Cimicifuga racemosa

Cimicifuga racemosa (Black cohosh) Indena photo



Cimicifuga racemosa

Introduction

Black cohosh, known botanically as *Cimicifuga racemosa* (also as *Actaea racemosa* and *Actea macrotys*), has been used by Native Americans and Europeans for gynecological conditions predating settlement of the New World.¹ Black cohosh was first listed in the U.S. Pharmacopoeia in 1830 under the name "black snakeroot." Other common names for this plant are black root, bugbane, rattle root, rattle top, rattle squawroot, snake root and rattle weed.² This herb was introduced to the medical community in 1844 when Dr. John King prescribed it for rheumatism and nervous disorders. Eclectic physicians in the United States commonly used this herb in the mid-nineteenth century for chronic ovaritis, endometritis, amenorrhea, dysmenorrhea, menorrhagia, sterility, threatened abortion,

uterine subinvolution, severe after-birth pains,³ and to increase breast milk production.¹ Most recently, black cohosh has received attention as a therapy for menopausal symptoms.

Active Constituents

The chemical constituents of the roots and rhizomes of black cohosh include cycloartenol-type triterpenoids, cimicifugoside, and cinnamic acid derivatives (ferulic acid, isoferulic acid, and piscidic and fukiic esters).^{2,4} Although the estrogenic isoflavone formononetin is reportedly a chemical constituent of black cohosh,⁵ its presence was not detected in alcohol extracts of the root/rhizome.^{6,7}

Mechanism of Action

It has been postulated that black cohosh has an estrogenic effect affording this herb its beneficial effects in menopause This estrogen-like effect is highly controversial, due to recent studies that dispute previous research.⁸ However, in some studies, black cohosh extracts exhibited organ specific estrogenic effects and were characterized as selective estrogen-receptor modulators.⁹

Suppressive effects of black cohosh on luteinizing hormone (LH) have been observed in menopausal and ovariectomized rats; however, the methodology of this study is questionable, as baseline measurements were not performed.¹⁰ This effect on LH has not been duplicated in other clinical studies.^{11,12}

Black cohosh root extracts have been used to improve circulation and reduce blood pressure by dilating blood vessels. The constituents for these actions are resinous and are much more soluble in an alcohol-based extract or tincture than in tea.¹³ Additionally, the black cohosh rhizome has been shown to have anti-inflammatory,^{14,15} analgesic, and antipyretic effects.¹⁵

Clinical Indications

Menopause

Extracts of black cohosh appear to be a safe and effective alternative to estrogen therapy for the treatment of menopausal symptoms, particularly in women with intolerance or contraindications to traditional hormone replacement therapy. Clinically, black cohosh has been used to alleviate perimenopausal and postmenopausal symptoms, including hot flashes, depression, emotional liability, profuse sweating, and sleep disturbances. The German Commission E has approved the herb as a nonprescriptive medication for "premenstrual discomfort, dysmenorrhea, or climacteric (menopausal) neurovegetative ailments."¹⁶

Since 1982, at least 11 clinical trials have assessed the efficacy of a standardized formulation of black cohosh (standardized to 1 mg triterpenes calculated as 27-deozyacetein per 20 mg of extract) for the symptomatic treatment of menopausal symptoms, such as anxiety, hot flashes, profuse sweating, insomnia, and vaginal atrophy. Of the 11 trials, six were randomized, controlled, or comparison trials,^{10-12,17,19} and the other five were uncontrolled studies.²⁰⁻²⁴ A randomized, placebo-controlled trial by Liske et al followed 152 women with menopausal symptoms, comparing two doses of black cohosh root for 12 weeks (39 mg versus 127 mg per day).¹⁸ Comparison was made to a historical placebo controlled trial by Stoll et al.¹¹ Similar to the Stoll trial, the Liske trial demonstrated beneficial results in two weeks, with both dosage levels having equal therapeutic efficacy and safety. No effects on levels of LH, follicle-stimulating hormone (FSH), sex hormone-binding globulin, prolactin, estradiol, or vaginal cytology were observed.

Menstrual Migraine

Approximately 30 percent of women are afflicted with menstrually-related migraine headaches. Evidence suggests estrogen and progestin fluctuations may influence these types of headaches.²⁵ A randomized, placebo-controlled study was undertaken to examine the efficacy of a phytoestrogen combination in the prophylactic treatment of menstrual migraine.²⁶ Forty-nine patients were randomized to receive either placebo or a daily combination of 60 mg soy isoflavone, 100 mg dong quai, and 50 mg black cohosh (each standardized to its primary alkaloid) for 24 weeks. A significantly positive effect (56-percent reduction of headaches) was noted in the treatment group after one month.

