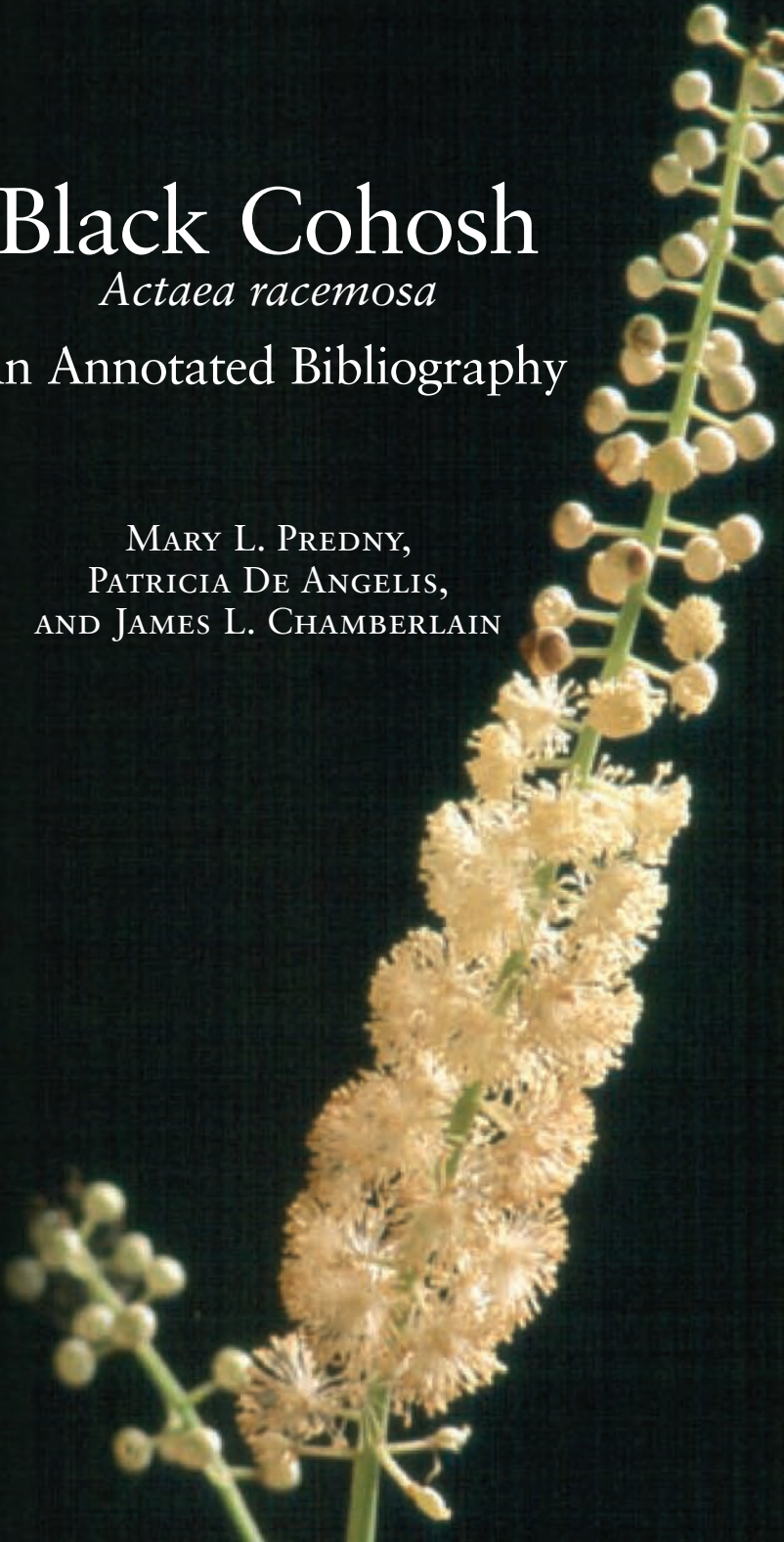


# Black Cohosh

*Actaea racemosa*

## An Annotated Bibliography

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## Abstract

Black cohosh (*Actaea racemosa*, Syn.: *Cimicifuga racemosa*), a member of the buttercup family (*Ranunculaceae*), is an erect perennial found in rich cove forests of Eastern North America from Georgia to Ontario. Native Americans used black cohosh for a variety of ailments including rheumatism, malaria, sore throats, and complications associated with childbirth. Europeans have used this important medicinal plant to treat menopausal symptoms for over 40 years. Recent clinical evidence supports the efficacy and safety of black cohosh for these symptoms. Recent decisions by the U.S. Food and Drug Administration on hormone replacement therapy have increased the demand for black cohosh. In a 1-year period ending in 1998, retail sales increased more than 500 percent. In 2001, when retail sales in other segments of the herbal products industry were down, black cohosh sales increased about 2 percent to an estimated value of \$6.2 million. Nearly 100 percent of black cohosh raw materials is wild harvested. Though it has received an “apparently secure” ecological ranking on the global and national scales, conservation groups list the species as “at risk” in the United States and endangered in Illinois and Massachusetts. Research is underway to determine sustainable harvest levels and to establish suitable cultivation methods.

**Keywords:** Conservation, medicinal plants, menopause, nontimber forest products, phytoestrogens, poaching.

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## Nomenclature

The scientific name for black cohosh has changed several times throughout botanical history. According to Foster (1999), the first known classification was made in 1705 by Plukenet, as *Christopheriana facie, Herba spicata, ex Provincia Floridiana*. In pre-Linnaean times (before 1750) the plant was most commonly known as *Actaea*, though some botanists still used the genus *Christopheriana*. Linnaeus first classified black cohosh as *Actaea*, but later separated out the genus *Cimicifuga* based on differences in fruit characteristics, where *Actaea* had fleshy berries and *Cimicifuga* had dry follicles. The name *Cimicifuga* was used until Rafinesque noted that black cohosh did not fit clearly into Linnaeus’ classification and renamed the plant *Macrotrys*. Eton adopted this classification but dropped the second “r”, making it *Macrotys*. In the eclectic<sup>1</sup> pharmacopeias of the late 1800s

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<sup>1</sup> Eclectic physicians were doctors who treated patients with herbal medicines between the late 1800s and early 1900s.



Figure 1—Black cohosh plant (Britton and Brown 1913).

and early 1900s, *Macrotys* was commonly used both as the genus and the common name. The species name varied along with the genus name, though the most commonly used were “*canadensis*,” “*spicata*,” “*racemosa*,” or “*serpentaria*.” Modern botanists reverted back to *Cimicifuga*, the genus assigned by Linnaeus, until 1998 when Compton and others evaluated morphological traits and deoxyribonucleic acid (DNA) sequences and put all of the species in *Cimicifuga* and *Souliea* back under *Actaea* (Compton and others 1998a, 1998b; Foster 1999). There are differences of opinion in the botanical community about whether black cohosh should be treated as a separate genus; however, for the purposes of this publication, the authors have agreed to use *Actaea racemosa*.

## Botany and Ecology

Black cohosh is an erect perennial that grows from 3 to 8 feet in height with a 2-foot spread (Foster 2000, Harding 1936). Leaves have sharply toothed edges, are alternate, three-pinnately compound, and terminate with a three-lobed leaflet (Foster and Duke 2000) (fig. 1).

In North America, several closely related plants that resemble black cohosh are harvested both intentionally to add bulk, and unintentionally due to misidentification (Ramsey 1986, 1988, 2000; Upton 2002). Black cohosh is often confused with other plants in *Actaea*, particularly yellow cohosh (*A. podocarpa* Syn.: *Cimicifuga americana*) or baneberry (*A. pachypoda* and *A. rubra*) (Upton 2002).



Flowers are hermaphroditic and apetalous, with showy greenish-white stamens in tufts (Fern 1997–2000, Missouri Botanical Garden 2002). Flowers, buds, and seedpods are simultaneously borne on a tall arching raceme, ½ to 2 feet in length, from July through September (Foster and Duke 2000, Harding 1936, Sievers 1930). The flowers are pollinated by bees (*Apis* spp. and *Bombus* spp.)<sup>2</sup> or flesh flies (*Sarcophaga* spp.) (Strauch 1995). After the flowers have faded, the seedpods remain on the raceme throughout the winter. The dry seeds rattle in their pods when disturbed by wind, making the distinctive noise that is the source for the lesser used common names for black cohosh of “rattleroot,” “rattle snakeroot,” “rattletop,” and “rattleweed” (Sievers 1930).

The flowers are said to have an unpleasant odor, a trait of the genus *Cimicifuga* (Foster 2000). The name *Cimicifuga* comes from the Latin “Cimex,” the genus name for the bed bug, and “fugare,” meaning to put to flight or repel (Foster 2000, Missouri Botanical Garden 2002). Also known by the common names “bugbane” or “bugwort,” similar species in Europe were traditionally used as insect deterrents with leaves or flowers stuffed into pillows or mattresses (Foster 2000, Harding 1936).

The common name “cohosh” comes from an Algonquian Indian word meaning “rough,” which describes the dark, hard, and knotted rhizomes that contain the plant’s medicinal properties (Tetherow 2001). The rhizome is harvested in early autumn after the flowers have faded to fruit and the leaves have died back (Grieve 1931, Sievers 1930), then cut into pieces and dried (Harding 1936). Rhizomes can be divided in the spring to propagate new plants (Botany.com 2004, Fern 1997–2000).

Black cohosh tolerates a variety of soil types, but prefers rich cove habitats—cool, well-drained, moist, semishaded woodland locations (Fern 1997–2000, Missouri Botanical Garden 2002). The hardiness range for the plant is 4A to 10A (Hortocopia, Inc. 2001). Black cohosh is found from southern Ontario to northern Georgia and west to Wisconsin and Arkansas (Foster and Duke 2000; U.S. Department of Agriculture, Natural Resources Conservation Service 2001) (fig. 2). Plants growing in the warmer southern extent of the range require more shade and water (Blakley and Renaud 1999).

Several thousand populations of black cohosh are estimated to be extant rangewide—including 100 in Indiana, “hundreds” in Maryland, 750 to

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<sup>2</sup> Personal communication. 2004. Lorna Lueck, Research Fellow, Medicinal Plant Program, University of Massachusetts, Amherst, MA 01003.

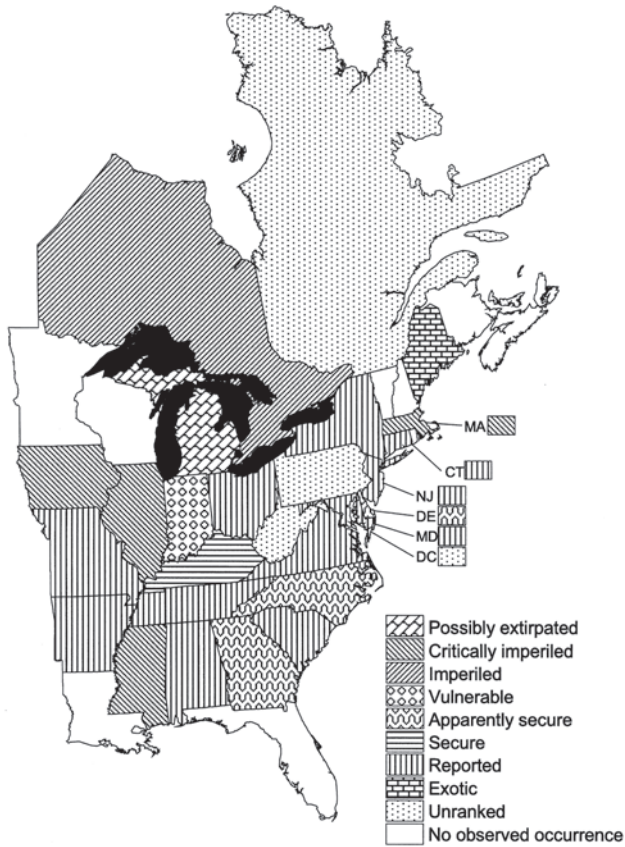


Figure 2—Black cohosh range and distribution map (adapted from NatureServe Explorer 2002 and U.S. Department of Agriculture, Natural Resources Conservation Service 2001).

1,000 on national forest lands in North Carolina, thousands in New York, 20 to 30 in South Carolina, and “hundreds” in Tennessee (NatureServe Explorer 2002). In general, black cohosh is considered to be relatively more abundant in the southern portion of its range (NatureServe Explorer 2002). A standard rich cove forest in North Carolina may contain an estimated 2,000 to 5,000 individual plants, or approximately 400 to 600 individuals per acre (1,000 to 1,500 individuals per ha<sup>3</sup>). Field data by Lueck (see footnote 2) reports population sizes between 80 (Delaware) and 50,000 (West Virginia), with typical populations consisting of several hundred to several thousand individuals.

<sup>3</sup> Personal communication. 2001. Gary Kauffman, Botanical Forest Products Specialist, U.S. Department of Agriculture Forest Service, National Forests in North Carolina, Asheville, NC 28804.

McGraw and others (2003) evaluated natural areas in northcentral West Virginia using habitat suitability models based on ecological characteristics of known populations. The population models indicated a large potential niche for black cohosh, but many factors limit the actual occurrence of the species. These include slow recovery after harvest, reproduction limitations, and increasing harvest due to market demand.

Vegetative reproduction is by regrowth of buds from underground rhizomes. Mature plants also produce seeds. Across the range, seed set can begin as early as June and continue well into August. Seeds require a warm period to break radicle dormancy and a cold period to break epicotyl dormancy (Baskin and Baskin 1985, Strauch 1995). Under normal conditions, complete germination (both radicle and epicotyl) can occur in 6 months. However, if seeds are sown after temperatures have dropped in late autumn, radicle emergence will be delayed until after summer the following year (complete germination in 18 months). Cotyledons do not emerge until after radicles have broken dormancy (Baskin and Baskin 1985).

Black cohosh has not been cultivated on any large scale (Miller 1988), and most of what is grown is for landscape use (Blakley and Renaud 1999). The main source of black cohosh rhizomes for the medicinal herb industry is wildcrafting (see the section Wild Harvest). As demand increases, there is an increasing interest in cultivation as a means to conserve wild resources (Popp and others 2003). Several groups are conducting research on germination and cultivation requirements, pest and disease problems, and cost/yield assessments for large-scale production (Adam 2002, Blakley and Renaud 1999, Popp and others 2003, Thomas and others 2001).

## **Medicinal Uses**

### **Historical**

Black cohosh was widely used by Native Americans, mainly as a treatment for various female conditions and for rheumatism, but also for malaria, general malaise, kidney malfunctioning, sore throat, childbirth, and snakebite (American Botanical Council 2002, Foster 2000, Foster and Duke 2000, Moerman 1999). Common names that denote these early uses include “snakeroot,” “black snakeroot,” and “squawroot” (Foster 2000, Grieve 1931). Early European settlers and eclectic physicians learned of these uses and incorporated them into their own medicinal practices, and also used the roots as a treatment for smallpox or chorea (Cook 1869, Ellingwood 1919, Felter 1922, Felter and Lloyd 1898, Petersen 1905, Potter 1902). Black cohosh was the principal ingredient in Lydia Pinkham’s Vegetable

Compound, a tonic sold in the late 1800s and early 1900s as a general treatment for women's ailments (Tyler 1995).

## Modern

Medicinal actions ascribed to black cohosh include hypoglycemic, sedative, anti-inflammatory, antirheumatic, antispasmodic, alterative, antidote, astringent, cardiogenic, diaphoretic, diuretic, emmenagogue, expectorant, and vasodilator (Fern 1997–2000, Foster and Duke 2000, Grieve 1931)

Europeans have used black cohosh to treat menopausal symptoms for over 40 years. According to the American Botanical Council (2002), 10 million retail units of standardized black cohosh ethanolic and isopropanolic extracts were sold in Germany, the United States, and Australia in 1996. In Germany, the German Commission E has approved black cohosh as a treatment for premenstrual discomfort or dysfunction (dysmenorrhea), and for menopausal symptoms such as hot flashes, heart palpitations, nervousness, irritability, sleep disturbances, tinnitus, vertigo, perspiration, and depression (American Botanical Council 2002, Blumenthal 1998). The recommended dosage is 40 mg per day of crude drug (Blumenthal 1998, Liske and Wüstenberg 1998). Because of the lack of long-term safety studies, it is recommended that the use of black cohosh be limited to a maximum of 6 months (American Botanical Council 2002, Blumenthal 1998).

