

The Longwood Herbal Task Force  
(<http://www.mcp.edu/herbal/default.htm>) and  
The Center for Holistic Pediatric Education and Research  
(<http://www.childrenshospital.org/holistic/>)

## **Black Cohosh (*Cimicifuga racemosa*)**

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**Principal Proposed Use:** Menopausal symptoms

**Other Proposed Uses:** Premenstrual syndrome (PMS), menstrual symptoms, labor inducer, mood stabilizer and sedative; treatment for tinnitus

### ***Overview***

Black cohosh (*Cimifuga racemosa*) is a popular herbal remedy for women's health problems such as premenstrual syndrome (PMS), menstrual problems, and menopausal symptoms. Other uses include the treatment of rheumatoid arthritis and tinnitus. In randomized clinical trials, *C. racemosa* decreases hot flashes, vaginal dryness, anxiety, and depression associated with menopause. There are few studies of *C. racemosa*'s use in the treatment of menstrual disorders, tinnitus and rheumatoid arthritis. The herb has been used in Germany for more than 40 years with no evidence of serious side effects and no reported drug interactions<sup>1</sup>. Due to its historical use as an emmenagogue, *C. racemosa* is not recommended in early pregnancy. There are no studies of the safety of its use by children or lactating women.

### ***Historical and Popular Uses***

Black cohosh (*C. racemosa*) is an herb native to North America. The name *cohosh* comes from an Algonquian word meaning "rough", referring to the feel of the rhizome, and *black* refers to the dark color of the rhizome. The Latin name *cimicifuga* means insect repellent, and the plant has been used for this purpose<sup>2</sup>. Native North Americans, who used the herb to treat malaise, kidney ailments, malaria, sore throat, bronchitis, indigestion, rheumatism and snakebites, introduced it to the European colonists<sup>3 4, 5</sup>. Other traditional uses include joint pain, myalgia, neuralgia, sciatica,

fever, hysteria, pruritis, dyspepsia, whooping cough, chorea, hypertension, tinnitus, congested airways, and nervous disorders<sup>3, 6, 5, 2, 7</sup>. It is thought to possess astringent, diuretic, diaphoretic, antirheumatic, antitussive, antispasmodic, aphrodisiac, emmenagogue, nervine, sedative, stomachic and emmenagogue properties<sup>7, 4, 3</sup>. *C. racemosa* was a popular nineteenth century remedy for female disorders such as PMS, menstrual disorders, and general gynecologic complaints<sup>5</sup>. It was traditionally used, and is still used today, to stimulate labor<sup>8</sup>.

Today *C. racemosa* is widely used in Europe as a treatment for menopausal symptoms, i.e. hot flashes, vaginal dryness, anxiety, and depression. Since 1956, over 1.5 million women in Germany have used *C. racemosa* extract, and in 1994 over 6.5 million monthly dosages of *C. racemosa* extract were used by menopausal women in Germany, Scandinavia, and Austria<sup>9</sup>. The German Commission E recommends it for premenstrual discomfort and dysmenorrheic as well as climacteric neurovegetative complaints<sup>10</sup>.

## ***Botany***

*Medicinal species:* *Cimicifuga racemosa*

*Common names:* Black snake root, bugbane, bugwort, baneberry, rattleroot, rattleweed, squaw root<sup>11</sup>

*Botanical family:* Ranunculaceae

*Plant description:* A tall perennial herb growing up to eight feet tall, with long plumed white flowers on a wand-like raceme. Its leaves have an irregular shape and are tooth-edged. It has knobby black roots or rhizomes.

*Where it's grown:* North America and Europe

## ***Biochemistry***

### **Black Cohosh (*C. racemosa*): Potentially Active Chemical Constituents**

- Triterpene glycosides: actein, deoxyactein, cimigaside, cimcifugoside, 27-deoxyactein, racemoside, 12-acetylactein<sup>2 12</sup>
- Flavonoid: formononetin , keampferol<sup>12</sup>,
- Aromatic acids: isoferulic acid, salicylic acid
- Tannins
- Alkaloids: n-methylcytisine<sup>7</sup>
- Other constituents: butyric acid, formic acid, oleic acid, palmitic acid, racemosin, biochanine, phytosterins, fukiic acid and piscidic acid<sup>2 13, 7</sup>.
- Cimicifugin

*C. racemosa* contains numerous active chemical constituents, listed in the table above.<sup>2, 7, 12, 14, 15 16 13</sup>.

The *triterpene glycosides* appear to be the major constituents with endocrine and reproductive effects. They also possess hypocholesterolemic activity *in vitro*<sup>7</sup>.

*Isoferulic acid* exhibits an anti-inflammatory effect by inhibiting interleukin-8 production in response to influenza virus<sup>17</sup>.

