosh in medical education, (5) available full text, and (6) published in the specified time frame.

Articles screened

After conducting the initial search, we identified 1173 articles in the searched database. We then excluded duplicates of 13 articles. In the initial screening, 869 articles that were irrelevant to the topic were excluded. Initially, we identified 291 articles, of which 281 articles were excluded because they did not meet the inclusion criteria (such as only abstracts were available, were not in English, and were old studies), and thus, we selected 10 articles for the final review.

The final review included 10 articles from 2006 to 2023 [Figure 1].

Table 1 shows the randomized control trials on black cohosh use in menopausal symptoms.

Black Cohosh

Black cohosh, rattle weed, wanzenkraut, and black snakeroot are topped with white blooms that extend from a broad base of twisted greenery.[19] The black cohosh rhizome contains substances that resemble estrogen. The most abundant triterpenes, especially Actin and 23 epi-26-deoxyactin, are used as standardisation markers for black cohosh preparation. Phenolic acids include ferulic acid, fumarolic acid, and other pharmaceutically active components in this herbal mixture.[8,19] Black cohosh is the 7th best-selling herb.[20,21] *C. racemosa*, another name for the perennial black cohosh, is native to Canada and eastern North America. The Ranunculaceae family includes this plant. Rhizomes that creep up to 2 m are formed.[4] Black cohosh has an estrogenic activity that contains isoflavones, which can affect female LH in an estrogenic manner LH secretion. Hot flushes have been associated with pulsed release of LH. Black cohosh has dopaminergic, serotonergic, and gamma-aminobutyric acid (GABAergic) actions but no direct effects on hormone receptors.[22] It has become more popular as an adequate treatment alternative in recent decades, particularly in Europe and Asia.[23] Since black cohosh is believed to have a serotonergic rather than estrogenic impact, it has been recommended to treat vasomotor symptoms associated with tamoxifen-taking breast cancer patients. Black cohosh for women taking tamoxifen has significantly decreased the frequency and intensity of hot flashes compared to placebo and improved fatigue levels, sleep, and irregular sweating.[24]

Bioactive Compounds, Effects, and Mechanisms

There are a variety of biologically active substances within the black cohosh rhizome fatty acids, resins, caffeic, ferulic, and isoflavone acids, in addition to the activity of triterpene glycosides and cimicifugoside.[19] Black cohosh preparations do not appear to simulate estrogen in any way and do not significantly affect endometrial thickness or bloodstream sex.[25] Two oral herbal formulations were introduced, including a solution with an ethanolic extract and tablets with the isopropanol extract of *C. racemosa*.[26] Black cohosh has been associated with unpleasant side effects in more recent scientific trials, with no discernible advantage over placebo in reducing hot flashes. In Thai women, a 40 mg/day black cohosh compound was not more successful in decreasing the symptoms of menopause versus placebo or enhancing the QOL rating. Like the placebo effect, a concentrated extract taken daily for a year at 125 mg was also ineffective.[25] Black cohosh has been associated with various tissue-dependent activities, such as inhibiting estrogen cell growth through cholinergic, antioxidant, and anti-inflammatory signaling[27] and observed a decrease in hot flashes in women who received a black cohosh extract for 12 weeks that contained 2.5% triterpenes. Twelve weeks of washout time allowed the impact to recover to its baseline. Furthermore, it was shown that whether estrogen was