The most common side effect is occasional transient gastric upset (Dog and others 2003, Huntley and Ernst 2003, Stolze 1982). Overdose can result in vertigo, headache, nausea, vomiting, and vision or circulation impairments (American Botanical Council 2002, Foster 2000). Recently, a few case studies have reported a possible link between black cohosh and liver damage (Laino 2003, Lontos and others 2003, Whiting and others 2002). In some cases, the products causing the hepatotoxic reaction contained a combination of herbs, which suggests that more research is needed to determine if black cohosh was the cause of the reaction (Dog and others 2003, Vitetta and others 2003). In addition, the products were not evaluated and may have contained contaminants. Several clinical studies examining potential toxicity in both humans and animals have determined that black cohosh is safe when used in moderate doses (Johnson and van Breemen 2003; Korn 1991; National Institutes of Health, National Toxicology Program 1999, 2002).

The bioactivity of black cohosh is not well understood. Medicinally active chemical constituents in black cohosh commonly used as markers for standardization include the triterpene glycosides actein, cimicifugoside,

and 23-epi-26-deoxyactein (formerly classified as 27-deoxyactein) (Bedir and Khan 2000; Chen and others 2002b; Linde 1964, 1967a, 1967b; McKenna and others 2001; Newall and others 1996; Shao and others 2000; Upton 2002; Watanabe and others 2002; Wende and others 2001). Commercially available black cohosh products such as Remifemin<sup>®</sup> are usually standardized to contain 1 mg of 23-epi-26-deoxyactein per tablet (Tetherow 2001). Although it was once believed that black cohosh contained phytoestrogens such as the flavonoid formononetin (Jarry and others 1985), more recent studies have failed to find formononetin or significant levels of other flavonoids in various commercially available products (Foster 1999, Kennelly and others 2002, Liske 1998, Liske and Wüstenberg 1998, Struck and others 1997). One study suggests that black cohosh roots do not contain any isoflavones (Hagels and others 2000). Other active compounds have been isolated, including aromatic acids such as ferulic acid, salicylic acid, and caffeic acid (Hagels and others 2000, Kruse and others 1999, Li and others 2003). Black cohosh roots also contain tannins, resins, fatty acids, starch, and sugars (American Botanical Council 2002, Foster 1999, Newall and others 1996, Upton 2002). Several clinical studies have evaluated the methods used to analyze black cohosh preparations to determine the quality and quantity of active constituents (Ganzera and others 2000, He and others 2000, Li and others 2003, Xu and others 2001). A recent study used DNA fingerprinting to detect related plant species that can be misidentified and contaminate black cohosh bulk material (Zerega and others 2002).

## **Clinical Research**

Most of the initial clinical research on black cohosh focused on the safety and efficacy of using it to treat menopausal symptoms. Early case studies simply observed and reported on beneficial effects in patients (Brücker 1960, Langfritz 1962, Stefan 1959, Stiehler 1959). Later research used various assessment scales such as the Kupperman Menopausal Index Scale for neurovegetative symptoms (hot flashes, profuse sweating, headache, vertigo, heart palpitation, and tinnitus) and the Profile of Mood States, Self-Assessment Depression Scale, or Hamilton Anxiety Scale for psychological complaints (nervousness, irritability, sleep disturbances, and depression). Most studies demonstrated statistically significant improvements (Daiber 1983, Foldes 1959, Vorberg 1984). Comparisons between black cohosh, hormone replacement therapy (HRT), and placebos determined black cohosh to be a safe and effective alternative to HRT (Lehmann-Willenbrock and Riedel 1988, Petho 1987, Stoll 1987, Stolze 1982, Warnecke 1985), though one study showed no significant difference between black cohosh and a placebo (Jacobson and others 2001).

Early research on the physiological actions of black cohosh debated the presence of compounds that could bind to estrogen receptors and, thus, reduce symptoms caused by the loss of estrogen production during menopause. Several studies claimed that black cohosh had an estrogen-like effect (Eagon and others 1997, 1999). However, a few studies on ovariectomized rats did not detect the appropriate physical and physiological changes (e.g., increase in uterine weight and changes in vaginal cytology) associated with estrogen and concluded that black cohosh did not have a hormonal effect (Einer-Jensen and others 1996, Knüvener and others 2000, Liske and others 1998). Jarry and Harnischfeger (1985), Jarry and others (1985), and Düker and others (1991) found that black cohosh reduced surges in the secretion of luteinizing hormone (LH) associated with hot flashes and sweating. Though the exact mechanism of action was not identified, it was believed that several constituents acted simultaneously in different ways to produce an overall estrogenic effect. Wade and others (1999) suggested that black cohosh had both estrogen-agonistic and estrogen-antagonistic effects on various target organs, indicating tissue selectivity. Contradictions in early clinical studies were most likely caused by variations in the dosage, duration of the study, number of participants, and lack of a standardized extract that was free of contaminants (Borrelli and Ernst 2002, Borrelli and others 2003). Most current research uses standardized commercial preparations Remifemin<sup>®</sup> or Klimadynon<sup>®</sup>/Menofem<sup>®</sup> (CR BNO extract 1055).

Contradicting estrogenic or antiestrogenic actions were also clarified by the discovery of two different types of estrogen receptors (ERs): ER- $\alpha$  and ER- $\beta$ . Whereas ER- $\alpha$ s are primarily found in the reproductive organs, ER- $\beta$ s are found in the skeletal and central nervous systems (Seidlová-Wuttke and Wuttke 2000). Researchers are investigating the possibility that constituents in the rhizomes act as selective ER modulators. Clinical research indicates that black cohosh may reduce hot flashes and sweating by reducing the secretion of LH from the hypothalamus/pituitary system in the brain through either mixed competitive binding to serotonin receptors (Burdette and others 2003, Seidlová-Wuttke and Wuttke 2000, Seidlová-Wuttke and others 2003, Wuttke and others 2003) or unidentified ERs (Jarry and others 2003), or through dopaminergic/antidepressant activity (Löhhning and Winterhoff 2000, Winterhoff and others 2003). Black cohosh has also been associated with a significant reduction in the bone loss that leads to osteoporosis (Nisslein and Freudenstein 2000; Seidlová-Wuttke and others 2000; Wuttke and others 2000, 2003).

The growing awareness of contraindications for HRT for individuals with estrogen-positive breast cancer has also raised concerns about the potential negative effects of phytoestrogens (plant chemicals that act like

estrogen). Several studies have shown that black cohosh does not cause the proliferation of cancer cells (Amato and others 2001, Freudenstein and others 2002, Lupu and others 2002, Morris and others 2003), and may even possess cancer-fighting properties (Dixon-Shanies and Shaikh 1999, Dog and others 2003, Hostanska and others 2004). Einbond and others (2004) found that ethyl acetate extracts and the triterpene glycoside actein, both active constituents in black cohosh, demonstrated significant inhibition of both estrogen-positive and estrogen-negative tumors. Studies on drug interactions have shown that black cohosh can increase the effectiveness of some anticancer drugs (Freudenstein and Bodinet 1999, Muñoz and Pluchino 2003, Nesselhut and others 1993, Rockwell and others 2003), but can also increase the toxicity of others (Rockwell and others 2003). One study conducted on female mice found that groups treated with black cohosh had significantly higher rates of tumor metastasization to the lungs than the control groups (Davis and others 2003). Critics have responded that this study was conducted on mice that were specifically bred to develop cancer, and that black cohosh may not demonstrate the same physiological effect on humans (Decker 2003, Murray 2003).

Several studies have looked at other medicinal applications of black cohosh. Burdette and others (2002) found that black cohosh possesses antioxidant activity and may protect against damage to DNA by reactive oxygen species. Burke and others (2002) examined the use of black cohosh to treat menstrual migraines. Takahira and others (1998) examined the antimalarial activity of triterpene glycosides found in black cohosh. Most recently, Sakurai and others (2004) discovered several constituents in black cohosh rhizomes that have moderate or potential anti-HIV activity.

Patents have been issued for the use of black cohosh for treating menopause symptoms (Fasano 2003, Newmark and Schulick 2001), reducing hair loss (McCullough 2000), treating estrogen-dependent tumors (Nesselhut and others 2001), and reducing levels of peptides in the brain believed to contribute to the onset of Alzheimer's disease (Eckman and others 2003).

## **Other Uses**

Black cohosh is used in the landscape as a native border or woodland plant in moist, shady locations (Missouri Botanical Garden 2002, Perry 2001).

## Market Trends

In 1936, Harding indicated a price range for black cohosh roots of \$0.02 to \$0.03 per pound. In 1988, Miller quoted a price of \$0.80 per pound paid to harvesters for dried roots, \$2.00 per pound for cut and sifted roots, and retail prices starting at \$3.90 per pound. At that time the domestic market was estimated at < 50 tons, with some export to Germany (Miller 1988, Forest Service 1993).

A summary by Lyke (2001) reported that the price for black cohosh raw materials peaked at \$12.00 to \$17.00 per pound of dry root in 2000. High prices paid to harvesters increased the wild collection of rhizomes. When the market became saturated, prices dropped. Greenfield and Davis<sup>4</sup> listed a price range of \$1.15 to \$4.00 per pound of dried root in 2001. As stockpiles of black cohosh rhizomes are depleted and demand continues to increase, prices are expected to slowly increase. The 2003 price was \$3.00 per pound.<sup>4</sup>

In 2004, Internet vendors listed the following retail prices: \$9.50 to \$10.00 per fluid ounce, and \$5.00 to \$20.00 per 100 tablets or capsules of varying potencies (EstroGentle, no date; Green Canyon Inc., no date; NatureServe Explorer 2002; Nature's Way Herbs, no date; Remifemin<sup>®</sup>, no date; RippleCreek.com, no date).

According to Blumenthal (1999), retail sales of black cohosh increased 511 percent between 1997 and 1998, and rose another 477 percent in 1999. In 2001, when total retail sales in the mainstream herbal supplement market were down 15 percent, black cohosh sales were up 2 percent, with an estimated sale of 936,979 units at a value of \$6,153,796 (Blumenthal 2002). The 2003 estimated market demand for black cohosh was 500,000 pounds of dried root per year<sup>4</sup>. Estimated black cohosh supplement sales totaled \$9.5 million from August 2001 to August 2002 (Brown 2002).

## Wild Harvest

Black cohosh is primarily harvested from wild rather than cultivated sources. In 2001, Indiana, Kentucky, Missouri, Ohio, Tennessee, and West Virginia were the main States supplying wild-harvested material (Johannesen 2001). In 2003, Kentucky and Tennessee were the primary producers, followed by Georgia, Michigan, North Carolina, South Carolina,

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<sup>4</sup> Greenfield, J.; Davis, J. 2003. Western North Carolina non-timber forest products. 81 p. plus appendices. Draft final report. On file with: Forest Service, Southern Research Station, 1650 Ramble Road, Blacksburg, VA 24060.



and Wisconsin. Ohio, Virginia, and West Virginia are also significant producers.<sup>5</sup>

Because the species is not monitored throughout its range, there is no accurate measure of actual harvest levels of black cohosh. At present, the sum of our knowledge is based on inferences from cultivation data and conservative estimates of harvest based on reports from the herbal industry and Federal collection permits.

### Herbal Industry Reports: American Herbal Products Association Tonnage Surveys

The American Herbal Products Association (AHPA) conducted two surveys to determine wild-harvest levels of several popular native plant species (American Herbal Products Association 2000, 2003). Due to the voluntary nature of the surveys and the unknown percentage of the total market represented by the survey respondents, the information provided by these surveys should be taken as a conservative estimate of actual harvest. According to these tonnage surveys, almost 1,400,000 pounds (dry weight) of black cohosh was harvested between 1997 and 2001, nearly 98 percent wild-harvested (table 1). It should be noted that three of the five major bulk traders in black cohosh (as identified in 2001) are not AHPA members. A large herb dealer based in the Southern Appalachians sold 55,000 to 60,000 pounds (dry) in 1999 (NatureServe Explorer 2002), almost half of what AHPA reported for the entire year.

**Table 1—Harvest of black cohosh according to the American Herbal Products Association (2003) tonnage survey**

Harvest year	Cultivated	Wild	Total	Wild harvest <i>percent</i>
1997	0	227,002	227,002	100
1998	35,430	725,984	761,414	95
1999	2,600	145,367	147,967	98
2000	149	117,843	117,992	99
2001	6,521	177,681	184,202	96
Total (pounds)	44,700	1,393,877	1,438,577	
<b>Average</b>				<b>97.6</b>

<sup>5</sup> Suggs, R. 2003. Market profile: black cohosh. 12 p. Unpublished document. On file with: Forest Service, Southern Research Station, 1650 Ramble Road, Blacksburg, VA 24060.

When experts were asked how many black cohosh rhizomes made up 1 pound of dry material, they provided a broad range of estimates—from 14<sup>6</sup> to 18 (see footnote 3), to as many as 40 (Johannesen 2001). Using a conservative estimate of 14 roots per dried pound, the number of individual plants wild-harvested during the 5-year period covered by the surveys exceeded 19.5 million.

## **Permit Sales**

Wild-harvesting is mostly done on public land, where plants are generally more accessible (Lyke 2001). Harvest is not allowed on national park land, but is permitted on Forest Service land. Examining black cohosh collection permits is one way to estimate wild-harvest; however, this method does not provide precise numbers because the amount of actual harvest is not monitored, and poaching is not taken into account.

According to NatureServe Explorer (2002), the Forest Service issued black cohosh collection permits for 2,200 pounds in 1997, 12,000 pounds in 1998, and 2,150 pounds in 1999. This amounts to the harvest of nearly 229,000 individual plants (estimating 14 roots per dry pound) during the 3-year period. As there is no requirement to “weigh out” after harvest, the actual harvest weight cannot be stated with certainty. According to Matthew Albrecht,<sup>7</sup> the number of black cohosh permits declined after 2000, possibly due to the market decline.

## **Seed Harvest**

The pressure that the horticultural industry exerts on wild black cohosh seed production is not quantifiable. Despite the development of several popular cultivars, pure black cohosh remains popular among horticulturalists. Whole plants and seeds are the primary commodities sold by the horticultural industry. Currently, there is no mechanism to monitor the trade in black cohosh seeds. Because black cohosh reproduces primarily from seed, the ability to quantify the seed trade is vital to the conservation of the species.

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<sup>6</sup> Personal communication. 2001. Joe-Ann McCoy, Curator (Medicinals), U.S. Department of Agriculture, Agricultural Research Service, North Central Regional Plant Introduction Station, Ames, IA 50014.

<sup>7</sup> Personal communication. 2003. Matthew Albrecht, Doctoral Candidate, Ohio University, Athens, OH 45701.

Joe-Ann McCoy<sup>8</sup> will soon publish a report on long-term population studies of several black cohosh populations that may help determine acceptable levels of seed harvest.

## Export

The actual amount of black cohosh raw materials exported from the United States is unknown. Estimates can be gleaned from industry market reports, phytosanitary certificates, and U.S. Customs port data.

## Phytosanitary Certificates

Phytosanitary certificates (PCs) are required by the International Plant Protection Convention for exports of living plant material, including seeds, to document the inspection of plant materials for harmful insects or disease. In the United States, PCs are issued and recorded by the U.S. Department of Agriculture. PCs issued for black cohosh exports at U.S. ports between 1999 and 2002 are shown in table 2.

**Table 2—Phytosanitary certificates for black cohosh exports, 1999–2002<sup>a</sup>**

Year	Pounds	Roots	Bags/bales	Seeds
1999	1,199 ≈ 16,786 roots	150	0	0
2000	8,623 ≈ 120,722 roots	0	234	0
2001	9,100 ≈ 127,400 roots	5,600	179	0
2002	33,080 ≈ 463,120 roots	21,720	0	12 oz.
Total	55,002 ≈ 728,028 roots	27,470	413 ≈ ? roots	12 oz. ≈ 144,000

<sup>a</sup> There are no standard reporting volumes on phytosanitary certificates. Quantities may be reported in pounds, roots, bags/bales, or seeds.

It should be noted that there is no standard reporting volume on PCs. Thus, shipments are reported variously in pounds, roots, bags, bales, or seeds. This makes it difficult to interpret the data. For exports reported as bags or bales, there is insufficient information to determine either the amount (i.e., size), weight, or the nature of the material (i.e., roots or whole plants), being exported. It is estimated that 12 ounces of seeds equals approximately 144,000 seeds.<sup>9</sup>

<sup>8</sup> Personal communication. 2003. Joe-Ann McCoy, Curator (Medicinals), U.S. Department of Agriculture, Agricultural Research Service, North Central Regional Plant Introduction Station, Ames, IA 50014.

<sup>9</sup> Personal communication. 2004. Russ Richardson, Registered Forester, Weston, WV 26452.