*Cimicifugin*, an amorphous resinous substance, makes up approximately 15-20 % of the root<sup>2</sup>.

## *Experimental Studies*

### **Black Cohosh (*C. racemosa*): Potential Clinical Benefits**

1. Cardiovascular: Hypotensive
2. Pulmonary: none
3. Renal and electrolyte balance: none
4. Gastrointestinal/hepatic: none
5. Neuro-psychiatric: Mood regulator and sedative; tinnitus
6. Endocrine: Hypoglycemic. See also Reproductive
7. Hematologic: none
8. Rheumatologic: none
9. Reproductive: Menopausal symptoms, premenstrual syndrome (PMS), menstrual symptoms, labor induction
10. Immune modulation: none
11. Antimicrobial: none
12. Antineoplastic: Antineoplastic
13. Antioxidant: none
14. Skin and mucus membranes: none
15. Other/miscellaneous: none

1. **Cardiovascular:** Hypotensive
  - i. *In vitro data*: none
  - ii. *Animal data*: Liquid *C. racemosa* extract reduced blood pressure, heart contractility and heart rate<sup>19</sup>. In rabbits and cats, and inconsistently in dogs, actein acted as a peripheral vasodilator and had a hypotensive effect<sup>18</sup>.
  - iii. *Human data*: none
2. **Pulmonary:** none
3. **Renal and electrolyte imbalance:** none
4. **Gastrointestinal/hepatic:** none
5. **Neuro-psychiatric:** Mood regulator and sedative, tinnitus
  - a. Mood regulator and sedative

- i. In vitro data: none
  - ii. *Animal data*: none
  - iii. *Human data*: Clinical reports have noted *C. racemosa* to have a sedative effect and positive effects on the mood swings, depressive disorders and psychological instability sometimes associated with hormonal imbalances<sup>20</sup>. In a clinical trial of 41 pre- and perimenopausal women who received a standardized *C. racemosa* extract (Remifemin<sup>®</sup>, one tablet TID) or placebo, *C. racemosa* had a sedative effect<sup>20</sup>.
- b. Tinnitus: Traditional use; no data
- 6 **Endocrine**: Hypoglycemic. See also **Reproductive** section below for *C. racemosa*'s modulating effects on LH (luteinizing hormone) , FSH (follicular stimulating hormone) and estrogen
- i. *In vitro data*: See **Reproductive** section below.
  - ii. *Animal data*: *C. racemosa* had a hypoglycemic effect in animal studies<sup>19</sup>.
  - iii. *Human data*: none
7. **Hematologic**: none
8. **Rheumatologic**: none
9. **Reproductive**: Menopausal symptoms, premenstrual syndrome (PMS), menstrual symptoms, labor induction
- a. Menopausal symptoms
    - i. *In vitro data*: Studies of *C. racemosa*'s physiologic effects have had mixed results. Originally, it was believed that *C. racemosa* had estrogenic effects, but now there is evidence to dispute this claim<sup>6</sup>. *C. racemosa* attaches to estrogen receptors in rat uterus and pituitary glands and suppressed luteinizing hormone in ovariectomized rats<sup>21 22</sup>, <sup>23</sup>. In ovariectomized rats, *C. racemosa* reduced the serum LH concentration<sup>24</sup>. A lipophilic extract of *C. racemosa* bound to estrogen receptor binding sites *in vitro*<sup>25</sup>.
    - ii. *Animal data*: Animal studies have shown conflicting results. In rats and mice, *C. racemosa* induced estrus and increased uterine weight in a dose-dependent manner<sup>20</sup>. In mice, triterpene glycosides led to an improved proliferation of vaginal epithelium<sup>26</sup>. *C. racemosa* significantly increased uterine weight in ovariectomized rats<sup>27</sup>. Also in

ovariectomized rats, a lipophilic extract of *C. racemosa* reduced LH secretion<sup>25</sup>; in another study, actein and formononetin suppressed LH secretion but had no effect on FSH and prolactin levels<sup>26</sup>.

In contrast, in immature mice, three days of 6, 60 or 600 mg/kg of *C. racemosa* aqueous-alcoholic extract did not affect uterine growth, while in ovariectomized rats, three days of 6, 60, 600 mg/kg *C. racemosa* did not lead to cornification of vaginal cells<sup>28</sup>.