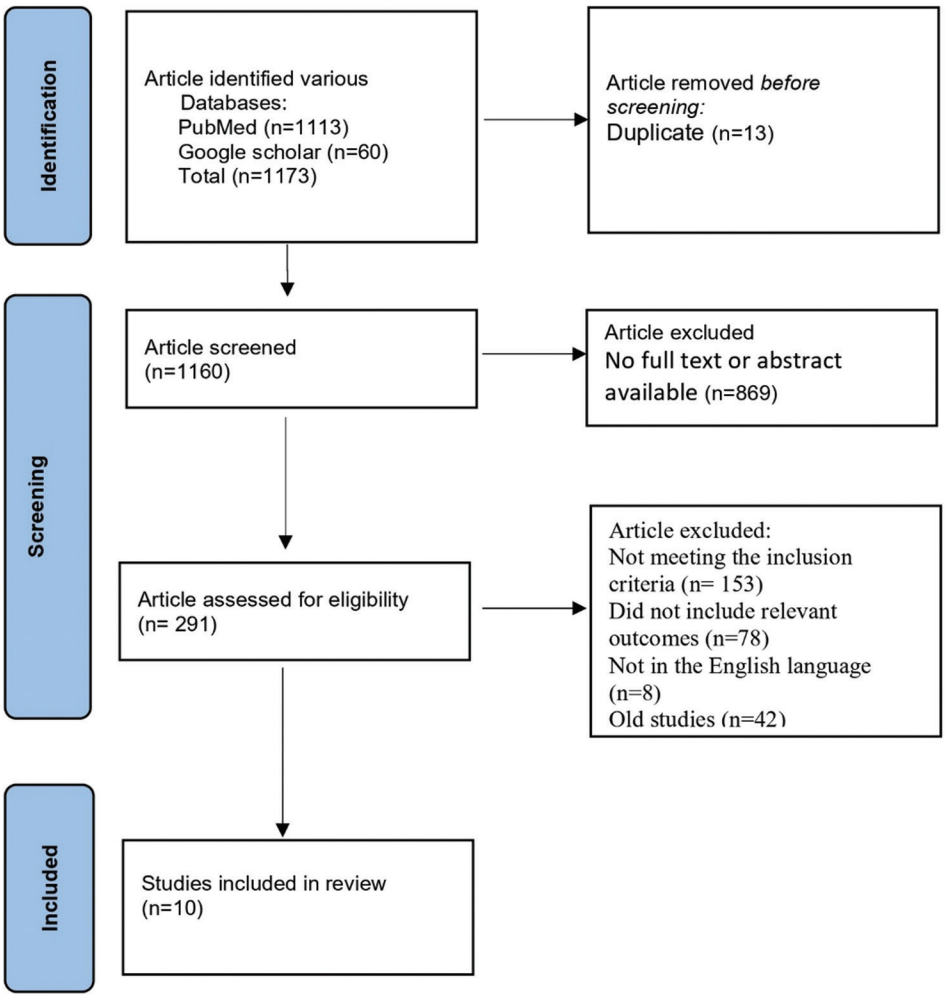

Figure 1: Flowchart for selection of articles

present or absent, black cohosh isopropyl extract did not affect uterine weight and genital epithelium.[28]

Black cohosh sometimes does not behave through an estrogenic mechanism. Instead, it starts to act on serotonin receptors, which can reduce menopausal symptoms and raise mood.[29] A meta-analysis involving four randomized clinical trials on black cohosh indicated that three of the four trials found black cohosh helpful in treating menopausal symptoms. Black cohosh reduces hot flashes and night sweats most effectively. It is important to note that the fourth trial did not show a significant improvement with black cohosh treatment. Black cohosh may be a viable option for women seeking relief from menopausal symptoms, particularly those experiencing mood disturbances.[30] Reviews of several randomized clinical trials have shown the effectiveness of *C. racemosa* in treating menopausal symptoms. In a 2009 controlled double-masked clinical experiment, randomized, placebo, red clover, and black cohosh were tested for their ability to cure hot flashes.[30,31]

Uses of Black Cohosh

In America, Asia, Europe, and Australia, *A. racemosa* is commonly used to treat various female health issues, particularly the adverse effects of traditional hormonal therapy in people with polycystic ovarian syndrome.[32] Liver damage has been associated with the use of black cohosh. The Japanese Ministry of Health, Education, and Welfare updates other national ministries' warnings against the possibility of an unfavorable hepatic response caused by items containing black cohosh.[33,34] This plant is often called black snakeroot, macros, black cohosh, and rattle weed. Herbal formulations of black cohosh rhizome are sold as herbal medicines in various European nations. It is one of the popular herbal items that native people have used to treat menopausal symptoms, such as hot flashes.[4,35]

Using the similarity of the spectrum to single component standards and retention duration, a total of seven components for black cohosh were found.[36] Based on biological and chemical information, the black cohosh