Breast Cancer

Hormone replacement therapy, a common menopausal treatment, is contraindicated in women with breast cancer due to concerns regarding the potential for breast cell proliferation. An in vitro study was performed to examine the effect of an extract of black cohosh on the proliferation of estrogen receptor-positive breast cancer cells (MCF-7).²⁷ Under estrogen-deprived conditions, the extract significantly inhibited MCF-7 cell proliferation. Additionally, application of the extract inhibited estrogen-induced proliferation of MCF-7 cells. Moreover, the proliferation-inhibiting effect of tamoxifen was enhanced by the black cohosh extract. This study suggests a non-estrogenic, or estrogen-antagonistic effect, of black cohosh extract on human breast cancer cells. This study further suggests black cohosh can be used safely in the treatment of menopausal symptoms in women with a history of breast cancer.

In a study of 85 women with a history of breast cancer (59 on tamoxifen and 26 not on tamoxifen), patients were randomly assigned to receive either 40 mg of standardized black cohosh extract or placebo.¹² After 60 days there were no significant differences between treatment groups in frequency and duration of hot flashes (decreased in both groups); however, there was a significantly greater decrease in sweating in the treatment group. There were no notable changes in FSH or LH levels in either group.

Tinnitus

As a central nervous system depressant, black cohosh directly inhibits vasomotor centers involved with inner ear balance and hearing. As such, black cohosh has been used clinically for relief of ringing in the ears.²⁸

Drug-Botanical Interactions

There have been no human studies documenting possible drug interactions with this herb; however, *in vitro* studies with breast cancer cell lines indicate it may have additive antiproliferative effects when used with tamoxifen.²⁹ Black cohosh has also been found to potentiate the effects of antihypertensive medications in rabbits, but not in dogs or humans.³⁰

Side Effects and Toxicity

In human trials, black cohosh, at the recommended dose, has been generally well tolerated, producing only mild gastrointestinal symptoms in some cases. In large doses (5-12 g) black cohosh can produce vertigo, tremors, low pulse, low blood pressure, vomiting, and nervous system irritation.

Dosage

Most research cited in this review used a standardized black cohosh extract at a dose of 40-80 mg daily (standardized to contain 1 mg of triterpenes calculated as 27-deozyacetein per 20 mg of extract).³¹

Warnings and Contraindications

Empirical data suggest black cohosh should be avoided during pregnancy because of its possible uterine-stimulating effect, and during lactation as it may cause colic.³²

References

- 1. Foster S. Black cohosh (*Cimicifuga racemosa*): a literature review. *Herbalgram* 1999;45:35-49.
- 2. Mahady GB, Fong HHS, Farnsworth NR. Rhizoma *Cimicifuga racemosae*. In: *WHO Monographs on Selected Medicinal Plants*, *Volume II*. Geneva, Switzerland: World Health Organization; 2002.
- Lloyd J, Lloyd C. Drugs and Medicines of North America, Volume 1. Cincinnati, OH: Lloyd, Lloyd; 1884-1885:287.

- 4. Kruse SO, Lohning A, Pauli GF, et al. Fukiic and piscidic acid esters from the rhizome of *Cimicifuga racemosa* and the *in vitro* estrogenic activity of fukinolic acid. *Planta Med* 1999;65:763-764.
- 5. Jarry H, Harnischfeger G. Endocrine effects of constituents of *Cimicifuga racemosa*. 1. The effect on serum levels of pituitary hormones in ovariectomized rats. *Planta Med* 1985 Feb;(1):46-49. [Article in German]
- 6. Struck D, Tegtmeier M, Harnischfeger G. Flavones in extracts of *Cimicifuga racemosa*. *Planta Med* 1997;63:289-290.
- McCoy J, Kelly W. Survey of *Cimicifuga* racemosa for phytoestrogenic flavonoids. Book of Abstracts, 212th ACS National Meeting. Orlando, FL: American Chemical Society; August 25-29, 1996.
- 8. Liu J, Burdette JE, Xu H, et al. Evaluation of estrogenic activity of plant extracts for the potential treatment of menopausal symptoms. *J Agric Food Chem* 2001;49:2472-2479.
- 9. Winterhoff H, Butterweck V, Jarry H, Wuttke W. Pharmacologic and clinical studies using *Cimicifuga racemosa* in climacteric complaints. *Wien Med Wochenschr* 2002;152:360-363. [Article in German]
- 10. Duker EM, Kopanski L, Jarry H, Wuttke W. Effects of extracts from *Cimicifuga racemosa* on gonadotropin release in menopausal women and ovariectomized rats. *Planta Med* 1991;57:420-424.
- 11. Stoll W. Botanical medicine influences on atrophic vaginal epithelium: double-blind study: Cimicifuga vs. estrogenic substances. *Therapeutikon* 1987;1:7-15. [Article in German]
- 12. 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.
- 13. Benoit PS, Fong HH, Svoboda GH, Farmsworth NR. Biological and phytochemical evaluation of plants. XIV. Antiinflammatory evaluation of 163 species of plants. *Lloydia* 1976;39:160-171.
- 14. Hirabayashi T, Ochiai H, Sakai S, et al. Inhibitory effect of ferulic acid and isoferulic acid on murine interleukin-8 production in response to influenza virus infections *in vitro* and *in vivo*. *Planta Meda* 1995;61:221-226.