For exports reported in pounds, it is estimated that 1 pound of dried black cohosh roots is equal to approximately 14 roots. Thus, during the 4-year period from 1999 to 2002, in excess of 755,498 black cohosh roots were exported. Note the spike in 2002 exports, which coincides with damaging revelations about the risks of synthetic HRT.

Note: PCs represent only a conservative estimate of actual exports because:

1. Not all countries require PCs, so not all shipments of black cohosh will be accompanied by a PC.
2. When required, many countries request PCs only for live or fresh material; so shipments of dried material, derivatives, or processed material may not be accompanied by a PC.
3. Shipments are not reported in standard units; thus, PCs may not record sufficient information to determine the amount or type of material being exported.
4. Information from PCs is neither centrally available nor electronically recorded, making it difficult to get accurate information and to follow up on inconsistencies.

### Port Data

Table 3 shows U.S. Customs port data from July 2001 through October 2002 (PIERS Exports 2003). Because PIERS is available only in 18-month increments the information spans portions of 2 years. The database reports that, between mid-2001 and late 2003, 40,124 pounds of black cohosh were exported to four European countries (PIERS Exports 2003). Previous import records showed that about 13 tons of black cohosh powder were imported into the United States from May 1998 to February 1999. This suggests that black cohosh exported as raw materials (dried roots) is re-imported as powder.

**Table 3—Port data for black cohosh exports (PIERS Exports 2003)<sup>a</sup>**

Year	Pounds	Equivalent number of plants (14 roots per dry pound)
6-12/2001	28,984	405,776
1-10/2002	11,140	155,960
Total	40,124	561,736

<sup>a</sup> PIERS data is available in 18-month increments, thus the information in this table spans portions of 2 years.

Note:

1. PIERS data reflects a conservative estimate of black cohosh exports because black cohosh does not have its own source code. Examples of the source codes that black cohosh may be exported under include “crude natural drugs and herbs,” “leaves, moss, polle, roots, veg prod,” “miscellaneous,” “herbs and spices,” “vat dyes,” “flavors, essences, esters,” etc.
2. The PIERS control officer may not record the common or scientific name of the plant material.
3. Because PIERS is available only in 18-month increments, it is difficult to obtain accurate information for more than one harvest season.

Further analysis of the PCs and port data revealed that the exports from these two sources do not overlap, but represent different shipments. Thus, by adding the total exports from these two data sources, a more accurate reflection of exports of black cohosh from 1999 through 2002 would be around 1,317,234 roots.

## Conservation Status

Wild-harvest and habitat destruction have led to the decline or disappearance of many black cohosh populations. Black cohosh is listed as endangered in Illinois and Massachusetts (U.S. Department of Agriculture, Natural Resources Conservation Service 2001), and is included on the United Plant Savers “At-Risk” list (United Plant Savers, no date). According to NatureServe (2002), black cohosh has a secure (G4) global heritage status rank; however, NatureServe acknowledges that increased market demand has put pressure on wild populations, and recommends that the conservation status be reviewed within the next 2 or 3 years (NatureServe Explorer 2002). In 2001, as evidence of conservation threats began mounting, black cohosh was considered for Appendix II listing on the Convention on International Trade in Endangered Species of Wild Fauna and Flora; lack of information led to its withdrawal from consideration (Lyke 2001).

Industry, academia, and the Federal Government are conducting research into various aspects of conservation. The Medicinal Plant Working Group, Forest Service, U.S. Fish and Wildlife Service, and Garden Club of America are cooperating on a long-term monitoring study to determine regeneration rates and the impact of varying harvest levels on black cohosh (Ford 2000, Kauffman 2002, Schlosser 2002). The University of Massachusetts and the New York Botanical Garden are collaborating on a rangewide study of the genetic diversity of black cohosh. Results from this study on the relatedness

of natural populations will provide information to help managers make conservation decisions (see footnote 2). Samples collected from natural populations by Lueck and McCoy are housed at the U.S. Department of Agriculture, Agricultural Research Service, North Central Regional Plant Introduction Station in Ames, IA, as part of the National Germplasm Collection.

## Discussion

Over the past few years, black cohosh has received increasing attention from industry, consumers, clinical researchers, biologists, conservationists, dealers, and wildcrafters. With the growing awareness of the harmful side effects of HRT, more women are turning to herbal remedies to alleviate symptoms of menopause. Research results are mixed on the safety and efficacy of extracts from certain plants, such as black cohosh, soy (*Glycine max*), dong quai (*Angelica sinensis*), and others, as safe and effective alternatives; particularly for women at risk of developing estrogen-related cancers. Products that contain black cohosh can be found in the mainstream market both within the United States and internationally.

Rising demand and higher profits for harvesters have increased pressure on wild populations. Increased sales of permits to collect black cohosh reflect the growing popularity of the herb in the world market. The amount of plant material collected illegally is estimated to be equal to or greater than the amount collected with permits. More data on the distribution and abundance of black cohosh is needed to determine the sustainability of current harvest levels.

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**Xu, H.; Fabricant, D.S.; Johnson, H.E. [and others].** 2001. Using random amplified polymorphic DNA (RAPD) markers to identify plant species and variants. [Abstract]. In: Botanical dietary supplements: natural products at a crossroads; 2001 November 8-11; Asilomar, CA. Washington, DC: American Society of Pharmacognosy and Council for Responsible Nutrition: p. 32.

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## Annotated Bibliography

### Research Literature

**Adam, K.L.** 2002. Ginseng, goldenseal, and other native roots. Hortic. Tech. Note. Fayetteville, AR: Appropriate Technology Transfer for Rural Areas. 12 p. <http://attra.ncat.org/attra-pub/ginsgold.html>. [Date accessed: September 13, 2004].

Provides well-documented overviews for American ginseng (*Panax quinquefolius*), goldenseal (*Hydrastis canadensis*), black cohosh, and blue cohosh (*Caulophyllum thalictroides*) that cover cultivation, regulations, and production. Covers research on black cohosh propagation and cultivation by several groups, including the New Crop Opportunities Center at the University of Kentucky, and the MU Center for Phytonutrient & Phytochemical Studies in Missouri. Provides resources on black cohosh cultivation.

Keywords: Cultivation, propagation, regulatory status.

**Amato, P.; Christophe, S.; Mellon, P.L.** 2001. Estrogenic activity of herbs commonly used as remedies for menopausal symptoms. Menopause. 9(2): 145-150.

Evaluates the effects on the proliferation of breast cancer cells of four herbs used to treat menopausal symptoms. Dong quai (*Angelica sinensis*) and American ginseng (*Panax quinquefolius*) were found to induce growth of breast cancer cells, whereas black cohosh and licorice root (*Glycyrrhiza glabra*) did not.

Keywords: Cancer, research.

**American Cancer Society.** 2004. Black cohosh. [http://www.cancer.org/docroot/eto/content/eto\\_5\\_3x\\_black\\_cohosh.asp?sitearea=eto](http://www.cancer.org/docroot/eto/content/eto_5_3x_black_cohosh.asp?sitearea=eto). [Date accessed: September 13, 2004].

Discusses research on black cohosh and cancer. Medicinal uses are described. Although black cohosh has estrogen-like effects, there has been no evidence that it increases the risk of developing estrogen-associated cancers. There are reports that black cohosh can actually reduce cancer risk, but these have not been substantiated by clinical research.

Keywords: Cancer, medicinal uses, research reviews.

**American Chemical Society.** 2003. Black cohosh may reduce hot flashes by targeting brain's thermostat. <http://www.intelihealth.com/IH/ihtIH/WSIHW000/333/28815/369064.html>. [Date accessed: September 13, 2004].

Reports on a study presented at the 226<sup>th</sup> national meeting of the American Chemical Society. The study showed that black cohosh reduced hot flashes by binding to serotonin receptors in the brain. Previous research had shown that these receptors play a role in regulating body temperature, though the chemical constituents responsible for this mechanism of action had not been identified.

Keywords: Hot flashes, physiological actions, research.

**American Herbal Products Association.** 2000. 1999 tonnage survey results. Silver Spring, MD: American Herbal Products Association. 14 p.

Provides harvest data from 1997 to 1999 for the most widely traded medicinal herbs.

Keywords: Harvest, market.

**American Herbal Products Association.** 2003. 2000–2001 tonnage survey of North American wild-harvested plants. Washington, DC: American Herbal Products Association. 19 p.

Reports harvest levels for several medicinal herbs based on surveys of herb dealers. Surveys were sent to 221 American Herbal Products Association members and 20 industry nonmembers. Of the 59 respondents, only 21 indicated that they were primary raw material producers of the herbs specified in the study. According to those respondents, black cohosh

harvests peaked in 1998 at 381 tons, then dropped to 61 tons in 2000. Harvest levels of both wild and cultivated roots are provided from 1997 through 2001.

Keywords: Harvest, market.

**Baillie, N.; Rasmussen, P.** 1997. Black and blue cohosh in labour. New Zealand Medical Journal. 110(1036): 20-21.

Responds to a report by Gunn and Wright (1996) that implicates the use of blue cohosh (*Caulophyllum thalictroides*) and black cohosh in the neurological dysfunction of a newborn infant whose mother had been given herbs by a midwife. The authors point out that the dosage, type of preparation, and administration of the herbs was not specified. They note that without this information it cannot be proven that the herbs themselves caused the birth defects, as it is possible that they were not used correctly by the midwife.

Keywords: Dosage, medicinal uses, preparations, side effects.

**Baskin, J.M.; Baskin, C.C.** 1985. Epicotyl dormancy in seeds of *Cimicifuga racemosa* and *Hepatica acutiloba*. Bulletin of the Torrey Botanical Club. 112(3): 253-257.

Examines the epicotyl dormancy of black cohosh seeds. Seeds require a warm period to break radicle dormancy and a cold period to break epicotyl dormancy. Complete germination in good conditions requires 6 months, but can take up to a year and a half if seeds are sown after temperatures have dropped in late autumn; in this case, radicle emergence is delayed until after the summer of the following year. Cotyledons do not emerge until after radicles have broken dormancy. This process allows the root system to begin development before the cotyledons emerge, facilitating the uptake of nutrients and water to the developing leaves.

Keywords: Research, seeds.

**Beck, V.; Unterrieder, E.; Krenn, L. [and others].** 2003. Comparison of hormonal activity (estrogen, androgen, and progestin) of standardized plant extracts for large scale use in hormone replacement therapy. Journal of Steroid Biochemistry and Molecular Biology. 84: 259-268.

Evaluates the chemical constituents and *in vitro* estrogenic activity of black cohosh, soy (*Glycine max*), and red clover (*Trifolium pratense*).

Black cohosh did not show estrogenic activity through binding to estrogen receptors, progesterone receptors, or androgen receptors. It is possible that metabolic action is required in order to produce estrogenic effects.

Keywords: Chemical constituents, clinical studies, physiological actions.

**Bedir, E.; Khan, I.A.** 2000. Cimicracemoside A: a new cyclolanostanol xyloside from the rhizome of *Cimicifuga racemosa*. Chemical and Pharmaceutical Bulletin. 48(3): 425-427.

Describes a recently identified compound isolated from black cohosh roots.

Keywords: Chemical constituents.

**Blakley, T.; Renaud, E.** 1999. Black cohosh: adaptability to production, sunlight levels and identifying stratification and propagation methods for high yield of cultivated black cohosh. Research Farm Proposal No. 6078. National Center for the Preservation of Medicinal Herbs. <http://home.frognet.net/~rural8/6078A.html>. [Date accessed: September 13, 2004].

Outlines research on black cohosh cultivation. Cultivation is best suited for hardiness zones 4 to 7, in woodlands and simulated woodland habitats. This project covers various cultivation issues such as overcoming seed dormancy, yield and cost production for seed vs. rootstock crops, optimum light levels, soils with or without added compost, water needs for various light conditions, identification of pest and disease problems, drying and storage of roots for commercial use, and budget analysis for crops under various light levels. Methods are described in detail in this in-progress research proposal.

Keywords: Cultivation, hardiness range, light requirements, propagation, research, seeds, soil requirements, water requirements.

**Boblitz, N.; Liske, E.; Wüstenberg, P.** 2000. Black cohosh: efficacy effect and safety of *Cimicifuga racemosa* in gynecology. Deutsche Apotheker Zeitung. 140(24): 107-114. In German.

Discusses the use of black cohosh in gynecology.

Keywords: Medicinal uses, safety.

**Borrelli, F.; Ernst, E.** 2002. *Cimicifuga racemosa*: a systematic review of its clinical efficacy. *European Journal of Clinical Pharmacology*. 58: 235-241.

Reviews four randomized clinical trials on the use of black cohosh to treat menopausal symptoms in women, and summarizes *in vitro* and *in vivo* assays to determine the mechanism of action of the medicinal constituents in the rhizome. The randomized clinical trials yielded conflicting results: three studies showed that black cohosh significantly improved physical and psychological symptoms of menopause, though one of these studies also showed significant improvement in the placebo group. The fourth study showed no change in symptoms. The differing results may be due to variations in dosage, number of participants, and/or duration of the study. Early research on mice and rats indicated estrogenic effects; recent studies, however, have suggested a dopaminergic activity. Because earlier research did not use standardized extracts, estrogenic results may have been caused by contaminants.

Keywords: Clinical studies, physiological actions, research reviews.

**Borrelli, F.; Izzo, A.A.; Ernst, E.** 2003. Pharmacological effects of *Cimicifuga racemosa*. *Life Sciences*. 73(10): 1215-1229.

Investigates the physiological actions of black cohosh by analyzing *in vivo* and *in vitro* experiments. Early studies suggested that black cohosh increased uterine weight and induced menstruation in ovariectomized rats by binding to estrogen receptors, reducing levels of luteinizing hormone. The chemical constituent believed to cause these phytoestrogenic effects was later identified as an adulterant not found in black cohosh roots and rhizomes. Current research using a standardized extract at recommended doses suggests that black cohosh reduces hot flashes through a dopaminergic effect on the brain. The effects of black cohosh on estrogen-sensitive cancer has not yet been determined; research has produced conflicting results.

Keywords: Cancer, chemical constituents, clinical studies, hot flashes, luteinizing hormone, physiological actions, research reviews.

**Brücker, A.** 1960. Essay on the phytotherapy of hormonal disorders in women. *Medizinische Welt*. 44: 2331-2333. Abstract available at [http://www.chiro.org/nutrition/ABSTRACTS/Essay\\_on\\_the\\_Phytotherapy.shtml](http://www.chiro.org/nutrition/ABSTRACTS/Essay_on_the_Phytotherapy.shtml). [Date accessed: September 13, 2004].

Concludes that black cohosh is safe and effective in treating symptoms of menopause, based on four years of clinical experience involving 517 female patients. Effects of the treatment are described as hormone-like and slightly euphoric. No adverse side effects, such as unphysiological bleeding, were observed.

Keywords: Case studies, menopause, safety.

**Burdette, J.E.; Chen, S.; Lu, Z. [and others].** 2002. Black cohosh (*Cimicifuga racemosa* L.) protects against menadione-induced DNA damage through scavenging of reactive oxygen species: bioassay-directed isolation and characterization of active principles. *Journal of Agriculture and Food Chemistry*. 50: 7022-7028.

Shows that certain constituents of black cohosh act as antioxidants and can reduce damage to DNA caused by reactive oxygen species. The process of oxidative damage and the constituents of black cohosh that are capable of protecting DNA are thoroughly discussed.

Keywords: Antioxidant properties, clinical studies, medicinal uses.

**Burdette, J.E.; Liu, J.; Chen, S. [and others].** 2003. Black cohosh acts as a mixed competitive ligand and partial agonist of the serotonin receptor. *Journal of Agriculture and Food Chemistry*. 51: 5661-5670.

Investigates the mechanism of action by which black cohosh reduces hot flashes. Previous research focused on the ability of constituents in the rhizomes of black cohosh to bind to estrogen receptors and, thus, reduce the levels of luteinizing hormone (LH), the same mechanism by which hormone replacement therapy reduces hot flashes. In this study, various signs of estrogenic activity were evaluated, including changes in body weight, uterine weight, vaginal cell differentiation, and direct binding to estrogen receptors. Anti-estrogenic activity was evaluated by combining black cohosh with estradiol to determine if black cohosh blocked the effects of estrogen. No estrogenic or anti-estrogenic activity was observed. Certain anti-depressant medications, particularly selective serotonin reuptake inhibitors, have been shown to reduce hot flashes. Serotonin inhibits secretion of LH from the hypothalamus/pituitary system; therefore, the effect of black cohosh on serotonin receptors was evaluated as a possible mechanism of action. Black cohosh demonstrated mixed competitive binding for specific serotonin receptors. The active constituents were not identified.

