



THERAPEUTIC EFFECTS OF CIMICIFUGA RACEMOSA-A SHORT REVIEW

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ABSTRACT

Cimicifuga racemosa is one of the most important of all the indigenous remedies. Its range of action is quite extensive; it has been quite thoroughly proven; the clinical experience with it is already large; and it has great possibilities for future development. This plant is considered to be safe and natural treatment for menopausal complaints such as hot flashes, profuse sweating and sleep disturbances.

Key words:

Cimicifuga Racemosa,
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INTRODUCTION

Cimicifuga racemosa is one of the most important of all the indigenous remedies. Its range of action is quite extensive; it has been quite thoroughly proven; the clinical experience with it is already large; and it has great possibilities for future development. Cimicifuga racemosa commonly going by the name of black cohosh, (Latin names: Actaea racemosa and Cimicifuga racemosa) is a perennial plant member of the buttercup family, a herb indigenous to North America^[1] and Europe, and its rhizomes have long been used for the treatment of a variety of ailments such as diarrhea, sore throat, and rheumatism. Now, black cohosh has become a well-known alternative herbal medicine with health benefits in treating painful menstrual periods and menopausal disorders. Black cohosh has been revealed to contain triterpene monoglycosides with the cycloartane skeleton, isoflavones, alkaloids, and phenylpropanoids, among which the cycloartane glycosides are its main secondary metabolites and are considered to partially contribute to the pharmacological effects of this herbal medicine.^[2-8] Menopause, which occurs at ages 45–55 years in women, is a physiological process defined by the cessation of menstruation for more than 6 months, caused by ovarian function diminishing naturally or after surgery. The common symptoms such as hot flashes, night sweats, and dyspareunia, dry eyes and dry mouth are seen significantly.^[9]

Therapeutic Effects

- **Anti-climacteric effects:** According to study, black cohosh was found to be consistent with a human mu opiate receptor (hMOR) agonist, which may explain its purported beneficial role in alleviating menopausal symptoms.^[10]
- **Anti-coagulation effects:** Native black cohosh contains small amounts of salicylic acid.
- **Anti-inflammatory activity:** The constituent isoferulic acid has also been reported to have anti-inflammatory effects and may decrease muscular spasm. Furthermore, salicylic acid is found in small quantities in black cohosh, and it is presumed that the salicylic acid contributes to the anti-inflammatory and analgesic properties of black cohosh.^[11,12]
- **Antineoplastic effects:** Based on a systematic review, there is laboratory evidence of antiproliferative properties of black cohosh but a lack of confirmation from clinical studies for a protective role in cancer prevention. *In vitro* studies have reported black cohosh to possess inhibitory effects on estrogen responsive cancer cell lines/breast cancer cells. Furthermore, in a cell line study, relatively low concentrations of actein or the methanol/water fraction of black cohosh may cause synergistic inhibition of human breast cancer cell proliferation when combined with different classes of chemotherapy agents. Actein may activate genes that respond to DNA damage and unfolded protein responses, and enhance apoptosis and repressed cell cycle genes. In an *in vitro* study conducted on human prostate cancer cells with black cohosh extract, the extract killed hormone-responsive or hormone-

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unresponsive prostate cancer cells by induction of apoptosis and activation of caspases. Another *in vivo* study demonstrated inhibited PC3 prostate cancer tumor growth with black cohosh and other herbal extracts. The mechanism behind tumor inhibition appeared to be anti-angiogenic by decreasing intratumoral microvessel density.^[13-25]