- iii. *Human data*: In numerous case series, standardized *C. racemosa* monodrug preparations have been used to treat menopausal symptoms, menstrual disorders (amenorrhea, oligomenorrhea, dysmenorrhea, polymenorrhea, PMS), and complaints during pregnancy. The literature describes the efficacy of *C. racemosa* in approximately 1500 patients with menopausal disorders, citing distinct and clear improvements in the clinical picture and good to very good therapeutic responses<sup>6, 20</sup>. By 1960, 1256 case reports in 111 published studies by gynecologists, general practitioners, internists and neurologist had evaluated the use of Remifemin<sup>®</sup> for the treatment of menopausal symptoms with positive effects and few side effects<sup>20</sup>.

(Most of the clinical trails assessing the use of *C. racemosa* for menopausal complaints have been carried out using Remifemin<sup>®</sup> [Schaper& Brummer Gmb & Co.]. Remifemin is standardized with respect to triterpene glycoside content, with each 20-mg tablet containing 1 mg of 27–deoxyactein; it is also available in a standardized liquid extract. For an assessment tool, many studies have used the Kupperman Menopausal Index, which is a weighted sum of ten individual symptoms: hot flashes, outbreaks of sweating, sleep disorders, nervousness, irritability, dizziness, difficulty in concentration, joint pains, headaches and palpitations<sup>29</sup>.)

In a multicenter open label study, 629 menopausal patients were treated with Remifemin (40 drops twice daily) for six to eight weeks. Neurovegetative symptoms (hot flashes, profuse sweating, headache, vertigo, heart palpitations, tinnitus) and psychological symptoms (nervousness, irritability, insomnia, depressive moods) improved in 80% of women after four weeks. None of the patients discontinued taking

Remifemin due to side effects, although transitory GI complaints were observed in 7% of participants<sup>6,30</sup>.

In an open, multicenter, post-marketing surveillance study, 812 women received a combination of *C. racemosa* and *Hypericum perforatum* (St. Johns wort). Patients and practitioners reported improvement in symptoms, especially difficulty concentrating and hot flashes, in up to 90% of patients. After three weeks, treatment success was apparent in most patients and 70% continued therapy after termination. Two percent experienced side effects (GI symptoms)<sup>31</sup>.

In two open studies in gynecological practices, a total of 86 menopausal patients received Remifemin (40 drops twice daily) for three months<sup>32, 33</sup>. After 12 weeks, there were statistically significant improvements in all rating scales. There was a highly significant improvement in Clinical Global Impressions, improvement in Profile of Mood States scales (a decrease in weariness, despondency and ill humor, an increase in motivation and an elevated mood state), and a highly significant decrease in the Kupperman Menopausal Index (less than 15). In all cases, tolerability was described as good to very good. Four patients reported mild GI complaints at the beginning of the therapy<sup>33</sup>.

In an open randomized controlled trial, 60 patients with moderate menopausal symptoms received either a) Remifemin (40 drops twice daily), b) conjugated estrogens (0.625 daily), or c) diazepam (2 mg daily) for twelve weeks. The three groups had equivalent improvement in symptoms with a statistically significant decrease in the Kupperman Menopausal Index, Self-evaluation Depression Scale, and the Hamilton Anxiety Scale (HAMA). The three groups were equivalent in the Clinical Global Impressions scale. A positive estrogen stimulation of vaginal mucosa occurred with Remifemin and conjugated estrogen as early as four weeks. No adverse effects were noted.<sup>34</sup>

In an open controlled placebo study, 110 patients with menopausal symptoms, who had received no estrogen replacement therapy for six months, received either Remifemin (2 tablets BID of 20 mg of dried extract) or placebo for eight weeks. LH but not FSH levels were significantly reduced in patients taking Remifemin<sup>35</sup>.

In a double blind, randomized placebo-controlled trial, 80 patients with menopausal symptoms received either *C. racemosa* extract (two tablets twice daily), conjugated estrogen (0.625 mg/day), or placebo. After four weeks, the *C. racemosa* group improved on the Kupperman Menopausal Index and HAMA scale compared to the placebo group, and after 12 weeks the *C. racemosa* had significantly decreased scores on both measures compared to both the placebo and estrogen groups. Also after 12 weeks of therapy, the *C. racemosa* group had significant improvements in somatic parameters and a notable increase in the degree of proliferation of the vaginal epithelium compared to the estrogen and placebo groups. No adverse effects were noted<sup>36</sup>.

In a double blind randomized clinical study, 153 menopausal patients received either 40 mg or 127 mg of Remifen<sup>®</sup> isopropanolic *C. racemosa* extract. There was a decrease in the Kupperman Menopausal Index after two weeks, and after six months, 90% of the subjects had a decrease in the Kupperman Menopausal Index. The levels of LH, FSH, SHBG, prolactin, and estradiol, as well as vaginal cytology, were not influenced by the *C. racemosa* extract. Both dosages showed similar efficacy and safety<sup>37</sup>.