Keywords: Chemical constituents, clinical studies, hormone replacement therapy, hot flashes, physiological actions.

**Burke, B.E.; Olson, R.D.; Cusack, B.J. 2002.** Randomized, controlled trial of phytoestrogen in the prophylactic treatment of menstrual migraine. *Biomedical Pharmacotherapy*. 56(6): 283-288.

Examines the use of phytoestrogens to reduce menstrual migraines. Soy (*Glycine max*), dong quai (*Angelica sinensis*), and black cohosh all showed significant effectiveness starting at 9 weeks after treatment until the completion of the study at 24 weeks.

Keywords: Medicinal uses, migraines, phytoestrogens.

**Cech, R. 1999.** Balancing conservation with utilization: restoring populations of commercially valuable medicinal herbs in forests and agroforests. *United Plant Savers Newsletter*. Winter: 4.

Discusses sustainable wildcrafting techniques for black cohosh, goldenseal (*Hydrastis canadensis*), and ginseng (*Panax quinquefolius*).

Keywords: Conservation.

**Chen, S.; Fabricant, D.S.; Lu, Z. [and others]. 2002a.** Cimiracemosides I-P, new 9,19-cyclolanostane triterpene glycosides from *Cimicifuga racemosa*. *Journal of Natural Products*. 65(10): 1391-1397.

Identifies eight new triterpene glycosides in the rhizomes of black cohosh.

Keywords: Chemical constituents.

**Chen, S.; Li, W.; Fabricant, D.S. [and others]. 2002b.** Isolation, structure elucidation, and absolute configuration of 26-deoxyactein from *Cimicifuga racemosa* and clarification of nomenclature associated with 27-deoxyactein. *Journal of Natural Products*. 65(4): 601-605.

Reports on the isolation of several triterpene glycosides from the rhizomes of black cohosh and discusses their chemistry. One constituent, 26-deoxyactein, was a newly identified compound. Another constituent, previously identified in the literature as 27-deoxyactein, was evaluated by guidelines set by the International Union of Pure and Applied Chemistry standards and reclassified as 23-epi-26-deoxyactein. This constituent has been used to standardize tablets containing black cohosh (such as Remifemin®) to contain 2.5 percent triterpene glycosides.

Keywords: Chemical constituents.

**Compton, J.A.; Culham, A.; Gibbings, J.G.; Jury, S.L.** 1998a. Phylogeny of *Actaea* including *Cimicifuga* (Ranunculaceae) inferred from nrDNA ITS sequence variation. *Biochemical Systematics and Ecology*. 26: 185-197.

Continues previous DNA analysis of *Actaea*, *Cimicifuga*, and *Souliea*. The results of this study suggested the reclassification of *Cimicifuga racemosa* to *Actaea racemosa*.

Keywords: Classification, research.

**Compton, J.A.; Culham, A.; Jury, S.L.** 1998b. Reclassification of *Actaea* to include *Cimicifuga* and *Souliea* (Ranunculaceae): phylogeny inferred from morphology, nrDNA ITS, and cpDNA trnL-F sequence variation. *Taxon*. 47: 593-634.

Reports on the analysis of the morphology and DNA sequences of plants in *Actaea*, *Cimicifuga*, *Souliea*, *Eranthis*, and *Anemonopsis*. The results supported reverting to the original classification by Linnaeus in 1753 where *Souliea* and *Cimicifuga* are part of the monophyletic clade with *Actaea*.

Keywords: Classification, research.

**Daiber, W.** 1983. Menopause symptoms: success without hormones. *Ärztliche Praxis*. 35: 1946-1947. Abstract available at [http://www.chiro.org/nutrition/ABSTRACTS/Success\\_without\\_Hormones.shtml](http://www.chiro.org/nutrition/ABSTRACTS/Success_without_Hormones.shtml). [Date accessed: September 13, 2004].

Summarizes an open study of 36 women using Remifemin® to relieve menopausal symptoms. Significant improvements were observed in climacteric and psychological symptoms based on standardized tests. No side effects were observed.

Keywords: Case studies, menopause, Remifemin®, side effects.

**Davis, V.L.; Jayo, M.J.; Hardy, M.L. [and others].** 2003. Effects of black cohosh on mammary tumor development and progression in MMTV-neu transgenic mice. American Association for Cancer Research. Abstract Number R910. Abstract available at <http://www.annieappleseedproject.org/blacchohnmam.html>. [Date accessed: September 13, 2004].

Investigates the effects of black cohosh on breast cancer cells in female mice. Although primary tumor development (both incidence and latency) was not significantly different between the study and control group,



metastasis of cancer to the lungs was higher in groups taking black cohosh (27.1 percent, n = 96 treatment group, versus 10.9 percent, n = 110, control group) after 14 weeks of treatment. The number of lung tumors increased with longer exposure to black cohosh. The results indicated that black cohosh did not increase the possibility of developing breast cancer in healthy individuals, but could accelerate metastasis of existing tumors.

Keywords: Cancer, clinical studies.

**Dixon-Shanies, D.; Shaikh, N.** 1999. Growth inhibition of human breast cancer cells by herbs and phytoestrogens. *Oncology Reports*. 6: 1383–1387.

Evaluates the abilities of various agents to protect against breast cancer. Black cohosh extract was found to inhibit growth of T-47D cancer cells.

Keywords: Cancer, clinical studies, phytoestrogens, research.

**Dog, T.L.; Powell, K.L.; Weisman, S.M.** 2003. Critical evaluation of the safety of *Cimicifuga racemosa* in menopause symptom relief. *Menopause*. 10(40): 299-313.

Reviews clinical research on the safety of black cohosh for treating menopausal symptoms. Reports from both the U.S. Food and Drug Administration, Special Nutritional Adverse Events Monitoring System and the World Health Organization Collaborating Center for International Drug Monitoring are presented. Adverse effects reported included headache, high blood pressure, heart attack, diarrhea, chest pain, anxiety, and weakness. In most cases, the patients used a combination product that contained black cohosh and other herbs. The products named in the report were not investigated, and the cause of the reaction only speculated. A postmarketing survey conducted by the manufacturers of Remifemin® found that 7 percent of patients experienced temporary, mild gastrointestinal upset. No serious side effects were reported. Numerous clinical studies on the effect of black cohosh *in vivo* and *in vitro* are reviewed. These studies suggested that black cohosh is safe when used in the recommended dosage for a period of 6 months and possibly longer. Studies on black cohosh and estrogen receptor-positive breast cancer showed that black cohosh did not stimulate cell proliferation, and may have actually inhibited the development of tumors. The authors concluded that the long history of medicinal usage, low incidence of adverse effects, and numerous clinical studies demonstrating improvement in menopausal symptoms with a lack of serious side effects

prove that black cohosh is a safe alternative to hormone replacement therapy.

Keywords: Adverse events, cancer, history, hormone replacement therapy, medicinal uses, research reviews, side effects, toxicity.

**Düker, E.M.; Kopanski, L.; Jarry, H.; Wuttke, W.** 1991. Effects of extracts from *Cimicifuga racemosa* on gonadotropin release in menopausal women and ovariectomized rats. *Planta Medica*. 57(5): 420-424.

Investigates the effects of black cohosh on luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels. After 8 weeks, menopausal women receiving the treatment showed reduced levels of LH but not FSH. A black cohosh extract was subjected to Sephadex chromatography, and separate fractions were tested for their effects on LH levels in ovariectomized rats. Three types of active compounds were identified: one that did not bind to estrogen receptor sites but did decrease LH levels, one that did bind to estrogen receptor sites and suppress LH levels, and one that did bind to the estrogen receptor site but did not suppress LH levels. The authors believed that these three compounds act synergistically to reduce LH levels.

Keywords: Chemical constituents, clinical studies, luteinizing hormone, physiological actions.

**Eagon, C.L.; Elm, M.S.; Eagon, P.K. [and others].** 1996. Estrogenicity of traditional Chinese and Western herbal remedies [Abstract #1937]. *Proceedings of the American Association for Cancer Research*. 37: 284.

Studies the estrogenic activity of several herbs. Black cohosh did not inhibit estrogen receptor binding.

Keywords: Physiological actions.

**Eagon, P.K.; Elm, M.S.; Teepe, A.G. [and others].** 1997. Medicinal botanicals: estrogenicity in rat uterus and liver [Abstract #1967]. *Proceedings of the American Association for Cancer Research*. 38: 293.

Evaluates the estrogenic activity of black cohosh and other herbs used to treat menopausal symptoms *in vivo* using rat studies. Three weeks of treatment with black cohosh caused uterine weight gain in ovariectomized rats, indicating that the herb has estrogenic activity.

Keywords: Clinical studies, physiological actions.

**Eagon, P.K.; Tress, N.B.; Ayer, H.A. [and others].** 1999. Medicinal botanicals with hormonal activity [Abstract #1073]. Proceedings of the American Association for Cancer Research. 40: 161-162.

Investigates the hormonal activity of several herbs used to treat menopausal symptoms, using *in vitro* estrogen or progesterone receptor binding assays and *in vivo* observations of ovariectomized rats. Black cohosh showed a dose-dependent inhibition of estradiol binding at estrogen receptor sites *in vitro*, and both uterine weight increases and hypothalamic/pituitary response in female rats. These results indicated an estrogen-like activity for black cohosh.

Keywords: Clinical studies, physiological actions.

**Eckman, C.B.; Yager, D.; Haugabook, S.; Abdul, F.,** inventors; Mayo Foundation for Medical Education and Research, assignee. 2003. Methods of reducing .beta.-amyloid polypeptides. U.S. patent 6,649,196. November 18. 1 p. Int. Cl<sup>2</sup> A61K 035/78. <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=/netahtml/search-bool.html&r=1&f=G&l=50&col=AND&d=ptxt&s1=6,649,196.WKU.&OS=PN/6,649,196&RS=PN/6,649,196>. [Date accessed: September 13, 2004].

Patents the use of black cohosh to reduce levels of .beta.-amyloid polypeptides. The accumulation of these peptides in the hippocampus and neocortex is believed to contribute to the onset of Alzheimer's disease.

Keywords: Medicinal uses, patents.

**Einbond, L.S.; Shimizu, M.; Xiao, D. [and others].** 2004. Growth inhibitory activity of extracts and purified components of black cohosh on human breast cancer cells. Breast Cancer Research and Treatment. 83: 221-231.

Examines various extracts and chemical constituents of black cohosh to determine their effects on human breast cancer cells. *In vitro* assays were performed with three extracted fractions: hexane, ethyl acetate, and water. The ethyl acetate fraction inhibited growth of estrogen positive MCF7 and estrogen negative MDA-MB-453 human breast cancer cell lines at the highest potency of the three extracts. Three specific constituents—the triterpene glycosides actein, 23-epi-26-deoxyactein, and cimracemoside

A—inhibited growth of MCF7 human breast cancer cells and induced cell cycle arrest. Actein was the most potent constituent identified.

Keywords: Cancer, chemical constituents, clinical studies, medicinal uses, physiological actions.

**Einer-Jensen, N.; Zhao, J.; Andersen, K.P.; Kristoffersen, K.** 1996.

*Cimicifuga* and *Melbrosia* lack oestrogenic effects in mice and rats. *Maturitas*. 25(2): 149-153.

Examines the estrogen-like effects of *Cimicifuga* and *Melbrosia*. Biological changes in animals tied to estrogen included uterine growth in immature mice and vaginal cornification in ovariectomized rats. *Cimicifuga* and *Melbrosia* were separately administered to immature mice and ovariectomized rats in doses of various potencies for three days. No signs of estrogen-like biological effects were observed.

Keywords: Clinical studies, physiological actions.

**Fabricant, D.; Li, W.; Chen, S.N. [and others].** 2001. Geographical and diurnal variation of chemical constituents of *Cimicifuga racemosa* (L.) Nutt. [Abstract]. In: Botanical dietary supplements: natural products at a crossroads; 2001 Nov 8-11; Asilomar, CA. Washington, DC: American Society of Pharmacognosy & Council for Responsible Nutrition: p. 34.

Discusses variations in chemical constituents for different populations of black cohosh.

Keywords: Chemical constituents, ecology, research.

**Fasano, S.**, inventor; [No assignee recorded], 2003. Herbal composition.

U.S. patent 6,586,018. July 1. 1 p. Int. CI2 A01N 065/00; A61K 035/78. <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=/netahtml/search-bool.html&r=1&f=G&l=50&co1=AND&d=ptxt&s1=6,586,018.WKU.&OS=PN/6,586,018&RS=PN/6,586,018>. [Date accessed: September 13, 2004].

Patents an herbal composition containing sage (*Salvia* spp.) leaf, red raspberry (*Rubus idaeus*) leaf, bayberry (*Myrica cerifera*) bark, capsicum (*Capsicum frutescens*) pepper, damiana (*Turnera diffusa*) leaf, ginger (*Zingiber officinalis*) root, licorice (*Liquiritiae radix*) root, valerian (*Valeriana officinalis*) root, black cohosh root, red clover (*Trifolium pratense*) extract, and kudzu (*Pueraria lobata*) root.

Keywords: Medicinal uses, patents.

**Foldes, J.** 1959. The actions of an extract of *Cimicifuga racemosa*. *Ärztliche Forschung*. 13(12): 623-624.

Summarizes a series of experiments assessing the estrogenic effects of black cohosh root (alcoholic extract Remifemin®). Various experiments on ovariectomized rats showed estrogenic effects that included a dose-dependent induction of estrus within three days of treatment and increased uterus weight in four days of treatment. However, one experiment showed a lack of estrogenic effect with no histological changes in the ovaries of rats after two weeks of treatment. Other research on the effects of black cohosh on rats found no suppression of thyroid function, changes in thyroid hormone mobilization, or sedative effect. A later experiment on the sedative effects of black cohosh proved positive in 31 out of 41 pre- and perimenopausal women. Three of the 41 women experienced gastric symptoms as a result of the black cohosh treatment, but no other side effects were observed. The author concluded that black cohosh was beneficial for treating symptoms of pre- and perimenopause, with a sedative effect and a hormone-like action.

Keywords: Chemical constituents, physiological actions, Remifemin®, research reviews, side effects.

**Ford, P.** 2000. Pilot inventory study of the medicinal herb black cohosh (*Actaea racemosa* L.) in a mesophytic forest type of Southern Appalachian. Plant Conservation Alliance Medicinal Plant Working Group. <http://www.nps.gov/plants/medicinal/pubs/pilotbcohosh.htm>. [Date accessed: September 13, 2004].

Provides an overview of a monitoring study done by the Medicinal Plant Working Group in cooperation with the Forest Service, U.S. Fish and Wildlife Service, and Garden Club of America. The objectives of this study were to track changes in a population of black cohosh and determine regenerations rates after harvest. This summary describes data collection in the first year of this ongoing study.

Keywords: Conservation, harvest, monitoring.

**Freudenstein, J.; Bodinet, C.** 1999. Influence of an isopropanolic aqueous extract of *Cimicifugae racemosae rhizoma* on the proliferation of MCF-7 cells. In: Abstracts of 23<sup>rd</sup> International LOF-Symposium on Phyto- oestrogens. Belgium: University of Gent: 1.

Examines the effects of an isopropanolic black cohosh extract (Remifemin<sup>®</sup>) on human estrogen-receptor-positive breast cancer (MCF-7) cells that were induced by hormone replacement therapy. The authors concluded that the extract did not stimulate proliferation of these MCF-7 cells; instead, in a dose-dependent manner, it inhibited the harmful DNA-synthesis estrogenic actions of estradiol. The anti-proliferative effects of tamoxifen were accentuated when used with black cohosh. The authors, therefore, concluded that Remifemin<sup>®</sup> was safe for use by patients with a history of breast cancer.

Keywords: Cancer, clinical studies, hormone replacement therapy, Remifemin<sup>®</sup>, safety.

**Freudenstein, J.; Dasenbrock, C.; Nisslein, T.** 2002. Lack of promotion of estrogen-dependent mammary gland tumors *in vivo* by an isopropanolic *Cimicifuga racemosa* extract. *Cancer Research*. 62: 3448-3452.

Evaluates whether black cohosh can be used to treat menopausal symptoms without increasing the proliferation of estrogen-receptor-positive breast cancer. Black cohosh extract was tested *in vivo* in ovariectomized rats with mammary tumors. After a six-week treatment, there was no significant increase in tumor number or size, suggesting that black cohosh could be used as a safe alternative to hormone replacement therapy.

Keywords: Cancer, clinical studies, hormone replacement therapy, safety.

