OVERVIEW
Black cohosh is indigenous to the eastern U.S. and Canada, with a long and widely recognized medicinal tradition. Native Americans and early colonists used black cohosh root to treat conditions including general malaise, malaria, rheumatism, abnormalities in kidney function, sore throat, menstrual irregularities, and childbirth. In Chinese medicine, rhizomes of many different species have been traditionally used to treat inflammation, fever, headache, pain, sore throat, and chills. Black cohosh has been used in Europe for more than 40 years to treat symptoms associated with menopause. In 1996, nearly 10 million retail units of a standardized ethanolic and isopropanolic extract were sold monthly in Germany, Australia, and the U.S. The herb has become increasingly popular as a dietary supplement in the U.S., with retail sales in mainstream markets in 2000 ranking 14th of all herbals. Currently, black cohosh root is approved to treat premenstrual discomfort, dysmenorrhea, and neurovegetative complaints associated with menopause by the German Commission E.

PRIMARY USES
- Neurovegetative complaints associated with menopause, including hot flashes, heart palpitations, nervousness, irritability, sleep disturbances, tinnitus, vertigo, perspiration, depression
- Premenstrual discomfort
- Dysmenorrhea

OTHER POTENTIAL USES
- Surgical ovarian deficiencies

PHARMACOLOGICAL ACTIONS
Estrogenic activity (with alcoholic fractions) inhibits LH secretion but not FSH secretion in menopausal women; proliferates vaginal epithelium. However, other studies have refuted estrogen-like activity and further research needs to be conducted to determine the mechanism of action.

DOSAGE AND ADMINISTRATION
The German Commission E Monograph recommends a maximum treatment duration of six months. In Germany, prescriptions for hormone replacement therapy (HRT) are limited to a six-month duration in order to ensure that women return to their healthcare providers for general check-ups. In the case of black cohosh, the Commission E has based its limitations of therapy with black cohosh on the same criteria as used for HRT.

Black cohosh (crude drug): 40 mg–80 mg (or oral dose equivalent) per day.
Dried rhizome and root: 40–200 mg.
Decoction: 240 ml boiling water poured onto 40–200 mg black cohosh (crude drug), simmered for 10–15 minutes.
Fluid extract: 1:1 (g/ml) 90% alcohol, 0.3–1.0 ml, or 0.3–2.0 ml, or 5–30 drops.
Tincture: 1:10 (g/ml) 40–60% alcohol, 0.4–2.0 ml, or 2–4 ml, or 40 drops twice daily.
Extract: 40%–60% ethanolic or isopropyl alcohol extracts of the rhizome with monitoring of active compounds (triterpene glycosides) corresponding to 40 mg of black cohosh daily.

CONTRAINDICATIONS
None known. Since black cohosh is considered to be a phytoestrogen, it was originally contraindicated in patients with a history of breast cancer. However, recent studies suggest that this contraindication needs to be reevaluated.

Pregnancy and Lactation: Not recommended during pregnancy due to its emmenagogue and uterine-stimulant effect (based on empirical observations). Not recommended during lactation (based on empirical observations).

ADVERSE EFFECTS
Occasional gastrointestinal discomfort has been reported. Vertigo, headache, nausea, vomiting, impaired vision, and impaired circulation have been reported in cases of overdose.

DRUG INTERACTIONS
None known.
Of 10 clinical studies, including a total of 1,371 participants, nine of these studies demonstrated positive effects for menopausal symptoms. Numerous clinical trials with varied methods and designs have been conducted on the standardized isopropanolic/ethanolic extract of black cohosh root, Remifemin®, from 1981 to the present. Five of the studies were open-label, and evaluated the effectiveness of the extract as a monotherapy for the treatment of menopausal complaints. Two studies compared black cohosh extract to conventional hormonal therapy in the treatment of complaints associated with menopause or hormonal deficiencies in ovariectomized/hysterectomized patients. One open-label, randomized, controlled study compared the efficacy of three different black cohosh therapies to conjugated estrogens and diazepam for menopausal problems. One R, DB study compared two dosages of Remifemin® for the treatment of menopausal symptoms. A decrease in the Kupperman-Menopause Index (KPI) was reported in five clinical studies on black cohosh extract.
Black Cohosh

Actaea racemosa L. (syn. Cimicifuga racemosa [L.] Nutt.)
[Fam. Ranunculaceae]

**Overview**
Black cohosh, a plant commonly found in the eastern U.S. and Canada, was a botanical remedy of Native Americans. It has been used in Europe for over 40 years. Today, black cohosh root is approved by the German government as a treatment for premenstrual discomfort, painful menstruation, and menopausal symptoms.