Table 1: Randomized controlled trials on black cohosh use in menopausal symptoms

Author's	Years	Conclusions	Findings
Bani *et al*.[5]	2013	Folic acid effectively reduces the severity, duration, and frequency of hot flashes during menopause	Significant variation in hot flashe's mean severity, duration, and frequency before and after therapy. The mean intensity of hot flashes in the second, third, and fourth weeks varies considerably amongst the groups when comparing the findings
Tumsutti *et al*.[10]	2022	Supplementation with the blend of four herbal extracts supports skin health in postmenopausal women. The blend of herbal extracts improves antioxidant status in women after menopause	Significant improvement in skin roughness at week 6. Compared to placebo, there was significant improvement in skin elasticity, roughness, smoothness, scaliness, and wrinkles at week 12
Mehrnoush *et al*.[11]	2021	Menopause therapy needs more research and caution	Aromatherapy, massage, yoga, acupuncture, and some dietary and herbal supplements were identified as effective in alleviating psychological symptoms
Friederichsen *et al*.[12]	2020	Menopausal symptoms improved significantly in both groups (MHT and CR)	MHT and CR extract improved menopausal symptoms. Body weight and serum metabolic parameters did not change in MHT or CR-treated women
Shahnazi *et al*.[13]	2013	Menopausal vasomotor symptoms can be efficiently treated with black cohosh, a natural medication	By controlling the intensity of vasomotor symptoms and the number of hot flashes before the intervention, a significant difference was seen between the two groups concerning the intensity and duration of hot flashes in weeks 4 and 8
Mohammad-Alizadeh-Charandabi *et al*.[14]	2013	Black cohosh reduced menopausal symptoms during treatment	Black cohosh reduced the GCS total score and all GCS subscale scores (vasomotor, psychiatric, physical, and sexual symptoms) during 4 and 8 weeks of treatment
Yang *et al*.[15]	2012	BSSG-P was superior to BSSG in improving the physical and psychological symptoms of menopausal women with mood disorders	BSSG-P and BSSG markedly decreased the total score of Greene, SDS, and SAS. BSSG-P exerted a superior effect after 8-week treatment and 4-week follow-up. BSSG-P also reduces the score of Greene, SDS, and SAS for menopausal women with a moderate mood disorder at the end of the 8th and 12th week when compared with BSSG
Amsterdam *et al*.[16]	2009	Black cohosh does not have anxiolytic benefits for menopause-related anxiety symptoms. Sample size and choice of dosage may have limited the identification of advantages	There is no anxiolytic benefit of black cohosh over placebo. Adverse events did not differ between groups
Maki *et al*.[17]	2009	Black cohosh and red clover do not have cognitive effects	Verbal memory did not alter in the two herbal therapy groups compared to the placebo group. Letter fluency increased, and instantaneous digit recall decreased due to CEE/MPA
Newton *et al*.[18]	2006	Black cohosh has little potential for relieving vasomotor symptoms. The naturopathic approach differs significantly from the interventions used in the study	Black cohosh, multibotanicals, soy, and placebo had little potential in relieving vasomotor symptoms, while hormone therapy was effective but had serious risks

MHT: Menopausal hormone therapy, CR: *Cimicifuga racemosa*, GCS: Greene Climacteric Scale, BSSG-P: Bushen-Shugan granule and psychotherapy, BSSG: Bushen-Shugan granule, SDS: Self-Rating Depression Scale, SAS: Self-Rating Anxiety Scale, CEE: Conjugated equine estrogen, MPA: Medroxyprogesterone acetate

extract was standardized for medical studies.[37] The most typical menopausal symptoms treated with black cohosh are night sweats and hot flashes, commonly referred to as vasomotor symptoms. Menopause also causes vaginal dryness, heart palpitations, tinnitus, vertigo, difficulty falling asleep, restlessness, and annoyance. These physical symptoms, menopause, can also cause emotional changes such as mood swings, irritability, and depression. Many women also experience weight gain and a decrease in libido during this stage of life. It is important to note that while black cohosh has been used as a natural remedy for menopausal symptoms, its effectiveness and safety have not been fully established through scientific research.[38] Plants, including Dong Quai and black cohosh, have phytoestrogens in addition to soy products. These phytoestrogens can mimic the

effects of estrogen in the body, making them popular natural alternatives for hormone replacement therapy. Dong Quai, also known as "female ginseng," has been used in traditional Chinese medicine to treat menopause symptoms. Similarly, black cohosh has been traditionally used by Native Americans to alleviate menstrual cramps and hot flashes.[39] To keep the blind intact and disguise the allocation, black cohosh or placebo pills were placed in sequentially numbered sealed envelopes of identical size and shape.[15]

Effects of Black Cohosh

There has been conflicting evidence on black cohosh's impact on early menopausal symptoms. However, there were a couple of minor adverse effects, including headaches, dizziness, nausea, and vomiting.[15] If this medication is used in the prescribed dose, it will be well accepted and will not have serious adverse effects.[14] The herbal remedy reduces menopausal symptoms to a lesser extent than tibolone and has fewer side effects than tibolone.[40] There are many biological effects of *Cimicifuga* species; investigated topics include osteoprotective quality, ovariectomized cartilage degradation, and preventing metabolic disorders.[41]