**Ganzer, M.; Bedir, E.; Khan, I.A.** 2000. Separation of *Cimicifuga racemosa* triterpene glycosides by reversed phase high performance liquid chromatography and evaporative light scattering detection. *Chromatographia*. 52(5/6): 301-304.

Provides a detailed report on high performance liquid chromatography to separate three main triterpene glycosides from black cohosh market products and crude plant material. The method was successful in both determining quality and quantity of active constituents and in differentiating species of *Cimicifuga*.

Keywords: Chemical constituents, research.

**Genazzani, E.; Sorrentino, L.** 1962. Vascular action of acteina: active constituent of *Actaea racemosa* L. *Nature*. 194: 544-545.

Describes the vascular action of black cohosh liquid extracts in various experiments. In the studies covered, black cohosh had a hypotensive effect on rabbits and cats. It did not have a hypotensive effect on dogs or humans, though it did increase peripheral blood flow. The authors concluded that black cohosh acted by either directly or indirectly inhibiting or stimulating the vasomotor centers in the body.

Keywords: Chemical constituents, physiological actions.

**Georgiev, D.B.; Iordanova, E.** 1997. Phytoestrogens – the alternative approach [Abstract]. *Maturitas*. 27(Suppl. 1): 213.

Evaluates the effects of black cohosh extracts used by 50 postmenopausal women. Effectiveness was evaluated subjectively by the Kupperman Menopausal Index and the Hamilton Anxiety Scale, and objectively by physical indicators such as vaginal smears and measures of endometrial thickness. At the completion of the six-month study, 90 percent of patients showed significant improvement in subjective evaluations. Vaginal maturation was positively influenced in 40 percent of the patients, whereas endometrial thickness did not change for any patients.

Keywords: Assessment scales, medicinal uses, phytoestrogens, research.

**Green, M.** 2003. Cool the menopausal heat: black cohosh may help eliminate hot flashes and other symptoms. *Natural Foods Merchandiser*. 24(3): 110, 112. [http://www.newhope.com/nfm-online/nfm\\_backs/mar\\_03/cool.cfm](http://www.newhope.com/nfm-online/nfm_backs/mar_03/cool.cfm). [Date accessed: September 13, 2004].

Summarizes the medicinal uses and actions of black cohosh. Includes a review of clinical studies, history of medicinal uses, reported side effects, and recommended dosage.

Keywords: Medicinal uses, research reviews.

**Greenfield, J.; Davis, J.M.** 2003. Western North Carolina non-timber forest products. 81 p. plus appendices. Draft final report. On file with: Forest Service, Southern Research Station, 1650 Ramble Road, Blacksburg, VA 24060.

Presents findings from an ongoing study to define the non-timber forest products (NTFP) industry in western North Carolina and to estimate the social and economic values, as well as the market conditions, for black cohosh and other priority non-timber forest products.

Keywords: Market, research.

**Gruenwald, J.** 1998. Standardized black cohosh (*Cimicifuga*) extract clinical monograph. Quarterly Review of Natural Medicine. Summer: 117-125.

Reviews black cohosh research articles from Germany, including information on historical use, constituents, climacteric complaints and treatments, use in gynecology, treatment of postoperative deficiency symptoms, dosage, safety, and references.

Keywords: Chemical constituents, dosage, history, medicinal uses, research reviews, safety.

**Gunn T.R.; Wright, I.M.** 1996. The use of black and blue cohosh in labour. New Zealand Medical Journal. 109(1032): 410-411.

Reports on the use of blue cohosh (*Caulophyllum thalictroides*) and black cohosh by a midwife to induce labor that resulted in maternal vasodilation and hypotension and severe respiratory and neurological problems in the infant at birth. Authors implied that the herbs that were used contributed to the outcome.

Keywords: Case studies, safety, side effects.

**Hagels, H.; Baumert-Krauss, J.; Freudenstein, J.** 2000. Composition of phenolic constituents in *Cimicifuga racemosa* [Abstract P1B/03]. In: International Congress and 48<sup>th</sup> annual meeting of the Society of Medicinal Plant Research (GA) and 6<sup>th</sup> International Congress on Ethnopharmacology of the International Society for Ethnopharmacology (ISE). Zurich, Switzerland. Abstract P1B/03. [Publisher name and location unknown]: [page numbers unknown].

Suggests that black cohosh does not contain isoflavones, and that formononetin, indicated in previous studies as the active phytoestrogenic constituent of black cohosh, does not occur in the dried root.

Keywords: Chemical constituents, phytoestrogens, research.

**Hardy, M.L.** 2000. Herbs of special interest to women. Journal of the American Pharmaceutical Association. 40: 234-242.



Summarizes current research on several medicinal plants used for female ailments, particularly focusing on controlled studies. Includes history, mechanism of action, clinical studies, safety, recommendations for usage, and guidelines on herbal medicinal use for women who are pregnant or lactating.

Keywords: History, physiological actions, research reviews, safety.

**Harnischfeger, G.; Cillien, N.** 1996. Influence of *Cimicifuga racemosa* extract fractions on the proliferation of human carcinoma cells *in vitro* with regard to their estrogen receptor sensitivity. Gottingen, Germany: 44<sup>th</sup> Annual Congress of Georg August Universitat. P12: 40.

Examines the effects of black cohosh extracts on the proliferation of cancer cells *in vitro*.

Keywords: Cancer, clinical studies, physiological actions.

**Harnischfeger, G.; Stolze, H.** 1980. Well-proved active substances derived from natural products: black snakeroot. *Notabene Medici*. 10: 446-450.

Describes medicinally active chemical constituents of black cohosh roots.

Keywords: Chemical constituents.

**He, K.; Zheng, B.; Kim, C.H. [and others].** 2000. Direct analysis and identification of triterpene glycosides by LC/MS in black cohosh, *Cimicifuga racemosa*, and in several commercially available black cohosh products. *Planta Medica*. 66: 635-640.

Reports on the use of reverse-phase chromatography to identify and quantify triterpene glycosides in black cohosh commercial preparations. The results showed that the method was successful for determining the quality of black cohosh products.

Keywords: Chemical constituents, products, research.

**Hostanska, K.; Nisslein, T.; Freudenstein, J. [and others].** 2004. *Cimicifuga racemosa* extract inhibits proliferation of estrogen receptor-positive and negative human breast carcinoma cell lines by induction of apoptosis. *Breast Cancer Research and Treatment*. 84(2): 151-160.

Investigates the activity of isopropanolic and ethanolic black cohosh extracts on MCF-7 estrogen receptor-positive and MDA-MB231 estrogen receptor-negative breast cancer cells *in vitro*. Both extracts showed a dose-dependent response, causing apoptosis (preprogrammed early cell death) of cancer cells.

Keywords: Cancer, clinical studies, medicinal uses.

**Hunter, A.** 1999. *Cimicifuga racemosa*: pharmacology, clinical trials, and clinical use. *Materia Medica*. 5(1): 19-25.

Reviews German literature on black cohosh. Includes pharmacology, traditional use, current clinical use, clinical trials, Remifemin® clinical trials, conservation, and references.

Keywords: Clinical studies, conservation, medicinal uses, physiological actions, Remifemin®, research reviews.

**Huntley, A.; Ernst, E.** 2003. A systematic review of the safety of black cohosh. *Menopause*. 10(1): 58-64.

Reviews research on black cohosh, focusing on various international adverse event reports. The most prevalent adverse events were gastrointestinal upset or rash. Evidence suggested that adverse events were rare, mild, and reversible; though a few cases of hepatic, cardiac, or circulatory disorders indicated areas of concern. In many of these last cases, the causality was not definitive; the authors concluded that black cohosh was a safe medication.

Keywords: Adverse events, research reviews, side effects.

**Jacobson, J.S.; Troxel, A.B.; Evans, J. [and others].** 2001. Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer. *Journal of Clinical Oncology*. 19(10): 2739-2745.

Investigates the safety and effectiveness of using black cohosh to treat hot flashes for breast cancer patients. Patients were given either black cohosh or a placebo for 60 days. Data were collected on occurrences of hot flashes and changes in luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels. Both treatment and placebo groups reported a decrease in hot flashes and other menopausal symptoms. Changes in levels of LH and FSH were not statistically different between the two groups. The study concluded

that black cohosh was not more effective than a placebo; however, the authors stated that most women use black cohosh in doses higher than those used in this study.

Keywords: Cancer, dosage, hot flashes, luteinizing hormone, safety.

**Jarry, H.; Harnischfeger, G.** 1985. Studies on the endocrine efficacy of the constituents of *Cimicifuga racemosa*: 1. Influence on the serum concentration of pituitary hormones in ovariectomized rats. *Planta Medica*. 51(1): 46-49.

Reports on the measurement of levels of serum concentrations of pituitary hormones in ovariectomized rats. After 3 days, there was a significant reduction in luteinizing hormone (LH) levels, but the follicle-stimulating hormone and prolactin levels were unaffected. Spikes in LH release have been linked to occurrences of hot flashes, and so served as a measure of endocrinological activity. The agents responsible for this selective reaction were believed to be a glycoside fraction and a lipophilic fraction (triterpene glycosides). This study provides evidence of an endocrine-like efficacy for black cohosh root.

Keywords: Chemical constituents, clinical studies, hot flashes, luteinizing hormone.

**Jarry, H.; Harnischfeger, G.; Düker, E.** 1985. Studies on the endocrine efficacy of the constituents of *Cimicifuga racemosa*: 2. *In vitro* binding of constituents to estrogen receptors. *Planta Medica*. 51(4): 316-319.

Investigates the mechanism of action by which black cohosh reduces symptoms of menopause. Results showed an estrogenic effect on the hypothalamus/pituitary glands, which control the release of the luteinizing hormone associated with hot flashes. The black cohosh extract did not bind to estrogen receptors ( $\alpha$  or  $\beta$ ), but did show estrogenic action in human endometrium cytosol. The authors speculated that black cohosh possibly binds to an unidentified estrogen receptor, and/or has dopaminergic active compounds.

Keywords: Chemical constituents, clinical studies, luteinizing hormone, physiological actions.

**Jarry, H.; Metten, M.; Spengler, B. [and others].** 2003. *In vitro* effects of the *Cimicifuga racemosa* extract BNO 1055. *Maturitas*. 44(Suppl. 1): S31-S38.

As a follow up to previous findings by Jarry and Harnischfeger (1985), attempts to further understand the mechanisms by which the active constituents in black cohosh produce an endocrinological effect in *in vitro* estrogen receptor assays and in *in vivo* studies on ovariectomized rats. Three agents that competed with the hormone estradiol for binding at estrogen receptor sites were found: one fraction that did not bind to estrogen receptors but suppressed the release of luteinizing hormone (LH), a second fraction that did bind to receptor sites and suppressed LH release, and a third fraction that did bind to receptor sites but did not suppress LH release. The isoflavone formononetin was identified as one of the active constituents that did bind to estrogen receptor sites but did not suppress LH release. This led the authors to conclude that several active constituents may have acted together to produce an LH-suppressant effect.

Keywords: Clinical studies, luteinizing hormone, physiological actions.

**Johannesen, S.J.** 2001. An assessment of the threat to the survival of six medicinal plants native to the USA. Aberystwyth: University of Wales. Ph.D. dissertation for BSc Phytotherapy, College of Phytotherapy. Aberystwyth: University of Wales. 69 p.

Investigates factors that influence the survival of several medicinal plants.

Keywords: Conservation.

**Johnson, B.M.; van Breemen, R.B.** 2003. *In vitro* formation of quinoid metabolites of the dietary supplement *Cimicifuga racemosa* (black cohosh). Chemical Research in Toxicology. 16: 838-846.

Determines if the constituents of black cohosh are metabolized into toxic reactive metabolites. Urine samples from seven postmenopausal women taking black cohosh extracts at 32, 64, or 128 mg/day were evaluated. Eight electrophilic metabolites were detected; however, none of them were toxic. Black cohosh was concluded to be safe in moderate doses.

Keywords: Clinical studies, toxicity.

**Kam, I.W.; Dennehy, C.E.; Tsourounis, C.** 2002. Dietary supplement use among menopausal women attending a San Francisco health conference. Menopause. 9(1): 72-78.

Surveys the use of dietary supplements by peri- and postmenopausal women at a women's health conference in San Francisco. Out of 100 women, 29

percent used only hormone replacement therapy (HRT), 16 percent used HRT with dietary supplements, 32 percent used only dietary supplements, and 13 percent used no product or used supplements not included in the survey. The most commonly used dietary supplements were soy (*Glycine max*), ginkgo (*Gingko biloba*), and black cohosh. Respondents were asked whether black cohosh relieved various symptoms of menopause such as hot flashes, vaginal dryness, libido, and mood changes. The survey compared the various treatments in terms of perceived success and satisfaction.

Keywords: Hormone replacement therapy, menopause, surveys.

**Kauffman, G.** 2002. Black cohosh (*Cimicifuga racemosa*) harvest monitoring 2002. Plant Conservation Alliance Medicinal Plant Working Group. <http://www.nps.gov/plants/medicinal/pubs/2002bcohosh.htm>. [Date accessed: September 13, 2004].

Summarizes results of the second year of a field monitoring study in North Carolina on black cohosh. Twenty-five plots were established in the Nantahala National Forest; black cohosh plants were counted and measured in each plot. Nine plots were lightly harvested (33 percent), seven plots were heavily harvested (66 percent), and the remaining plots served as controls with no harvest. Harvested roots weighed an average of 61 grams, with a range of 4 to 301 grams. An estimated 15 to 20 plants made up a pound of dried root.

Keywords: Conservation, harvest, monitoring.

**Kennelly, E.J.; Baggett, S.; Nuntanakorn, P. [and others].** 2002. Analysis of thirteen populations of black cohosh for formononetin. *Phytomedicine*. 9: 461-467.

Reports on testing different populations of black cohosh for the presence of the isoflavone formononetin, using thin-layer chromatography and high-performance liquid chromatography. Two commercial products containing black cohosh were also evaluated. The compound formononetin was not present in any of the samples tested.

Keywords: Chemical constituents, clinical studies.

**Knüvener, E.; Korte, B.; Winterhoff, H.** 2000. *Cimicifuga* and physiological estrogens [Abstract]. *Phytomedicine*. 7(Suppl. 2): 12.

Evaluates black cohosh for estrogenic or antiestrogenic activity. Cornification of vaginal smears in castrated female mice was used as an indicator of estrogenic activity. Mice treated with mestranol or 17- $\beta$ -estradiol developed estrus, whereas mice treated with black cohosh did not. No antiestrogenic effects were observed in mice treated with both estrogen and black cohosh.

Keywords: Clinical studies, physiological actions.

**Koeda, M.; Aoki, Y.; Sakurai, N. [and others].** 1994. Three novel cyclolanostanol xylosides from *Cimicifuga* rhizome. Chemical and Pharmaceutical Bulletin. 42(10): 2205-2207.

Reports the isolation of three new xylosides from a commercial black cohosh rhizome. The structures and chemistry of the compounds are presented.

Keywords: Chemical constituents.

**Korn, W.D.** 1991. Six-month oral toxicity study with Remifemin<sup>®</sup>-granulate in rats followed by an 8-week recovery period. Hannover, Germany: International Bioresearch. [Number of pages unknown].

Investigates chronic toxicity over a six-month period of administering black cohosh granulate to rats at up to 1800 mg/kg body weight, 90 times the therapeutic dose. After an eight-week recovery period, no detectable toxic effects were observed.

Keywords: Research, toxicity.

**Kronenberg, F.; Fugh-Berman, A.** 2002. Complementary and alternative medicine for menopausal symptoms: a review of randomized, controlled trials. Annals of Internal Medicine. 137(10): 805-813.

Reviews research on several herbs used to treat menopausal symptoms. Triterpene glycosides, organic acids, esters, or the isoflavone biochanin have all been suggested as sources for the medicinal effects of black cohosh, though the active constituents and their physiological actions had not yet been identified at the time the article was published. Notes that no data was available on the long-term safety of using black cohosh.

Keywords: Chemical constituents, research reviews.

**Kruse, S.O.; Lohning, A.; Pauli, G.F. [and others].** 1999. Fukiic and piscidic acid esters from the rhizome of *Cimicifuga racemosa* and the *in vitro* estrogenic activity of fukinolic acid. *Planta Medica*. 65: 763-764.

Reports the isolation of new compounds from black cohosh rhizomes and discusses their potential pharmacological actions.

Keywords: Chemical constituents, physiological actions.