**Uses**
Menopausal complaints including hot flashes, heart palpitations, nervousness, irritability, sleep disturbances, ringing in the ears (tinnitus), whirling sense or dizziness (vertigo), perspiration, and depression; premenstrual discomfort; painful menstruation.

**Dosage**
The German Commission E Monograph recommends taking black cohosh for a period of six months, after which a check-up with your healthcare practitioner is advised before resuming further use.

**Average recommended dose**: 40mg-80mg (or oral dose equivalent) of black cohosh per day (available in tablet and liquid form).

**Dried rhizome and root**: 40–200 mg.

**Decoction**: Pour 240 ml boiling water onto 40–200 mg black cohosh root, simmer for 10–15 minutes.

**Fluid extract**: 1:1 (g/ml) 90% alcohol, 0.3–1.0 ml, 0.3–2.0 ml, 5–30 drops.

**Tincture**: 1:10 (g/ml) 40–60% alcohol, 0.4–2.0 ml, 2–4 ml, 40 drops twice daily.

**Contraindications**
None known.

**Pregnancy and lactation**: Patients who are pregnant and/or lactating should not use black cohosh. It is not recommended during pregnancy because it may promote menstrual flow or stimulate the uterus. Black cohosh is not recommended during breast-feeding.

**Adverse Effects**
Occasional gastrointestinal discomfort has been reported. Overdose may cause vertigo, headache, nausea, vomiting, impaired vision, and impaired circulation.

**Drug Interactions**
None known. Minimal side effects were noted when standardized black cohosh extracts and estrogen-replacement therapy were taken at the same time.

Comments
When using a dietary supplement, purchase it from a reliable source. For best results, use the same brand of product throughout the period of treatment. As with all medications and dietary supplements, please inform your healthcare provider of all herbs and medications you are taking. Interactions may occur between medications and herbs or even among different herbs when taken at the same time. Treat your herbal supplement as you would any type of medication by taking it as directed, storing it as advised on the label, and keeping it out of the reach of children and pets. Consult your healthcare provider with any questions.

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Black Cohosh
Actaea racemosa L. (syn. Cimicifuga racemosa [L.] Nutt.)
[Fam. Ranunculaceae]

**Overview**

Black cohosh is indigenous to the eastern U.S. and Canada, with a long and widely recognized medicinal tradition (Blumenthal et al., 2000; Liske, 1998). Native Americans and early colonists used black cohosh root to treat conditions including general malaise, malaria, rheumatism, abnormalities in kidney function, sore throat, menstrual irregularities, and childbirth (Blumenthal et al., 2000; Boon and Smith, 1999; Liske, 1998). In Chinese medicine, rhizomes of many different species have been traditionally used to treat inflammation, fever, headache, pain, sore throat, and chills (Foster, 1999; Liske, 1998). Black cohosh has been used in Europe for more than 40 years to treat symptoms associated with menopause (Foster, 1999). In 1996, nearly 10 million retail units of a standardized ethanolic and isopropanolic extract were sold monthly in Germany, Australia, and the U.S. (Blumenthal et al., 2000; Pizzorno and Murray, 1999). The herb has become increasingly popular as a dietary supplement in the U.S., with retail sales in mainstream markets in 2000 ranking 14th of all herbals (Blumenthal, 2001). Currently, black cohosh root is approved as a nonprescription drug to treat premenstrual discomfort, dysmenorrhea, and neurovegetative complaints associated with menopause by the German Commission E (Blumenthal et al., 1998; Liske, 1998).