Women transitioning to menopause benefited the most from superiority, and vasomotor symptoms had the most significant impact.[42] A study found that black cohosh did not influence verbal memory or the California verbal learning test.[43] Commercially sold black cohosh-based dietary supplements reduce the ability of some medications to cause side effects and may even increase those risks.[44] Black cohosh was labeled "possibly responsible" for a reported heartbeat in a 59-year-old woman in other cardiovascular events. Black cohosh is known to have an adverse reaction to slowed heart rate.[45] Additional side effects in clinical trials have included vaginal bleeding/spotting, muscular symptoms, and breast pain/enlargement infections, although their prevalence was comparable to that of black cohosh.[46]

The effects and mechanism of actions of plant species are explained [Table 2].

Conclusions

Black cohosh is a perennial plant that can potentially alleviate menopausal symptoms, scorching flashes, and night sweats. It is known for its serotonergic rather than estrogenic effects, making it a viable

Table 2: Effects and mechanism of actions of plant species

Plant species or scientific name	Mechanism of action	Effects
Black cohosh rhizome (*Cimicifuga racemosa*)	Estrogen receptors are unaffected in the long-term enhancement of brain metabolism and general activity[47]	Treatment for menopause symptoms includes headaches, flushes, sleeplessness, irritability, and nocturnal hyperhidrosis.[1] Minimize how uncomfortable colors are. Diminish vasomotor symptoms[48]
Chaste tree fruit (*Vitex agnus-castus*) fruit	A reduction in prolactin release after binding to dopamine receptors. Increased levels of LH and a slight restriction of follicle-stimulating hormone release will tip the estrogen–progesterone ratio in favor of progestin[4]	Reduces in sadness, edema, mental tension, migraines, and constipation. Chaste tree extract reduced physical symptoms. Plants work on bodily hormones to treat female disorders[49]
Evening primrose seed (*Oenothera biennis*)	Its fatty acid components are believed to have therapeutic effects on immune cells directly and indirectly by influencing the production of eicosanoids such as prostaglandins, cytokines, and cytokine mediators[50]	Less hot flashes, under control vasomotor symptoms, minimal side effects, and excellent safety[51]
Fenugreek (*Trigonella foenum-graecum*) seed	Changes in immune cell function, antioxidant properties, and nitric oxide activity may all play a role in how estrogen modifies the quantity and activity of cytokines[52]	Reduce thromboxane levels, diminish platelet clumping, and limit clotting to avoid clotting problems at high lipid levels. This herb reduces metabolic and inflammatory problems caused by menopause[52]
Hop (*Humulus lupulus*) inflorescence	6-OHDA was stopped by lower amounts of ROS and higher levels of endogenous antioxidants that caused PC12 cells to activate the mitochondrial apoptotic pathway, which may have protected neuronal cells[53]	The severity and frequency of hot flushes have been shown to be reduced by preparations based on hops[53]
Red clover (red clover *Trifolium pratense*) stem, leaf, flower	Red clover flavonoids operate differently from flavonoid compounds in terms of how they affect lipid metabolism due to their varied isoflavone compositions[54]	There is no discernible impact on maintaining body or uterine weight[55]
Soybean seed (*Glycine soja*)	Furthermore, soybean germ includes estrogenic lignans and pertinent anti-inflammatory, antioxidant, and estrogenic properties of flavonoids such as genistein, equol, and daidzein isoflavones[56]	The mental health is improved by isoflavone-rich food and medicine plants rich in isoflavones[56]

LH: Luteinizing hormone, ROS: Reactive oxygen species, OHDA: Hydroxydopamine, PC: Pheochromocytoma

option for women seeking alternatives to hormone therapy during menopause, especially breast cancer patients taking tamoxifen. Black cohosh has been found to have anti-inflammatory properties, which can help reduce joint pain and stiffness that are often experienced during menopause. This herbal remedy also has a calming effect on the nervous system, helping to manage anxiety and mood swings commonly associated with this transitional phase in the life of a woman. Black cohosh offers a natural and potentially effective solution for women who want to alleviate menopausal symptoms without the use of hormone therapy. Variability in dosage and assessment methods underscores the need for more rigorous research to establish efficacy and safety, including standardized trials. These trials will give women the information they need to make informed decisions about black cohosh as a menopausal treatment. Standardized trials will help health-care professionals understand the appropriate dosage and potential side effects. With this knowledge, health-care professionals can provide more accurate patient recommendations and ensure safety.

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Conflicts of interest

There are no conflicts of interest.

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