Monograph

- Sakurai N, Nagai M. Chemical constituents of original plants of Cimicifugae rhizoma in Chinese medicine. *Yakugaku Zasshi* 1996;116:850-865. [Article in Japanese]
- Blumenthal M, Busse W, Goldberg A, et al. *The Complete German Commission E Monographs – Therapeutic Guide to Herbal Medicines*. Austin, TX: American Botanical Council; 1998.
- 17. Lehmann-Willenbrock E, Riedel HH. Clinical and endocrinologic studies of the treatment of ovarian insufficiency manifestations following hysterectomy with intact adnexa. *Zentralbl Gynakol* 1988;110:611-618. [Article in German]
- Liske E, Hanggi W, Henneicke-von Zepelin HH, et al. Physiological investigation of a unique extract of black cohosh (*Cimicifugae* racemosae rhizoma): a 6-month clinical study demonstrates no systemic estrogenic effect. J Women's Health Gend Based Med 2002;11:163-174.
- 19. Warnecke G. Influencing menopausal symptoms with a phytotherapeutic agent. *Die Med Welt* 1985;36:871-874.
- 20. Daiber W. Climacteric complaints: success without using hormones – a phytotherapeutic agent lessens hot flashes, sweating, and insomnia. *Arztliche Praxis* 1983;35:1946-1947. [Article in German]
- 21. Petho A. Climacteric complaints are often helped with black cohosh. *Arzliche Praxis* 1987;38:1551-1553. [Article in German]
- 22. Stolze H. An alternative to treat menopausal complaints. *Gyne* 1982;1:14-16. [Article in German]
- 23. Vorberg G. Therapy for climacteric complaints. *Zeitschrift fur Allegmeinmedizin* 1984;60:626-629. [Article in German]
- 24. Nesselhut T, Liske E. Pharmacological measures in postmenopausal women with an isopropanolic aqueous extract of *Cimicifugae racemosae* rhizome. *Menopause* 1999;6:331.
- 25. Silberstein S, Merriam G. Sex hormones and headache 1999 (menstrual migraine). *Neurology* 1999;53:S3-S13.
- 26. Burke BE, Olson RD, Cusack BJ. Randomized, controlled trial of phytoestrogen in the prophylactic treatment of menstrual migraine. *Biomed Pharmacother* 2002;56:283-288.

- 27. Bodinet C, Freudenstein J. Influence of *Cimicifuga racemosa* on the proliferation of estrogen receptor-positive human breast cancer cells. *Breast Cancer Res Treat* 2002;76:1-10.
- 28. Genazzani E, Sorrentino L. Black cohosh. *Nature* 1962;194:544-545.
- Freudenstein J, Bodinet C. Influence of an isopropanolic aqueous extract of *Cimicifuga* racemosae rhizome on the proliferation of MCF-7 cells. Paper presented at 23rd International LOF-Symposium on Phyto-estrogens. Ghent, Belgium; Jan 15, 1999.
- Tyler V. Cimicfuga racemosa. In: Robbers J, ed. Tyler's Herbs of Choice: The Therapeutic Use of Phytomedicinals. Binghamton, NY: Hawthorn Press; 1994.
- Mahady GB, Fabricant D, Chadwick LR, Dietz B. Black cohosh: an alternative therapy for menopause? *Nutr Clin Care* 2002;5:283-289.
- Brinker F. Herb Contraindications and Drug Interactions, 2nd ed. Sandy, OR: Eclectic Medical; 1998:40.

Alternative Medicine Review ♦ Volume 8, Number 2 ♦ 2003