**Description**

Crude preparations of black cohosh consist of the dried rhizome and roots of Actaea racemosa L. (syn. Cimicifuga racemosa [L.]) (Foster, 1999; McGuffin et al., 2000) [Fam. Ranunculaceae], harvested in the fall (Blumenthal et al., 2000; Bradley, 1992). Some commercial extracts have been standardized based upon triterpene glycoside content (Liske, 1998; McKenna, 1998). Remifemin®, a German standardized oral formulation used in all of the black cohosh clinical studies published through 2000, contains 20 mg of black cohosh extract standardized to 1 mg triterpene glycosides (calculated as 27-deoxyactein) per tablet or twenty drops (Blumenthal et al., 2000; Liske, 1998; McKenna, 1998).

**Primary Uses**

Gynecology

- Menopause: Neurovegetative complaints associated with menopause, including hot flashes, heart palpitations, nervousness, irritability, sleep disturbances, tinnitus, vertigo, perspiration, and depression (Liske and Wüstenberg, 1998; Düker et al., 1991; Lehmann-Willenbrock and Riedel, 1988; Blumenthal et al., 1998; Bratman and Kroll, 1999; Pethö, 1987; Stoll, 1987; Warnecke, 1985; Vorberg, 1984; Däber 1983; Stolze 1982)
- Premenstrual discomfort (Blumenthal et al., 1998; Bratman and Kroll, 1999)
- Dysmenorrhea (Blumenthal et al., 1998; Bratman and Kroll, 1999)

**Other Potential Uses**

- Treatment of surgical ovarian deficiencies (Lehmann-Willenbrock and Riedel, 1988; Liske, 1998)

**Dosage**

In clinical studies before 1996, the dose was 2x2 tablets/day, or 2x40 drops/day, which is equivalent to 48–140 mg of black cohosh extract per day (Foster, 1999; Liske, 1998). A recent clinical trial comparing two different dosages of Remifemin® (40 mg vs. 127 mg daily), for six months, in 152 women with menopausal complaints, found similar safety and efficacy profiles for both doses (Liske and Wüstenberg, 1998). Based upon the results of this trial, a recommended dose equivalent to 40 mg of black cohosh (dried root) daily is currently recommended (Liske, 1998). Nevertheless, the dosage in most of the clinical trials shown in the table below is 80 mg daily of the extract (the doses in the studies using liquid preparation form at 40 drops twice daily are equivalent to 80 mg daily).

**Internal Crude Preparations**

- Dried rhizome and root: 40–200 mg (Bradley, 1992).
- Decoction: 240 ml boiling water poured onto 40–200 mg black cohosh (cut, dried root) and simmered for 10–15 minutes (Bradley, 1992).
- Fluid extract: 1:1 (g/ml) 90% alcohol, 0.3–1.0 ml (Karnick, 1994); 0.3–2.0 ml (Newall et al., 1996); 5–30 drops (Lust, 1974).
- Tincture: 1:10 (g/ml) 40–60% alcohol, 0.4–2.0 ml (Bradley, 1992); 2–4 ml (Newall et al., 1996; Wren, 1988). 40 drops are taken twice daily (Unter, 1999; Warnecke, 1985).
Standardized Preparations

**Extract:** 40%-60% ethanolic or isopropyl alcohol extracts of the rhizome with monitoring of active compounds (triterpene glycosides) (Liske, 1998; Liske and Wüstenberg, 1998), corresponding to 40 mg of black cohosh daily (Blumenthal et al., 1998).