**Kusano, G.; Hojo, S.; Kondo, Y.; Takemoto, T.** 1977. Studies on the constituents of *Cimicifuga* spp. XIII. Structure of cimicifugoside. *Chemical and Pharmaceutical Bulletin*. 25(12): 3182-3189.

Reports on the isolation of several compounds from the roots of black cohosh, and proposes chemical structures for each compound.

Keywords: Chemical constituents.

**Laino, C.** 2003. Dangers of black cohosh as HRT: popular herb linked to liver disease. *WebMD Medical News*. <http://my.webmd.com/content/article/75/89785.htm>. [Date accessed: September 13, 2004].

Reports on a case study of a woman who developed autoimmune hepatitis from taking black cohosh. Autoimmune hepatitis is an inflammation of the liver caused by an attack from the body's immune system; symptoms of the disease include fatigue, abdominal discomfort, aching joints, or itching. The patient developed symptoms three weeks after she started taking black cohosh. Two weeks after she stopped using the herb, the symptoms disappeared and the patient's liver function returned to normal within nine weeks. A search of medical literature showed five reports of liver problems resulting from black cohosh use.

Keywords: Case studies, toxicity.

**Langfritz, W.** 1962. Essay on the therapy of menstrual anomalies and their concomitant phenomena in young girls and young women. *Medizinische Klinik*. 35: 1497-1499.

Studies the effectiveness of black cohosh. Remifemin<sup>®</sup> has been used successfully to treat juvenile hormonal disorders such as dysmenorrhea, oligomenorrhea, premenstrual syndrome, and similar complaints. Seventy-three young female patients were treated with Remifemin<sup>®</sup> over a four-year period. All had uterine or ovarian hypoplasia, complaints of cold feet, and underdeveloped breasts. The Remifemin<sup>®</sup> treatment normalized these

disorders and relieved or eliminated associated neurovegetative symptoms without side effects. The author considered the treatment not to be a hormone substitute, but a modifier of the autonomic hormonal processes.

Keywords: Clinical studies, medicinal uses, Remifemin<sup>®</sup>, side effects.

**Lata, H.; Bedir, E.; Hosick, A. [and others].** 2002. *In vitro* plant regeneration from leaf-derived callus of *Cimicifuga racemosa*. *Planta Medica*. 68(10): 912-915.

Describes tissue culture of black cohosh.

Keywords: Tissue culture.

**Lehmann-Willenbrock, E.; Riedel, H.H.** 1988. Clinical and endocrinologic studies of the treatment of ovarian insufficiency manifestations following hysterectomy with intact adnexa. *Zentralblatt für Gynakologie*. 110(10): 611-618.

Compares the effectiveness of estriol, conjugated estrogens, estrogen-gestagen, and black cohosh for treating climacteric symptoms in hysterectomized patients. After 24 weeks of treatment, all groups showed significant improvements. There were no significant differences between the various treatment groups.

Keywords: Clinical studies, hormone replacement therapy, medicinal uses.

**Li, W.; Sun, Y.; Liang, W. [and others].** 2003. Identification of caffeic acid derivatives in *Actaea racemosa* (*Cimicifuga racemosa*, black cohosh) by liquid chromatography/tandem mass spectrometry. *Rapid Communications in Mass Spectrometry*. 17(9): 978-982.

Reports on the utilization of high-performance liquid chromatography electrospray ionization tandem mass spectrometry to identify constituents in black cohosh rhizomes.

Keywords: Chemical constituents, research.

**Lieberman, S.** 1998. A review of the effectiveness of *Cimicifuga racemosa* (black cohosh) for the symptoms of menopause. *Journal of Women's Health*. 7(5): 525-529.



Reviews eight human studies of black cohosh use, focusing specifically on the relief of menopause symptoms. The authors concluded that black cohosh is an effective and safe alternative to hormone replacement therapy. Review includes historical uses, clinical trials, constituents, safety, and references.

Keywords: Chemical constituents, history, hormone replacement therapy, medicinal uses, research reviews, safety.

**Linde, H.** 1964. The composition of *Cimicifuga racemosa*. 1. on the isolation of 2 glycosides. *Arzneimittelforschung*. 14: 1037-1039. In German.

Describes chemical constituents of black cohosh.

Keywords: Chemical constituents.

**Linde, H.** 1967a. Components of *Cimicifuga racemosa*. 3. Configuration of the A, B, and C rings of actein. *Archiv Pharmazie*. 300(12): 982-992. In German.

Describes chemical constituents of black cohosh.

Keywords: Chemical constituents.

**Linde, H.** 1967b. Contents of *Cimicifuga racemosa*. 2. On the structure of actein. *Archiv Pharmazie*. 300(10): 85-92. In German.

Describes chemical constituents of black cohosh.

Keywords: Chemical constituents.

**Liske, E.** 1998. Therapeutic efficacy and safety of *Cimicifuga racemosa* for gynecologic disorders. *Advances in Therapy*. 15(1): 45-53.

Reviews clinical research and standardized assessments of black cohosh products for safety and effectiveness. Includes case reports, drug monitoring studies, clinical studies, constituents, safety, side effects, and extensive references. The authors concluded that black cohosh is a safe and effective means of treating menopausal symptoms.

Keywords: Chemical constituents, medicinal uses, products, research reviews, safety, side effects.

**Liske, E.; Boblitz, N.; Henneicke-von Zepelin, H.H.** 2000. Therapy of climacteric complaints with *Cimicifuga racemosa*; data on effect and efficacy from a randomized controlled double-blind study. In: Rietbrock, N.; Donath, M.F.; Loew, D. [and others], (eds.). *Phytopharmaka VI*. Darmstadt: Steinkopff. p. 247-257. In German.

Describes a study on the effectiveness of black cohosh for treating climacteric complaints.

Keywords: Clinical studies, medicinal uses.

**Liske, E.; Wüstenberg, P.** 1998. Therapy of climacteric complaints with *Cimicifuga racemosa*: herbal medicine with clinically proven evidence. *Menopause*. 5(4): 250.

Compares the effects of two different dosages of Remifemin<sup>®</sup> (40 mg vs. 127 mg isopropanolic black cohosh extract) in a double-blind randomized 6-month clinical study of 152 female patients with climacteric complaints. The two dosages showed similar efficacy and safety. Levels of luteinizing hormone, follicle stimulating hormone, sex hormone binding globulin, prolactin and estradiol, and vaginal cytology were unaffected. The authors concluded that the product did not have an estrogen-like (hormone) effect.

Keywords: Clinical studies, dosage, Remifemin<sup>®</sup>.

**Liske, E.; Wüstenberg, P.; Boblitz, N.** 1998. Human-pharmacological investigations during treatment of climacteric complaints with *Cimicifuga racemosa* (Remifemin<sup>®</sup>): no estrogen-like effects. ESCOP, The European Phytojournal. <http://www.ex.ac.uk/phytonet/phytojournal/poster71.pdf>. [Date accessed: September 13, 2004].

Previous research has suggested estrogen-like effects for black cohosh, though recent findings have questioned this claim. This study, involving 152 patients, showed that the commercial preparation Remifemin<sup>®</sup> had no effect on concentrations of luteinizing hormone, follicle stimulating hormone, sex hormone-binding globulin, prolactin, or estradiol. The proliferation of vaginal mucosa did not change in an estrogenic manner; however, the Kupperman Menopausal Index indicated a significant improvement in climacteric symptoms. The authors found black cohosh a safe and effective alternative to hormone replacement therapy.

Keywords: Assessment scales, clinical studies, physiological actions, Remifemin<sup>®</sup>.

**Liu, J.; Burdette, J.E.; Xu, H. [and others].** 2001. Evaluation of estrogenic activity of plant extracts for the potential treatment of menopausal symptoms. *Journal of Agriculture and Food Chemistry*. 49(5): 2472-2479.

Evaluates the estrogenic activity of eight herbs commonly used to treat menopausal symptoms. Clinical research on black cohosh has shown decreased levels of the luteinizing hormone responsible for hot flashes. Yet, in this study, black cohosh did not demonstrate binding to estrogen receptors and was concluded to not have estrogen-like activity.

Keywords: Clinical studies, physiological actions.

**Liu, Z.; Yang, Z.; Zhu, M.; Huo, J.** 2001. Estrogenicity of black cohosh (*Cimicifuga racemosa*) and its effect on estrogen receptor level in human breast cancer MCF-7 cells. *Wei Sheng Yan Jiu (Journal of Hygiene Research)*. 30(2): 77-80.

Female mice receiving black cohosh showed an increased uterine weight and duration of estrus. The authors concluded that black cohosh showed an estrogen-like action.

Keywords: Clinical studies, physiological actions.

**Löhning, A.; Verspohl, E.J.; Winterhoff, H.** 1998. *Cimicifuga racemosa* *in vitro* findings using MCF-7 cells [Abstract]. *Phytopharmakaforschung* 2000: 72. In German.

Investigates the effects of black cohosh on cancer cells.

Keywords: Cancer, clinical studies, medicinal uses.

**Löhning, A.; Verspohl, E.J.; Winterhoff, H.** 1999. Pharmacological studies on the dopaminergic activity of *Cimicifuga racemosa*. In: 23<sup>rd</sup> international LOF-symposium on phyto-estrogens; 1999 Jan 15; Belgium. Belgium: University of Gent. [Number of pages unknown].

Describes research on the dopaminergic activity of black cohosh.

Keywords: Clinical studies, physiological actions.

**Löhning, A.; Winterhoff, H.** 2000. Neurotransmitter concentrations after three weeks treatment with *Cimicifuga racemosa* [Abstract]. *Phytomedicine*. 7(Suppl. 2): 13.

Reports on the detection of changes in neurotransmitter concentrations in response to treatment with black cohosh. Results showed that black cohosh had an antidepressant activity caused by the inhibition of monoamine oxidase.

Keywords: Clinical studies, physiological actions.

**Lontos, S.; Jones, R.M.; Angus, P.W.; Gow, P.J.** 2003. Acute liver failure associated with the use of herbal preparations containing black cohosh. *Medical Journal of Australia*. 179(7): 390-391.

Reports a case of liver failure caused by an herbal remedy containing fluid extracts of ground ivy (*Nepeta hederaceae*), goldenseal (*Hydrastis canadensis*), ginkgo (*Gingko biloba*), oats seed (*Avena sativa*), and black cohosh. Three months after beginning to use the herbal mixture, the patient had acute liver failure and required a transplant. The explanted liver showed massive hepatic necrosis. Based on previous reports of hepatic failure associated with black cohosh, the authors suggested that the adverse reaction was caused by the black cohosh in the herbal mixture.

Keywords: Case studies, toxicity.

**Löser, B.; Kruse, S.O.; Melzig, M.F.; Nahrstedt, A.** 2000. Inhibition of neutrophil elastase activity by cinnamic acid derivatives from *Cimicifuga racemosa*. *Planta Medica*. 66: 751-753.

Evaluates several chemical constituents of black cohosh rhizomes, and describes their mechanism of action.

Keywords: Chemical constituents, physiological actions.

**Lupu, R.; Mehmi, I.; Atlas, E. [and others].** 2002. Black cohosh, a menopausal remedy, does not have estrogenic activity and does not promote breast cancer cell growth. *International Journal of Oncology*. 23: 1407-1412.

Determines that black cohosh does not have estrogenic activity *in vitro*. Various assays indicated that black cohosh extracts did not bind to or otherwise modulate estrogen receptors, and did not cause estrogen-positive breast cancer cells to proliferate.

Keywords: Cancer, physiological actions.

**Lyke, J.** 2001. Summary of the conservation status of *Cimicifuga* ssp. (*Cimicifuga rubifolia*, *C. americana*, *C. racemosa*). <http://www.nps.gov/plants/medicinal/pubs/2001appendixf.htm>. [Date accessed: September 13, 2004].

Summarizes the conservation status of black cohosh, with references. Demand for black cohosh has steadily increased in the world herb market, with an estimated 97 percent of the supply from wildcrafting. The distribution and abundance of wild populations were estimated, but no formal tracking was in progress. An estimated 366,000 pounds of dried roots were collected from 1997 to 1999; at 25 roots per pound, this meant a total of 9.2 million plants. Permit sales, conservation status, and proposed government regulations are discussed.

Keywords: Conservation, distribution, harvest, market demand, permits, regulatory status, wildcrafting.

**Macht, D.I.; Cook, H.M.** 1932. A pharmacological note on *Cimicifuga*. Journal of the American Pharmaceutical Association. 21(4): 324-330.

Provides a historical account of black cohosh medicinal uses.

Keywords: History, physiological actions.

**Mahady, G.B.** 2003. What is the evidence for supplement use for menopausal symptoms? Bethesda, MD: NIH conference on dietary supplement use in the elderly. <http://dietary-supplements.info.nih.gov/pubs/elderly.14jan03.abst.mahady.pdf>. [Date accessed: September 13, 2004].

Discusses the safety of black cohosh as a treatment for menopausal symptoms. Although black cohosh has been shown to be effective for reducing hot flashes and vaginal dryness in healthy individuals, it has not been shown to be effective for individuals taking tamoxifen for the treatment of breast cancer. The article describes a one-year research trial in progress at the University of Illinois at Chicago, National Institutes of Health Center for Botanical Dietary Supplement Research in Women's Health.

Keywords: Cancer, clinical studies, medicinal uses.

**Mahady, G.B.; Fong, H.H.S.; Farnsworth, N.R.** 2001. Botanical dietary supplements: quality, safety, and efficacy. Lisse, The Netherlands: Swets & Zeitlinger B.V. 271 p.

Provides information on several medicinal herbs, including history, medicinal uses, clinical research, physiological actions, and safety information. Clinical research has indicated that black cohosh can relieve symptoms of menopause such as hot flashes, sweating, anxiety, and insomnia. Beneficial effects have been observed after four to twelve weeks of treatment. Side effects such as nausea, vomiting, headaches, and dizziness have been reported, but are not common. Clinical trials investigating the constituents, mechanisms of action, and efficacy of black cohosh are discussed.

Keywords: Medicinal uses, physiological actions, research reviews, side effects.

**McCoy, J.; Kelly, W.** 1996. Survey of *Cimicifuga racemosa* for phytoestrogenic flavonoids. In: 212<sup>th</sup> ACS national meeting. Washington, DC: American Chemical Society. [Number of pages unknown].

Analyzes the chemical constituents of black cohosh roots. The isoflavone formononetin, previously reported to be a constituent of black cohosh roots, was not detected in this study.

Keywords: Chemical constituents, phytoestrogens, research.

**McCullough, J.E.**, inventor; Hair Associates, LLC, assignee. 2000. Hair care formulations. U.S. patent 6,139,828. October 31. 1 p. Int. CI2 A61K 007/075, A61K 007/08. <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=/netahtml/search-bool.html&r=1&f=G&l=50&co1=AND&d=ptxt&s1=6,139,828.WKU.&OS=PN/6,139,828&RS=PN/6,139,828>. [Date accessed: September 13, 2004].

Patents a hair care formulation designed to cleanse the scalp and open hair follicles, thus promoting hair growth. The product contains black cohosh and surfactants.

Keywords: Medicinal uses, patents.

**McFarlin, B.L.; Gibson, M.H.; O'Rear, J.; Harman, P.** 1999. A national survey of herbal preparation use by nurse-midwives for labor stimulation. Review of the literature and recommendations for practice. *Journal of Nurse-Midwifery*. 44(3): 205-216.

Surveys the use of herbal preparations by midwives during childbirth. Black cohosh was used to stimulate labor, alone or in combination, by 45 percent of the respondents. Issues related to herbal use during childbirth are discussed, with a brief summary of black cohosh uses.

Keywords: Medicinal uses, preparations, surveys.

**McGraw, J.B.; Bailey, B.; Sanders, S.** 2003. Conservation status of medicinal plants in international trade. Award No. 1434—HQ-97—RU—01563. Morgantown, WV: West Virginia University. 48 p. [Technical report produced for the U.S. Fish and Wildlife Service].

Reports on the use of habitat suitability models to predict potential habitat for goldenseal (*Hydrastis canadensis*) and black cohosh. Factors that limit the abundance of the plants include slow recovery after harvest, limited reproduction, and increasing harvest due to market demand. Habitat suitability models were developed based on ecological characteristics of both known populations and confirmed areas of absence. Natural areas in north central West Virginia were evaluated as potential habitat, using variables such as land cover/use, elevation, terrain shape, slope, planiform curvature (convex or concave areas), profile curvature, aspect, topography, relative moisture index, solar insolation, and distance to streams. Goldenseal showed a high level of habitat specificity, whereas black cohosh was less restricted and more abundant. However, slow vegetative reproduction and limited seed dispersal have made black cohosh populations susceptible to depletion from the harvest of rhizomes for medicinal purposes. Results of interviews with herb dealers are presented, providing insight into general market trends in the medicinal botanical industry.