- Antioxidant effects: Extracts of black cohosh have protected against induced DNA damage through scavenging of reactive oxygen species.^[26-29]
- Bone metabolism effects: An isopropanolic extract of black cohosh has been shown to significantly diminish the urinary content of pyridinoline and deoxypyridinoline, specific markers for bone loss, and the morphometric correlates of bone loss associated with ovariectomy.^[30-32]
- CNS effects: Recent studies suggest that the mechanism of action of black cohosh may be centrally mediated, with possible action at the level of serotonin or dopamine receptors.^[33,34]
- Endocrine effects: Cimicifugoside contained in black cohosh is believed to affect hypothalamus-pituitary function.
- Estrogenic effects: It is not clear what constituent(s) of black cohosh, if any, possesses estrogenic properties. In animals and *in vitro*, initial reports of estrogen receptor binding activity stand in contrast with more recent data suggesting no significant estrogen receptor binding activity or estrogenic activities. Two *in vitro* studies found no effects of black cohosh alone on estrogen receptors, but reported that black cohosh antagonized proliferative effects on cells induced by estradiol. A similar *in vitro* study on estrogen sensitive breast cancer cells (MCF-7) reported isopropanolic black cohosh extract did not stimulate MCF-7 growth and exerted inhibitory effects on cellular proliferation, indicating strong estrogen-antagonist effects. Several studies have aimed to assess estrogen activity by measuring luteinizing hormone (LH), follicle stimulating hormone (FSH), or prolactin levels. One study reported lower FSH levels (but not LH) in patients treated with black cohosh vs. placebo, although baseline hormone levels were not known in either group. Results from other trials have found no effects on these hormone levels after up to six months of black cohosh therapy. *Cimicifuga racemosa* ethanolic extract, Ze 450, may inhibit cell proliferation and show antiestrogenic activity. The *Cimicifuga racemosa* extract bound to the progesterone receptor B1 but did not show progestin-like activity in the T-47D cell line. In an *in vitro* study using healthy breast tissue of pre- and postmenopausal women, incubation *in vitro* with black cohosh extract decreased local estrogen formation.^[35-57]
- Gastrointestinal effects: In an *in vitro* study, black cohosh extracts moderately but significantly inhibited estrone-3-sulfate (a typical organic anion-transporting polypeptide B (OATP-B) substrate) uptake. As OAT-B is involved in the intestinal absorption of various drugs, black cohosh may decrease the absorption of orally administered substrates of OATP-B.^[58]
- Neuropharmacologic effects: Black cohosh has been shown to exhibit an action on the central endogenous

opioid system in postmenopausal women as evidenced by suppression of mean luteinizing hormone pulse frequency following opioid receptor blockade.^[59]

- Serum glucose level altering effects: In a randomized trial peri- or post-menopausal women, black cohosh had no demonstrable effects on lipids, glucose, insulin, or fibrinogen.^[60]
- Serum insulin level altering effects: In a randomized trial peri- or post-menopausal women, black cohosh had no demonstrable effects on lipids, glucose, insulin, or fibrinogen.^[60]
- Serum lipid level altering effects: In a double-blind randomized, placebo controlled, study in 89 peri- or postmenopausal women experiencing climacteric symptoms, a combination of black cohosh (*Cimicifuga racemosa*) and St. John's wort (*Hypericum perforatum*) significantly increased HDL levels. However, in a randomized trial peri- or post-menopausal women, black cohosh had no demonstrable effects on lipids, glucose, insulin, or fibrinogen.^[61]
- Vascular effects: In a 1962 study, acteina, a constituent of black cohosh, was found to cause peripheral vasodilation, and has been noted to elicit hypotension.^[62]
- Vasoactive effects: Laboratory study of cimicifugic acids C and D, and fukinolic acid in the rhizome of black cohosh show vasoactive effects.^[63]
- Other: *In vivo* oral administration of black cohosh extract inhibited the anti-IgE-induced passive cutaneous anaphylaxis reaction.⁷ Black cohosh extract also showed inhibitory potential on histamine release. Cimicifugoside from *Cimicifuga simplex* has been found to inhibit cellular thymidine-³H uptake, and to act as a selective inhibitor of nucleoside transport into mammalian cells.^[64,65]

CONCLUSION

No known contradiction or interaction with other active substances have been demonstrated for *Cimicifuga racemosa*. Clinical and statistical data ensures that the THERAPEUTIC efficacy of *Cimicifuga racemosa* for moderate to severe neurovegetative symptoms of climacteric. Good tolerability and low risk of side effects have been confirmed in case reports and clinical studies. Experimental studies indicate that no toxic, mutagenic, carcinogenic, teratogenic effects are seen. This plant is considered to be safe and natural treatment for menopausal complaints such as hot flashes, profuse sweating and sleep disturbances.

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