**Duration of Administration**

The German Commission E monograph recommends a maximum treatment duration of six months (Blumenthal et al., 1998). Some authors have suggested that this is due to a lack of clinical trials longer than six months published at the time the monograph was compiled (Bratman and Kroll, 1999; MCKenna, 1998). According to Professor H. Schilcher, vice-president of the Commission E, the reason for this limitation is predicated on the Commission's desire to ensure that women return to their healthcare provider for periodic examinations at six-month intervals. The limitation is not based on any concerns about the long-term safety of black cohosh. Based on a long history (33 years) of black cohosh use in Germany at the time the monograph was written in 1989, and on the herb's general safety in long-term use (including data from clinical experience, post-marketing studies, and market data on daily doses prescribed, adverse events reports, etc.), the Commission E considered allowing unlimited duration of use of black cohosh without concern for safety. However, in Germany, prescriptions for hormone replacement therapy (HRT) are limited to a six-month duration in order to ensure that women return to their healthcare provider for general checkups; in the case of black cohosh, the Commission E treated it with the same limitations as HRT (Schilcher, 2001). The relative safety of black cohosh in long-term use is also supported by pharmacological and clinical research. In a six-month chronic toxicity study, followed by an eight-week recovery period, up to 1,800 mg/kg body weight, or roughly 90 times the therapeutic dose, of black cohosh granulate was administrated to rats, and no detectable anomalies or toxic effects were observed (Korn, 1991). Although this study may support long-term use of black cohosh (Pizzorno and Murray, 1999), studies of carcinogens in rats must typically be two years long to equate to long-term use in humans (Cott, 2000). Ames tests (in vitro Salmonella microsomal assays) performed on isopropanolic extracts showed no evidence of mutagenicity (Bratman and Kroll, 1999; Liske, 1998). Although long-term studies may be warranted to satisfy current standards in toxicology, these findings suggest that black cohosh may be considered relatively safe for long-term therapy (Liske, 1998; Pizzorno and Murray, 1999).

**Chemistry**

 Constituents of black cohosh root and rhizome include triterpene glycosides: actein, cimicifugoside, cimigoside, 27-deoxyactein, deoxyacetylacteol, and racemoside (Bradley, 1992; Bratman and Kroll, 1999; MCKenna, 1998; Newall et al., 1996). Eight new triterpene glycosides named cimiracemosides A-H have been identified (Shao et al., 2000). Some references state that it also contains isoflavones including formononetin (Bradley, 1992; Jarry et al., 1985; Pizzorno and Murray, 1999). Note: Although Jarry and coworkers reported the isolation of formononetin from a methanolic extract in 1985, more recent studies of Remifemin® (an isopropyl/ethanolic extract) along with five other commercial preparations failed to identify appreciable levels of the flavonoids (Liske, 1998; Liske and Wüstenberg, 1998; Foster, 1999; Stuck et al., 1997). A recent review suggests black cohosh does not contain isoflavones (Hagels et al., 2000). Constituents of black cohosh root and rhizomes also include the aromatic acids, isofolic acid and salicylic acid (Bradley, 1992; Newall et al., 1996; Pizzorno and Murray, 1999) and other constituents including tannins, resin, phytosterols, fatty acids, starch, and sugars (Bradley, 1992; Foster, 1999; Newall et al., 1996).

**Pharmacological Actions**

**Human**

 A good-clinical-practices-compliance study (40 mg vs. 127 mg daily) in postmenopausal women yielded no estrogen-like LH or FSH suppression. In addition, endogenous estradiol, sex hormone-binding globulin (SHBG), and prolactin levels remain unaffected (Liske et al., 1998; Liske and Wüstenberg, 1998). Estrogenic changes in vaginal cytological parameters (e.g., degree of vaginal proliferation) were not observed (Liske et al., 1998; Liske and Wüstenberg, 1998). No increase in thickness of the endometrium, no changes in vaginal cell status, and no changes in the hormone values of LH, FSH, prolactin, estradiol were observed before and after a black cohosh treatment (Nesselhut and Liske, 1999).

**Animal**

 No estrogen-like uterine effects or changes in vaginal cytology were detected in animal experiments using an ethanolic extract (Einer-Jensen et al., 1996). In rats with artificially (DMBA) induced breast tumors, it was demonstrated that different doses of an isopropanolic black cohosh extract (1x, 10x, 100x human therapeutic dose) did not cause stimulation of mammary tumors compared to the placebo group. Estrogen substitution with mestranol resulted in a progression of the tumors. No estrogenic-agonistic effects on prolactin, LH, FSH, or on the uterine tissue were seen (Freudenstein et al., 2000). Pyridinoline and deoxypyridinoline as markers of bone metabolism in rats declined significantly under black cohosh administration (isopropanolic extract) compared to the control, suggesting potential benefits in retarding bone loss (Nisslein and Freudenstein, 2000).