Keywords: Conservation, ecology, habitat, harvest, market.

**McKenna, D.J.; Jones, K.; Humphrey, S.; Hughes, K.** 2001. Black cohosh: efficacy, safety, and use in clinical and preclinical applications. *Alternative Therapies*. 7(3): 93-100.

Reviews and summarizes research conducted on Remifemin<sup>®</sup>, a commercial black cohosh product. Includes botanical data, classification and nomenclature, history and traditional uses, chemical constituents, therapeutic applications, preclinical studies, clinical studies, dosage, safety, side effects, drug interactions, precautions, a thorough discussion of pharmacological actions throughout the body, and extensive references.

Keywords: Chemical constituents, drug interactions, dosage, history, physiological actions, Remifemin<sup>®</sup>, research reviews, safety, side effects.

**Mielnik, J.** 1997. Extract of *Cimicifuga racemosa* in the treatment of neurovegetative symptoms in women in the perimenopausal period [Abstract]. *Maturitas*. 27(Suppl. 1): 215.

Describes the use of black cohosh by 34 postmenopausal women evaluated by the Kupperman Menopausal Index of menopausal symptoms. After the first month of treatment, 26 patients showed significant improvement. Four patients showed no improvement, and four discontinued treatment in favor of hormone replacement therapy. No side effects were observed.

Keywords: Assessment scales, clinical studies, hormone replacement therapy, medicinal uses.

**Morris, K.; Look, R.M.; Hudson, V. [and others].** 2003. The efficacy and safety of black cohosh for managing menopausal symptoms in breast cancer survivors. *Breast Cancer Research and Treatment*. 82(Suppl. 1): S159.

Investigates the safety of black cohosh use by breast cancer survivors. *In vitro* experiments showed that black cohosh did not cause proliferation of hormone sensitive (T-47D) or insensitive (HCC-1937) breast cancer cells. *In vivo* experiments on 21 women compared the efficacy of black cohosh to that of venlafaxine for two 60-day periods divided by a 7-day washout period. Although venlafaxine was more effective than black cohosh, both groups showed a significant reduction in hot flashes with no serious side effects.

Keywords: Cancer, clinical studies, side effects.

**Moyer, P.** 2002. ENDO: phytoestrogen black cohosh may have potential as a SERM. Doctor's Guide. <http://www.docguide.com/dg.nsf/PrintPrint/A947E7526A16116785256BE3004F23CA>. [Date accessed: September 13, 2004].

Summarizes a study on black cohosh as a potential selective estrogen receptor modulator for treating symptoms of menopause. The 62 participants in the study received either black cohosh, conjugated estrogen, or a placebo for a three-month period. Climacteric symptoms such as hot flashes were significantly reduced by both black cohosh and conjugated estrogen.

Keywords: Clinical studies, medicinal uses, phytoestrogens.



**Muñoz, G.H.; Pluchino, S.** 2003. *Cimicifuga racemosa* for the treatment of hot flushes in women surviving breast cancer. *Maturitas*. 44(Suppl. 1): S59-S65.

Examines the use of black cohosh (extract CR BNO 1055, found in Klimadynon<sup>®</sup>/Menofem<sup>®</sup>) to treat hot flashes for breast cancer survivors on tamoxifen. After mastectomy, radiation, and chemotherapy, patients were divided into two groups: one group received tamoxifen and black cohosh, the other received tamoxifen only. After 12 months of treatment, the group receiving black cohosh and tamoxifen showed a significant reduction in the number and severity of hot flashes compared to the group receiving only tamoxifen.

Keywords: Cancer, clinical studies, hot flashes, medicinal uses.

**Murray, M.T.** 2003. Black cohosh – is there really a concern? <http://www.doctormurray.com/newsletter/1-16-2003.htm>. [Date accessed: September 13, 2004].

Responds to a study by Davis and others (2003) that found that mice bred to express breast cancer, when fed a diet with black cohosh, showed significantly higher rates of breast cancer cells metastasizing to the lungs. The author discusses several issues related to this study: (1) the research was conducted on mice and not on humans, and black cohosh may not have the same effects on two different organisms; (2) the mice used in the study were specifically bred to develop breast cancer, which may have skewed the results; and (3) previous research has shown that black cohosh has an inhibitory effect on cancer cells. Research on the safety of black cohosh by Dog and others (2003) is summarized.

Keywords: Research reviews, toxicity.

**National Institutes of Health, National Toxicology Program.** 1999. Summary of data for chemical selection: black cohosh. <http://ntp.niehs.nih.gov/INDEX.CFM?OBJECTID=03DA9AE1-E585-C748-5328B384769DCD0F>. [Date accessed: January 7, 2004].

Summarizes data on the chemical constituents, mechanism of action, and safety of black cohosh. Includes information on human and animal exposure, manufacturers and distributors, usage, history, regulations, and biological effects.

Keywords: Chemical constituents, medicinal uses, physiological actions, products, side effects, toxicity.

**National Institutes of Health, National Toxicology Program.** 2002. Black cohosh. <http://ntp.niehs.nih.gov/index.cfm?objectid=07110B8E-B6F8-602B-BFB961E97D06B225>. [Date accessed: January 7, 2004].

Reviews research on black cohosh safety, including the identification and structure of chemical constituents, exposure information, use patterns, regulatory status, evidence for carcinogenic activity, biological effects, health effects of active constituents, and references.

Keywords: Cancer, chemical constituents, physiological actions, regulatory status, research reviews.

**Nesselhut, T.; Bodinet, C.; Schneider, P.; Freudenstein, J., inventors;** Schaper & Bruemmer GmbH & Co., assignee. 2001. Use of extract of *Cimicifuga racemosa*. U.S. patent 6,267,994. July 31. 1 p. Int. CI2 A61K 035/78. <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HI TOFF&p=1&u=/netahtml/search-bool.html&r=1&f=G&l=50&co1=AND &d=ptxt&s1=6,267,994.WKU.&OS=PN/6,267,994&RS=PN/6,267,994>. [Date accessed: September 13, 2004].

Patents the use of a black cohosh extract to treat estrogen-dependent tumors. Black cohosh has been found to increase the effectiveness of the anticancer drug tamoxifen, reducing the dosage needed to treat cancer. This is beneficial both because tamoxifen can be toxic in high doses, and because black cohosh can reduce hot flashes experienced by breast cancer survivors.

Keywords: Cancer, drug interactions, medicinal uses, patents.

**Nesselhut, T.; Borth, S.; Kuhn, W.** 1993. Influence of *Cimicifuga* extracts with estrogen-like activity on the *in vitro* proliferation of mamma carcinoma cells. Archives of Gynecology and Obstetrics. 254: 817-818.

Shows that Remifemin<sup>®</sup>, at concentrations of > 2.5 µgm/ml, inhibits the proliferation of E2 positive breast cancer cells. Inhibition decreased when Remifemin<sup>®</sup> was combined with estradiol, but increased when combined with tamoxifen, and was greater than for either Remifemin<sup>®</sup> or tamoxifen used alone. The authors suggested that the inhibition of breast cancer cells was mediated through the estrogen receptor and that the positive effects of tamoxifen were enhanced by black cohosh.

Keywords: Cancer, clinical studies, drug interactions, Remifemin<sup>®</sup>.

**Nesselhut, T.; Liske, E.** 1999. Pharmacological measures in postmenopausal women with an isopropanolic aqueous extract of *Cimicifuga racemosa rhizoma* [Abstract]. *Menopause*. 6(4): 331.

Evaluates the effects of a high dose of black cohosh (136 mg/day) on 28 postmenopausal patients for 98 days. No changes were observed in endometrial thickness or vaginal cells, though 80 percent of patients reported an improvement in symptoms after therapy. The authors concluded that black cohosh acted as a phyto-selective estrogen receptor modulator with a non-estrogenic effect.

Keywords: Clinical studies, medicinal uses, physiological actions.

**Newmark, T.; Schulick, P.**, inventors; [No assignee recorded], 2001. Herbal composition for promoting hormonal balance in women and methods of using same. U.S. patent 6,242,012. June 5. 1 p. Int. CI2 A61K 035/78; A01N065/00. <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=/netahtml/search-bool.html&r=1&f=G&l=50&col=AND&d=ptxt&s1=6,242,012.WKU.&OS=PN/6,242,012&RS=PN/6,242,012>. [Date accessed: September 13, 2004].

Patents an herbal composition containing ginger (species not specified), rosemary (*Rosmarinus officinalis*), evening primrose (*Oenothera biennis*), black cohosh, dong quai (*Angelica sinensis*), schizandra berry (*Schizandra chinensis*), and chaste tree berry (*Vitex agnus-castus*). The purpose of this herbal formula is to treat symptoms of hormonal imbalance in women, promote normal bone growth, improve sexual functioning, and act as an antioxidant to reduce signs of aging.

Keywords: Medicinal uses, patents.

**Nisslein, T.; Freudenstein, J.** 2000. Effects of black cohosh on urinary bone markers and femoral density in an OVX-rat model. *Osteoporosis International*. 11(Supplement 2): [Number of pages unknown]. Abstract number 504.

Suggests that black cohosh has potential benefits for retarding bone loss. Markers of bone metabolism declined significantly compared to controls in rats given black cohosh isopropanolic extract.

Keywords: Clinical studies, medicinal uses.

**Nisslein, T.; Freudenstein, J.** 2003. Effects of an isopropanolic extract of *Cimicifuga racemosa* on urinary crosslinks and other parameters of bone quality in an ovariectomized rat model of osteoporosis. *Journal of Bone Mineral Metabolism*. 21(6): 370-376.

Investigates the effects of black cohosh on bone loss associated with decreased estrogen levels. Ovariectomized rats on diets containing black cohosh showed significantly less bone loss starting 2 to 5 weeks after treatment began through the completion of the study at 7 weeks.

Keywords: Clinical studies, medicinal uses, physiological actions.

**Noguchi, M.; Naga, M.; Koeda, M. [and others].** 1998. Vasoactive effects of cimicifugic acids C and D, and fukinolic acid in *Cimicifuga* rhizome. *Biological and Pharmaceutical Bulletin*. 21(11): 1163-1168.

Examines the vasoactivity of several constituents of black cohosh.

Keywords: Chemical constituents, clinical studies.

**Onorato, J.; Henion, J.D.** 2001. Evaluation of triterpene glycoside estrogenic activity using LC/MS and immunoaffinity extraction. *Analytical Chemistry*. 73(19): 4704-4710.

Tests the estrogen-like activity of three triterpene glycosides present in the rhizomes of black cohosh. One glycoside, 27–deoxyacetyl aglycon, showed weak binding (4 percent), whereas none of the other glycosides or their metabolic products showed binding to estrogen receptor sites.

Keywords: Chemical constituents, clinical studies, physiological actions.

**Papps, F.A.** 2000. Therapeutic use and associated biochemistry of *Cimicifuga racemosa* in the treatment of menopausal symptoms. *Australian Journal of Medical Herbalism*. 12(1): 22-26.

Reviews research related to the use of black cohosh to treat symptoms of menopause, with a focus on biochemical mechanisms and chemistry.

Keywords: Chemical constituents, medicinal uses, research reviews.

**Pepping, J.** 1999. Black cohosh: *Cimicifuga racemosa*. *American Journal of Health-System Pharmacy*. 56(14): 1400-1402.

Reviews black cohosh research; includes uses, pharmacology, pharmacokinetics, clinical studies, dosage, adverse effects, drug interactions, contraindications, and references. The active constituents include triterpene glycosides such as actein, cimicifugoside, and 27-deoxyactein. The most popular commercial product, Remifemin<sup>®</sup>, is standardized to contain 1 mg of 27-deoxyactein per 20-mg tablet. Studies on the presence of the isoflavone formononetin have yielded conflicting results. Several clinical studies indicated estrogenic effects for black cohosh, such as decreased luteinizing hormone levels in menopausal women and increased uterine weight in rats. Other studies failed to show these results. Several clinical studies that demonstrated significant improvement in psychological and somatic symptoms of menopause as measured by the Kupperman Menopausal Index and the Hamilton Anxiety Scale are summarized. All studies utilized Remifemin<sup>®</sup> at dosages from 40 to 80 mg twice daily. Research conducted by the manufacturer resulted in a recommended dose of one tablet twice daily. Effects were apparent after two weeks of use, and maximum benefit seen after eight weeks. Side effects included gastrointestinal upset in a small percentage of consumers. Recent studies have concluded that black cohosh is safe for women with a history of estrogen-related cancer. The author noted that no drug interactions were known, and that black cohosh should not be used during pregnancy.

Keywords: Assessment scales, chemical constituents, dosage, medicinal uses, physiological actions, Remifemin<sup>®</sup>, research reviews, side effects.

**Petho.** 1987. Climacteric complaints are often helped with black cohosh. *Ärztliche Praxis.* 47: 1551-1553.

Reviews the effectiveness of Remifemin<sup>®</sup> for treating menopausal symptoms in an open study involving 60 female patients who replaced hormone injection therapy with black cohosh tablets (40 mg twice daily) over a 6-month period. The Kupperman Menopausal Index, subjective observations, and the number of hormone injections needed after initiation of Remifemin<sup>®</sup> therapy were used to measure efficacy. Eighty-two percent of patients reported the black cohosh therapy as good or very good, and 58 percent did not need additional hormone injections. No side effects were reported over the six-month period.

Keywords: Assessment scales, clinical studies, hormone replacement therapy, medicinal uses, Remifemin<sup>®</sup>, side effects.

**Popp, M.; Schenk, R.; Abel, G.** 2003. Cultivation of *Cimicifuga racemosa* (L.) Nuttall and quality of CR extract BNO 1055. *Maturitas*. 44(Suppl. 1): S1-S7.

Reports the results of experiments with propagation and cultivation techniques for black cohosh with the goal of producing a homogenized, standardized variety for pharmaceutical use. Germination of black cohosh seeds required two stratification periods. Gibberellic acid applications improved leaf development. Evaluation of triterpene glycoside content over several months showed peak levels in June, though extractable levels and quality of constituents peaked in August.

Keywords: Chemical constituents, cultivation, harvest, research, seeds.

**Ramsey, G.** 2000. *Actaea* and *Cimicifuga* identification. *Chinquapin*. 8(3): 26.

Identifies key points for distinguishing *Cimicifuga* from *Actaea* based on leaf characteristics.

Keywords: Identification.

**Ramsey, G.W.** 1986. A biometrical analysis of terminal leaflet characteristics of the North American *Cimicifuga* (Ranunculaceae). *Virginia Journal of Science*. 37(1): 3-8.

Identifies anatomical characteristics that can be used to differentiate Eastern North American *Cimicifuga* species, including stomatal apparatus length and number of stomates on terminal leaflets.

Keywords: Identification, related species.

**Ramsey, G.W.** 1988. A comparison of vegetative characteristics of several genera with those of the genus *Cimicifuga* (Ranunculaceae). *Sida*. 13(1): 57-63.

Offers an analysis of morphological features of *Cimicifuga*, *Actaea*, *Aruncus*, *Astilbe*, *Thalictrum*, *Caulophyllum*, and *Trautvetteria*, highlighting vegetative differences between the genera. A key is included to aid in field identification of specimens based on terminal leaflet characteristics.

Keywords: Identification.

**Robbins, C.** 1999. Medicine from U.S. wildlands: an assessment of native plant species harvested in the United States for medicinal use and trade and evaluation of the conservation and management implications. <http://www.nps.gov/plants/medicinal/pubs/traffic.htm>. [Date accessed: September 14, 2004]. [Prepared by TRAFFIC North America for the Nature Conservancy].

Provides information on black cohosh harvest and conservation status. A total of 4 permits were sold for black cohosh collection from national forests in 1995, 33 in 1996, and 50 in 1997.

Keywords: Conservation, harvest, permits.

**Robbins, C.** 2001. TRAFFIC analysis of U.S. exports and consumer interest in black cohosh (*Cimicifuga racemosa*). Washington, DC: TRAFFIC North America. 1 p.

Summarizes export data from the U.S. Department of Agriculture, Animal and Plant Health Inspection Service from 1999 to 2001. A total of 4245 kg of dried rhizomes were exported to Italy, France, Canada, Germany, and Switzerland. Sources of exported roots were Virginia, North Carolina, South Carolina, and Ohio.

Keywords: Export.