In a randomized clinical trial, 60 newly-hysterectomized patients under 40 years old, who all had at least one intact ovary but complained of climacteric symptoms, were treated with estriol (1 mg), conjugated estrogens (1.25 mg), estrogen-gestagen sequential therapy or Remifemin (2 tablets twice daily). All groups had equivalent significant improvement in symptoms and there were no significant differences in therapy success between groups<sup>38</sup>.

- b. Premenstrual syndrome. There have been clinical reports of the use of *C. racemosa* for PMS<sup>20</sup>.
  - i. *In vitro data*: none
  - ii. *Animal data*: none
  - iii. *Human data*: There are no clinical trial on the uses of black cohosh in premenstrual syndrome.
- c. Menstrual symptoms: Traditional use; no data

d. Labor induction: Traditional use: no data

10. **Immune modulation**: none

11. **Antimicrobial**: none

12. **Antineoplastic**: Antineoplastic

- i. *In vitro data*: *C. racemosa* extract inhibited proliferation of breast cancer cells<sup>39 40</sup>. *C. racemosa* does not have estrogen like effects in established estrogen receptor positive breast cancer cell lines whose growth is estrogen dependent<sup>6</sup>. *In vitro* studies with breast cancer cells lines indicate that the herb may have an additive antiproliferative effect with tamoxifen<sup>41</sup>.
- ii. *Animal data*: none
- iii. *Human data*: There are no clinical trials assessing the effectiveness or safety of *C. racemosa* with women who have or had breast cancer.

13. **Antioxidant**: none

14. **Skin and mucus membranes**: none

15. **Other/miscellaneous**: none

## ***Toxicity and Contraindications***

*All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, pharmaceuticals.*

*This is particularly concerning with imports from developing countries.*

*Furthermore, allergic reactions can occur to any natural product in sensitive persons.*

The FDA lists *C. racemosa* as an “Herb of Undefined Safety”<sup>7</sup>

*Allergic reactions to C. racemosa* have not been reported.

*Potentially toxic compounds in C. racemosa:* None found; unknown.

*Acute toxicity:* The most commonly documented side effect is mild gastrointestinal distress, occurring in less than 5% of patients enrolled in clinical trials. There are also rare reports of dizziness, headaches and weight gain<sup>29, 42</sup>. Overdoses produce nausea, vomiting, vertigo, headache, hypotension, impaired vision, impaired circulation, increased perspiration, and dizziness<sup>3, 43, 11, 7</sup>. There is a case report of a 45-year-old woman who experienced seizures that may have been related to the consumption of a herbal preparation containing black cohosh<sup>44</sup>.

*Chronic toxicity:* A six-month oral toxicity study in rats found no toxic potential even at very high doses (up to 5000 mg/kg of body weight); no abnormalities were noted in clinical, chemical, histopathologic or macroscopic organ examinations compared with the control group<sup>6</sup>. There have been no long-term studies of the use of *C. racemosa*.

*Limitations during other illnesses or in patients with specific organ dysfunction:* There are no studies assessing the safety of *C. racemosa* in women with estrogen-receptor positive breast cancer or osteoporosis.

*Interactions with other herbs or pharmaceuticals:* There are no studies assessing the safety of *C. racemosa* in women taking birth control pills or hormone replacement therapy.

*Safety during pregnancy and/or childhood:* There are no studies assessing the safety of *C. racemosa* in pregnant or lactating women or in children. Some herbalists do not recommend it during pregnancy due to its traditional use as an emmenagogue.<sup>45</sup> Extracts of *C. racemosa* have shown no teratogenicity or mutagenicity tested in any human or animal

studies<sup>19, 29, 46, 1</sup>, and *in vitro* salmonella microsome assays showed no evidence of a mutagenic potential<sup>47</sup>.

### ***Typical Dosages***

*Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.*

*Doses are given for single herb use and must be adjusted when using herbs in combinations.*

*Doses may also vary according to the type and severity of the condition treated and individual patient conditions.*

*Adult doses:*

*Root: 0.3-2.0 grams, boiled as a decoction (tea), three times daily<sup>7</sup>*

*Tincture (1:10 in 90% alcohol): 2-4 mL daily<sup>7</sup>*

*Fluid extract (1:1 in 90% alcohol): 0.3-2.0 mL three times daily<sup>7</sup>*

*Pediatric dosages: Unknown*

*Availability of standardized preparations: Remifemin, Cimicifuga Oligoplex, Cimifuga Pentakran, Black Cohosh Liquid Extract ( eg. Bio-pro, et al), Black Cohosh Root Powder (eg. Global Botanical, et al)<sup>2</sup>, Cefakliman mono capsules, Cimisan dried root stock extract, Femilla tincture, Klimadynon*

*Dosages used in herbal combinations: Variable*

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