**In vitro**

 Formononetin, the isoflavone thought to be an active estrogenic component of black cohosh in earlier studies (Jarry et al., 1985; Jarry and Harnischfeger, 1985), is not detected in the commercially available isopropanolic and ethanolic extract (Struck et al., 1997) and is not a constituent of the dried root (Hagels et al., 2000). An isopropanolic/alcoholic extract inhibits the proliferation of estrogen-receptor positive (ER+) human breast cancer cell lines (M D A M B 4355) (Nesselhut et al., 1993). Investigations show that an isopropanolic-aqueous extract does not stimulate the proliferation of ER+human breast cancer cell lines (M CF-7), but the extract does produce a dose-dependent inhibition of DNA synthesis, an antagonization of estradiol activity, and a synergistic increase in the anti-proliferative effect of tamoxifen (Freudenstein and Bodinet, 1999). An ethanolic black cohosh extract inhibited growth of T-47D human breast cancer cells (Dixon-Shanies and Shaikh, 1999).

Studies supporting the estrogenic activity of black cohosh:

**Human**

 Earlier research showed that black cohosh improves neurovegetative symptoms (hot flashes, increased perspiration, headache, vertigo, heart palpitations, tinnitus) and psychological complaints.
(nervousness, irritability, sleep disturbances, depressive mood) associated with menopause or hormonal deficiencies experienced by hysterectomized/ovariectomized patients (Stolze, 1982; Daiber, 1983; Vorberg, 1984; Warnecke, 1985; Stoll, 1987; Pethö, 1987; Lehmann-Willenbrock and Reidel, 1988; Lieberman, 1998; Liske, 1998; Liske and Wüstenberg, 1998), proliferation of vaginal epithelium (Stoll, 1987). Three alcoholic fractions produced endocrine effects that inhibit luteinizing hormone (LH) secretion, but not follicle-stimulating hormone (FSH) secretion, in menopausal women. The authors hypothesize that this is an estrogen-like effect (Dükert et al., 1991).

In vitro
A methanolic extract demonstrated endocrine activity in an in vitro estrogen-receptor assay. The three fractions identified were believed to compete with estradiol for binding sites on estrogen receptors (Jarry et al., 1985).

Mechanism of Action
Although estrogen-like effects, such as LH suppression, have been proposed as the primary mechanism of action in alleviating the symptoms of menopause, results of recent animal investigations and clinical studies indicate that the mode of action is not identical with estrogen. On the contrary, estrogen-agonistic and estrogen-antagonistic effects on different target organs indicate a tissue selectivity for black cohosh ingredients (Boblitz et al., 2000). Although some studies suggest black cohosh has an estrogen-like effect based on its observed LH-suppressive activity, a definite mechanism of action has not been established (Dükert et al., 1991). A recent animal study failed to detect estrogen-like uterine effects or changes in vaginal cytology with black cohosh administration. Thus, the authors concluded that LH suppression was associated with neurotransmitter interference instead of estrogenic activity (Einer-Jensen et al., 1996). Similarly, another study comparing two different dosages of Remifemin® (40 mg vs. 127 mg daily) showed no effect on hormonal levels of LH, FSH, SHBG, prolactin, or estradiol, or on vaginal cytological parameters; however, menopausal symptoms were clearly alleviated (Liske et al., 1998; Liske and Wüstenberg, 1998). Although the authors cannot definitively explain the mechanism responsible for the efficacy of black cohosh in the treatment of menopausal complaints, they agree that Remifemin® does not exert a hormonal (estrogenic) effect (Liske et al., 1998; Liske and Wüstenberg, 1998).

Contraindications
None known (Blumenthal et al., 1998; Pizzorno and Murray, 1999).

Note: Despite earlier concerns about the possible estrogenicity of black cohosh, and thus a possible contraindication for women with estrogen-positive breast cancer, as explained in the Pharmacology and Mechanism of Action sections above and in the discussion below, it is clearly established that black cohosh is not estrogenic. Thus, no such contraindication is warranted.

According to an in vitro study, the use of an isopropanolic aqueous extract of black cohosh reportedly inhibited the proliferation of estrogen-receptor positive (ER+) human breast cancer cells and, although still debated, the present data indicate that black cohosh does not increase the risk of developing breast cancer (Nessenhut et al., 1993). Another in vitro study reported that Remifemin® extract did not stimulate the proliferation of ER+ human breast cancer cells (Freudenstein and Bodinet, 1999). In addition, the extract inhibited DNA synthesis in a dose-dependent manner, antagonized the estrogenic activity of estradiol, and enhanced the anti-proliferative effect of tamoxifen (Freudenstein and Bodinet, 1999). In rats with artificially (DMBA) induced breast tumors, it could be demonstrated that different doses of an isopropanolic black cohosh extract (1x, 10x, 100x human therapeutic dose) did not cause any stimulation of mammary tumors compared to the placebo group. Estrogen substitution with mestranol resulted in a progression of the tumors. No estrogenic-agonistic effects on prolactin, LH, or FSH, or on uterine tissue were seen (Freudenstein et al., 2000).

Pregnancy and Lactation: Not recommended during pregnancy due to its emmenagogue and uterine-stimulant effect (based on empirical observations) (Brinker, 2001; McGuffin et al., 1997). Not recommended during lactation (based on empirical observations) (Brinker, 2001; McGuffin et al., 1997).

Adverse Effects
Occasional gastrointestinal discomfort has been reported (Blumenthal et al., 1998; Foster, 1999; McGuffin et al., 1997). Vertigo, headache, nausea, vomiting, impaired vision, and impaired circulation have been reported with overdose (Foster, 1999; McGuffin et al., 1997).

Drug Interactions
None known (Blumenthal et al., 1998; Brinker, 2001), including in cases of simultaneous administration of standardized black cohosh extracts and estrogen-replacement therapy (McKenna, 1998; Pethö, 1987; Warnecke, 1985).

American Herbal Products Association (AHPA) Safety Rating
Class 2b: Not to be used during pregnancy.
Class 2c: Not to be used while nursing (McGuffin et al., 1997).

Regulatory Status
Canada: Regulated as a drug if single dose is sufficiently high or as a potential "New Drug" for specific nontraditional use claims (HPB, 1993). Included in the Drugs Directorate "List of Herbs Unacceptable as Non-medicinal Ingredients in Oral Use Products" (Health Canada 1995a). When identified as a Traditional Herbal Medicine (THM) or as a homeopathic drug, black cohosh is regulated as a nonprescription over-the-counter (OTC) drug requiring premarket authorization and assignment of a drug identification number (DIN) (Health Canada, 1995b; Health Canada, 2001; WHO, 1998).

France: Traditional medicine.

Germany: Fresh or dried rhizome with attached roots is an approved nonprescription drug for oral use in the German Commission E Monographs (Blumenthal et al., 1998). The fresh rhizome and roots for preparation of hydro-alcoholic mother tincture and liquid dilutions are an official drug of the German Pharmacopoeia (DAB).

Italy: No information available.

Sweden: Classified as a natural remedy; intended for self-medication; require advanced application for marketing authorization. A monograph for the product Remifemin® is published in the Medical Products Agency (M PA) "Authorised Natural Remedies" (M PA, 1999, 2001; WHO, 1998).
SWITZERLAND: Approved as single-ingredient Herbal Medicine and as a component of multiple-ingredient Homeopathic Medicines, both classified by the Interkantonale Kontrollstelle für Heilmittel (IKS) as List D medicinal products with sales limited to pharmacies and drugstores, without prescription (M orant and Ruppanner, 2001; WHO, 1998).

U.K.: OTC herbal medicine specified in the General Sale List, Schedule 1 (medicinal products requiring a full product license), Table A (for internal or external use); 200 mg maximum single dose and maximum daily dose (GSL, 1990).

U.S.: Dietary supplement (USC, 1994). The homeopathic mother tincture 1:10 (v/v), 55% (v/v), of fresh or dried black cohosh root, is a Class OTC drug of the Homeopathic Pharmacopoeia of the United States (HPUS, 1990).

Clinical Review

Ten clinical studies are outlined in the following table, “Clinical Studies on Black Cohosh,” including a total of 1,371 participants. Nine of these studies demonstrated positive effects for menopausal symptoms. Numerous clinical trials with varied methods and designs have been conducted on the standardized isopropanolic/ethanolic extract of black cohosh root, Remifemin®, from 1981 to the present. Five of the studies were open-label, and evaluated the effectiveness of the extract as a monotherapy for the treatment of menopausal complaints (Pethö, 1987; Warnecke, 1985; Vorberg, 1984; Daiber, 1983; Stolze, 1982). Two studies, a randomized, double-blind (R,D,B) study (Liske et al., 1998), and a randomized study (Lehmann-Willenbrock and Reidel, 1988) compared black cohosh extract to conventional hormonal therapy in the treatment of complaints associated with menopause or hormonal deficiencies in ovariec-tomized/hysterectomized patients. One open-label, randomized, controlled study compared the efficacy of three different black cohosh therapies to conjugated estrogens and diazepam for menopausal complaints (Warnecke, 1985). One n.e., D,B study compared two dosages of Remifemin® for the treatment of menopausal symptoms (Liske et al., 1998). A decrease in the Kupperman-Menopause Index (KPI) was reported in five clinical studies on black cohosh extract (Liske et al., 1998; Lehmann-Willenbrock and Reidel, 1988; Stoll, 1987; Vorberg, 1984; Daiber, 1983).

Branded Products

Remifemin®: GlaxoSmithKline / One Franklin Plaza / Philadelphia, PA 19102 / U.S. / Tel.: (800) 366-8900. One tablet contains black cohosh extract corresponding to 20 mg of crude drug standardized to 1% 27-deoxyacteine.

Remifemin®: GlaxoSmithKline. Twenty drops correspond to 20 mg of crude drug. This product is no longer available.

References


Farinauworth N.R. Personal communication to M. Blumenthal. May 24, 1999.


GHP. See: German Homeopathic Pharmacopoeia.

GSL. See: General Sale List.


HPB. See: Health Protection Branch.

HPUS. See: Homeopathic Pharmacopoeia of the United States.


HPS. See: Health Protection Branch.

HPS. See: Homeopathic Pharmacopoeia of the United States.

### Clinical Studies on Black Cohosh (Actaea racemosa L., syn. Cimicifuga racemosa)

#### Gynecology

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Subject</th>
<th>Design</th>
<th>Duration</th>
<th>Dosage</th>
<th>Preparation</th>
<th>Results/Conclusion</th>
</tr>
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<tbody>
<tr>
<td>Jacobson et al., 2001</td>
<td>Menopausal complaints: Hot flashes in women with history of breast cancer</td>
<td>R, DB, PC, n=69 (randomized based on current tamoxifen use)</td>
<td>2 months</td>
<td>O, ne, 20 mg tablet, 2 x daily with meals</td>
<td>Remifemin®</td>
<td>Although both treatment and placebo groups self-reported declines in number and intensity of hot flashes, black cohosh was not found to be statistically more harmful or beneficial than placebo in treating menopausal symptoms. Sweating was the only symptom that did show significantly greater improvement over placebo in the black cohosh group (p=0.4). Subset analysis showing effects on patients taking tamoxifen was not reported.</td>
</tr>
<tr>
<td>Liske and Wüstenberg, 1998</td>
<td>Menopause complaints</td>
<td>R, DB n=152 (women ages 43–60 with climacteric complaints)</td>
<td>6 months</td>
<td>40 mg/day (crude drug) vs. 127 mg/day (crude drug)</td>
<td>Remifemin®</td>
<td>Decrease in the Kupperman-Menopause Index (KPI) (values ~31 at the beginning) was observable after 2 weeks of Remifemin® therapy. Similar results in safety and efficacy were observed for both dosages. After 6 months, a positive response (KPI&lt;35) was seen in ~90% of patients. No detectable changes were seen in hormone levels of LH, FSH, SHBG, prolactin, or estradiol. Remifemin® did not influence vaginal cytological parameters (degree of proliferation). The authors concluded that Remifemin may act as a selective estrogen receptor modulator (&quot;Phyto-SERM&quot;) (no statistics presented).</td>
</tr>
<tr>
<td>Düker et al., 1991</td>
<td>FSH and LH levels during menopause</td>
<td>PC n=110 female patients with menopausal complaints who have received no hormonal therapy for at least 6 months (mean age=52)</td>
<td>2 months</td>
<td>8 mg/day extract vs. placebo</td>
<td>Remifemin® tablet vs. placebo</td>
<td>Remifemin® showed an estrogen-like mode of action with selective LH suppression in menopausal women. No significant change in FSH was observed. Mean LH levels significantly reduced compared to placebo (p&lt;0.05).</td>
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<tr>
<td>Lehmann-Willenbrock and Riedel, 1988</td>
<td>Menopause complaints</td>
<td>R, Cm n=60 randomized into 4 treatment groups (Estriol, conjugated estrogen, estrogen gestation, black cohosh)</td>
<td>6 months</td>
<td>1 mg tablet/day or 1.25 mg tablet/day or 1 tablet/day or 48–140 mg/day</td>
<td>Remifemin®</td>
<td>Remifemin® extract was shown to produce a decline in modified KPI and improvement of complaints associated with postoperative ovarian function deficiencies. No significant differences were noted among treatment groups. No differences in LH or FSH levels were observed.</td>
</tr>
<tr>
<td>Pethö, 1987</td>
<td>Menopause complaints</td>
<td>O n=50 (female patients converting from hormone injections to black cohosh over 6 months)</td>
<td>6 months</td>
<td>48–140 mg/day</td>
<td>Remifemin® tablet</td>
<td>Hormone replacement therapy (Gynodian injection) may be switched to black cohosh extract with equivalent success. Of the patients, 82% reported black cohosh preparation good or very good; 56% of patients did not require additional hormone injections. No side effects were noted. Significant improvement in mean menopausal index after 2 months (p&lt;0.001).</td>
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### Clinical Studies on Black Cohosh (Actaea racemosa L., syn. Cimicifuga racemosa) (cont.)

#### Gynecology

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Subject</th>
<th>Design</th>
<th>Duration</th>
<th>Dosage</th>
<th>Preparation</th>
<th>Results/Conclusion</th>
</tr>
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<tbody>
<tr>
<td><strong>Stoll, 1987</strong></td>
<td>Menopause complaints</td>
<td>R, DB, PC, C</td>
<td>n=80 female patients (ages 46 to 56)</td>
<td>12 weeks</td>
<td>48-140 mg/day or 0.625 mg CE/day + 3 placebo tablets/day on days 1–21, then 2 placebo tablets 2x/day on days 22–28 or 2 placebo tablets 2x/day</td>
<td>Remifemin® tablet or conjugated estrogens (CE) or placebo</td>
</tr>
<tr>
<td><strong>Warnecke, 1985</strong></td>
<td>Menopause complaints</td>
<td>O, C, Cm</td>
<td>n=80 female patients (average age 54 years)</td>
<td>12 weeks</td>
<td>48-140 mg/day or 0.6 mg/day or 2 mg/day</td>
<td>Remifemin® drops or Conjugated estrogens or diazepam</td>
</tr>
<tr>
<td><strong>Vorberg, 1984</strong></td>
<td>Menopause complaints</td>
<td>0</td>
<td>n=80 menopausal women (39 patients showed contraindications to HRT, and 11 refused hormone treatment)</td>
<td>12 weeks</td>
<td>48-140 mg/day</td>
<td>Remifemin® drops</td>
</tr>
<tr>
<td><strong>Daiber, 1983</strong></td>
<td>Menopause complaints</td>
<td>0</td>
<td>n=56 menopausal women, hormone replacement therapy was refused or contraindicated for these subjects (ages 45–62 years)</td>
<td>12 weeks</td>
<td>48-140 mg/day</td>
<td>Remifemin® drops</td>
</tr>
<tr>
<td><strong>Stolze, 1982</strong></td>
<td>Menopause complaints</td>
<td>0, MC</td>
<td>n=704 female patients, 629 evaluated (mean age 51 years)</td>
<td>6 to 8 weeks</td>
<td>48-140 mg/day</td>
<td>Remifemin® drops</td>
</tr>
</tbody>
</table>