**Rockwell, S.; Fajolu, O.; Liu, Y. [and others].** 2003. The herbal medicine black cohosh alters the response of breast cancer cells to some agents used in cancer therapy [Abstract]. American Association for Cancer Research. Abstract available at: <http://www.annieappleseedproject.org/efofblaccoho.html>. [Date accessed: September 13, 2004].

Investigates the effects of black cohosh extracts on cancer cells *in vitro*. The black cohosh extract alone did not affect the growth of cancer cells. When combined with different anticancer drugs the results varied: black cohosh increased the efficacy of Cisplatin, but increased the toxicity of Adriamycin<sup>®</sup> and Taxotere<sup>®</sup>.

Keywords: Cancer, clinical studies, drug interactions, toxicity.

**Sakurai, N.; Wu, J.H.; Sashida, Y. [and others].** 2004. Anti-AIDS agents. Part 57: Actein, an anti-HIV principle from the rhizome of *Cimicifuga racemosa* (black cohosh), and the anti-HIV activity of related saponins. Bioorganic and Medicinal Chemistry Letters. 14(5): 1329-1332.

Evaluates constituents from black cohosh for anti-HIV activity. Actein, a tetracyclic triterpenoid, showed potent anti-HIV activity, and 12 saponins showed moderate anti-HIV activity.

Keywords: Chemical constituents, clinical studies, medicinal uses.

**Schaper and Brummer, GmbH.** 1997. Remifemin®: a plant-based gynecological agent. Salzgitter, Germany: Schaper and Brummer GmbH. [Number of pages unknown].

Summarizes a controlled, randomized, double-blind, multicenter clinical study involving 152 women before or after menopause (age 43 to 60 years) who were experiencing moderate neurovegetative climacteric complaints. Patients received either one or two 20-mg tablets twice daily for three months. Patients were examined before starting treatment, at 2, 4, and 8 weeks of treatment, and after the study ended. Effectiveness was evaluated using the Kupperman Menopausal Index, the Self-Assessment Depression Scale, the Clinical Global Impression scale, and vaginal cytology indices. Levels of luteinizing hormone, follicle stimulating hormone, estradiol-17 $\beta$ , prolactin, and globulin were also measured. Both dosages showed similar effectiveness and safety results; the Kupperman Menopausal Index and Self-Assessment Depression Scale showed significantly decreased scores, but no changes were seen in vaginal cytology or hormone levels. No details are given on adverse effects, though the treatment was rated as well tolerated by 95 percent of patients and 92 percent of their doctors, and as “good” or “very good” in 80 percent of cases. This brochure is provided by the manufacturers of Remifemin®.

Keywords: Assessment scales, clinical studies, dosage, luteinizing hormone, medicinal uses, menopause, Remifemin®

**Schlosser, K.K.** 2002. Counting cohosh. North Carolina Wildflower Preservation Society. 14(2): [Number of pages unknown]. <http://www.nps.gov/plants/medicinal/pubs/countingcohosh.htm>. [Date accessed: September 13, 2004].

Describes a monitoring study of black cohosh in the forests of North Carolina sponsored by the Plant Conservation Alliance - Medicinal Plant Working Group and the Forest Service, and executed by members of the Garden Club of America. In this study, black cohosh plants in designated 10 X 10-meter plots were counted, measured, and evaluated for health status. Plots were divided into one of three groups: controls with no harvest, 33 percent harvest, or 66 percent harvest. The purpose of the research is to



provide forest managers with information about the regeneration of black cohosh to ensure that harvest levels remain within sustainable limits.

Keywords: Conservation, harvest, monitoring.

**Seibel, M.M.** 2003. Treating hot flushes without hormone replacement therapy. *Journal of Family Practice*. 52(4): 291-296.

Summarizes information on herbs used as alternatives to hormone replacement therapy, including soy (*Glycine max*), dong quai (*Angelica sinensis*), black cohosh, evening primrose (*Oenothera biennis*), and red clover (*Trifolium pratense*).

Keywords: Hormone replacement therapy, medicinal uses.

**Seidlová-Wuttke, D.; Hesse, O.; Jarry, H. [and others].** 2003. Evidence for selective estrogen receptor modulator activity in a black cohosh (*Cimicifuga racemosa*) extract: comparison with estradiol-17beta. *European Journal of Endocrinology*. 149: 351-362.

Compares the selective estrogen receptor modulator (SERM) activity of the black cohosh extract BNO 1055 (Klimadynon<sup>®</sup>/Menofem<sup>®</sup>) to estrogen. After a 3-month treatment with black cohosh or estrogens, ovariectomized rats showed both decreased luteinizing hormone secretion and reduced bone loss. The estrogen group also showed uterine weight gain and progesterone receptor activity, whereas the group using black cohosh did not. Results indicated that black cohosh has SERM properties that act in the hypothalamus/pituitary system and prevent bone loss without stimulating the uterus. The active constituents remained unidentified.

Keywords: Chemical constituents, clinical studies, medicinal uses, physiological actions.

**Seidlová-Wuttke, D.; Jarry, H.; Heiden, I.; Wuttke, W.** 2000. Effects of *Cimicifuga racemosa* on estrogen dependent tissues [Abstract]. *Phytomedicine*. 7(Suppl. 2): 11.

Evaluates the activity of black cohosh in the uterus, bone, liver, and aorta. Subacute and chronic treatments with black cohosh extract BNO 1055 were compared to treatments with estradiol in rats. Black cohosh showed no effect on uterine weight, but acted similarly to estrogen in the bone, liver, and aorta. These results suggested that black cohosh has phytoselective estrogen receptor (ER) modulator activity acting mainly upon ER-β.

Keywords: Clinical studies, physiological actions.

**Seidlová-Wuttke, D.; Wuttke, W.** 2000. Selective estrogen receptor modular activity of *Cimicifuga racemosa* extract: clinical data [Abstract]. *Phytomedicine*. 7(Suppl. 2): 11.

Discusses the selective estrogen receptor (ER) modulator activity of black cohosh. Two types of estrogen receptors have been identified: ER- $\beta$  and ER- $\alpha$ . Black cohosh has shown beneficial effects in the central nervous system, bone, and arteries, but no effects on the uterus. The authors suggested that this indicates that black cohosh may selectively affect one type of estrogen receptor, though more research is needed to understand the mechanism of action. Recent studies have suggested that black cohosh may reduce hot flashes by influencing the hypothalamus, without estrogenic activity.

Keywords: Clinical studies, hot flashes, medicinal uses, physiological actions.

**Shao, Y.; Harris, A.; Wang, M. [and others].** 2000. Triterpene glycosides from *Cimicifuga racemosa*. *Journal of Natural Products*. 63: 905–910.

Reports the discovery of eight new triterpene glycosides in root extracts of black cohosh.

Keywords: Chemical constituents, clinical studies.

**Stefan, H.** 1959. An essay on the manifestations and therapy of hormone-related female biopathic syndrome. *Ringelbl Biol Umsch*. 10: 149-152; 11: 157-162.

Focuses on the use of black cohosh to treat juvenile menstrual irregularities, which can be accompanied by psychological symptoms such as mood swings, depression, and psychological instability. The author found that, within eight weeks of initiation, this treatment was particularly useful for restoring regular menstruation after disruptions caused by stress, transitions, or adjustment to new surroundings. The author concluded that, with its mild sedative action and hormone-like effect, black cohosh could be effectively used to treat females with hormone imbalances from pre-puberty to menopause. This conclusion was based on the study findings that the herb could induce normal menstruation without being habit-forming or having other negative side effects with long-term administration.

Keywords: Case studies, medicinal uses, mood, side effects.

**Stiehler, K.** 1959. On the use of a standardized *Cimicifuga* extract in gynecology. *Ärztliche Praxis*. 11(26): 916-917.

Concludes that black cohosh produces a normalizing effect by intervening with (without interfering with) hormonal mechanisms while still under pituitary control, in a study based on clinical observations of 53 patients. The author states that black cohosh was found useful for treating both premenopausal and menopausal symptoms and irregular menstruation with a shortened follicular phase in juveniles, but was not useful for menstrual disorders in general. A mild mood-enhancing effect was noted.

Keywords: Case studies, medicinal uses, mood, physiological actions.

**Stoll, W.** 1987. Phytotherapy influences atrophic vaginal epithelium. *Therapeuticon*. 1: 23-31. Abstract available at [http://www.chiro.org/nutrition/ABSTRACTS/Phytotherapy\\_Influences\\_Atrophic.shtml](http://www.chiro.org/nutrition/ABSTRACTS/Phytotherapy_Influences_Atrophic.shtml). [Date accessed: September 13, 2004].

Evaluates the effectiveness of black cohosh for treating symptoms of menopause. A double-blind study was conducted with 80 women for three months, comparing Remifemin® and a low-dose estrogen treatment to a placebo. At the end of the study, women taking Remifemin® showed significant improvement on the Kupperman Menopausal Index (measuring neurovegetative symptoms), the Hamilton Anxiety Scale (measuring psychological complaints), and proliferation of vaginal epithelium. The estrogen dose was too low for any significant results.

Keywords: Assessment scales, clinical studies, medicinal uses, Remifemin®.

**Stolze, H.** 1982. An alternative to treat menopausal complaints. *Gynakologe*. 3: 14-16.

Reviews objective evaluations by 131 general practitioners and gynecologists and subjective evaluations by 629 of their patients on the effectiveness of a black cohosh treatment (40 drops Remifemin® liquid twice/day) for menopausal complaints, in an open, multi-center, retrospective study. Favorable results were achieved in 80 percent of cases after six to eight weeks of treatment, and included varying degrees of relief from neurovegetative symptoms such as hot flashes, sweating, headache, vertigo, heart palpitation, and tinnitus. Varying degrees of relief were also found from psychiatric symptoms such as nervousness and irritability, sleep disturbances, and depressive moods. Symptoms were completely removed in 49 percent of cases, and 37.8 percent experienced improvement (but not cessation) of symptoms. Seven percent of the cases experienced transient

stomach upset, but none discontinued treatment. Physicians considered the black cohosh treatment advantageous over hormone replacement in 72 percent of the cases. The author concluded that black cohosh was a safe and effective nonhormonal treatment for menopausal symptoms.

Keywords: Clinical studies, medicinal uses, Remifemin®.

**Struck, D.; Tegtmeier, M.; Harnischfeger, G.** 1997. Flavones in extracts of *Cimicifuga racemosa*. *Planta Medica*. 63(3): 289.

Evaluates the active chemical constituents in black cohosh commercial preparations. Flavonoids were found in both extracts and medicines, but the isoflavone formononetin and the flavone kaempferol were not present in detectable amounts.

Keywords: Chemical constituents, products, research.

**Suggs, R.** 2003. Market profile: black cohosh. Robbinsville, NC: Yellow Creek Botanical Institute. 12 p. Unpublished document. On file with: U.S. Department of Agriculture, Forest Service, Southern Research Station, SRS-4702, 1650 Ramble Road, Blacksburg, VA 24060.

Describes the international market for black cohosh. Black cohosh is most commonly used to relieve symptoms of menopause and premenstrual syndrome. Although black cohosh is not currently threatened or endangered, increased demand in the late 1990s has qualified the herb for “At-Risk” status with the United Plant Savers, and the plant is considered a priority species for observation by the wildlife trade monitoring organization TRAFFIC. Black cohosh is regulated in the United States as a dietary supplement and is approved as a drug in Europe. Numerous clinical studies have supported the safety and efficacy of black cohosh, though the exact mechanism of action is not known. Active constituents in medicinal preparations are triterpene glycosides and flavonoids, often standardized to 1-mg triterpenes (27–deoxyactein) per tablet. In the field, yellow cohosh (*Cimicifuga americana*) is often confused with black cohosh, as the plants have similar characteristics and habitats. In China, sheng ma (*Cimicifuga foetida*) is substituted for black cohosh, though no clinical studies have evaluated this species. Market prices for black cohosh peaked in 1998 at \$4.50/lb for dried roots, with a total of 600,000 to 700,000 lbs of roots in the market at that time. An estimated 95 percent of this was supplied from the wild and only 5 percent cultivated. The high prices paid for rhizomes increased harvest and overstocked the market, causing prices to drop to \$1.40/lb in late 2000. As stocks are diminishing, prices are slowly rising

again. Major producers of black cohosh in the U.S. are in Kentucky and Tennessee, with additional harvest in Wisconsin, Michigan, North Carolina, South Carolina, Georgia, West Virginia, Virginia, and Ohio. An estimated 60 percent of the total harvest is exported, mostly to Germany and Italy. Price variations along the market chain from harvest to retail are included for wild, cultivated, and certified organic roots.

Keywords: Chemical constituents, conservation, harvest, prices.

**Sun, J.** 2003. Morning/evening menopausal formula relieves menopausal symptoms: a pilot study. *Journal of Alternative Complementary Medicine*. 9(3): 403-409.

Evaluates the efficacy of a combination herbal formula for treating menopausal symptoms. The regimen consisted of a morning pill with Asian ginseng (*Panax ginseng*), black cohosh, soy (*Glycine max*), and green tea (*Camellia sinensis*) extracts, and an evening pill with black cohosh, soy, kava (*Piper methysticum*), hops (*Humulus lupulus*), and valerian (*Valeriana officinalis*) extracts. Beneficial effects were achieved within two weeks. By the 8<sup>th</sup> week, significant reductions in hot flashes, anxiety, depression, and insomnia were observed.

Keywords: Clinical studies, medicinal uses.

**Takahira, M.; Kusano, A.; Shibano, M. [and others].** 1998. Antimalarial activity and nucleoside transport inhibitory activity of the triterpenic constituents of *Cimicifuga* spp. *Biological and Pharmaceutical Bulletin*. 21(8): 823-828.

Examines triterpene glycosides from *Cimicifuga* for their antimalarial activity and nucleoside transport inhibition. Effective concentrations and a discussion of the mechanism of action are provided.

Keywords: Chemical constituents, clinical studies, medicinal uses, physiological actions.

**Thomas, A.L.; Lubhan, D.; Folk, W. [and others].** 2001. Black cohosh cultivation in Missouri, and quantification of its medicinal compounds in response to various cultivation regimens. Mt. Vernon: Missouri Agricultural Experiment Station, Southwest Research Center. <http://aes.missouri.edu/swcenter/fieldday/page53.stm>. [Date accessed: September 13, 2004].

Describes research by the Center for Phytonutrient and Phytochemical Studies (a consortium between the University of Missouri, Columbia, and the Missouri Botanical Garden) that focuses on black cohosh cultivation. The article covers two experiments: one to evaluate ideal cultivation conditions to provide farmers with detailed recommendations, and the other to evaluate plants grown in various spacings and under various shade conditions to determine optimum growth and production of medicinal compounds.

Keywords: Cultivation, research.

**Thomassen, M.; Schmidt, M.** 2003. Hepatotoxicity from *Cimicifuga racemosa*? Recent Australian case report not sufficiently substantiated. *Journal of Alternative and Complementary Medicine*. 9(3): 337-340.

Disputes an article by Whiting and others (2002) which links a case of hepatotoxicity to the use of black cohosh.

Keywords: Side effects.

**Tyler, V.** 1995. Was Lydia Pinkham's Vegetable Compound an effective remedy? *Pharmacy in History*. 37: 24-28.

Discusses the modern clinical research on individual constituents of an herbal tonic that was popular in the early 1900s. Black cohosh was one of the main ingredients in this formula that was marketed for various female ailments.

Keywords: History, Lydia Pinkham's Vegetable Compound, research reviews.

**Vitetta, L.; Thomassen, M.; Sali, A.** 2003. Black cohosh and other herbal remedies associated with acute hepatitis. *Medical Journal of Australia*. 178(8): 411-412.

Responds to an article by Whiting and others (2002) on the association between black cohosh and acute hepatitis. The author points out that adverse effects may have been due to contaminants in the herbal product used, and that, without further investigation into the constituents of the product, black cohosh cannot be assumed to be the cause of the illness. Previous research has shown black cohosh to be a safe and effective herbal medicine.

Keywords: Research reviews, toxicity.

**Vorberg, G.** 1984. Treatment of menopause symptoms. *Zeitschrift Für Alternsforschung*. 60: 626-629.

Evaluates the effectiveness of Remifemin® in an open study with 50 women. After 12 weeks of treatment, significant improvements were observed for neurovegetative and psychological symptoms.

Keywords: Clinical studies, medicinal uses, Remifemin®.

**Wade, C.; Kronenberg, F.; Kelly, A.; Murphy, P.A.** 1999. Hormone-modulating herbs: implications for women's health. *Journal of the American Medical Women's Association*. 54(4): 181-183.

Reviews research related to black cohosh, particularly the effectiveness and safety of phytoestrogens. Phytoestrogens such as isoflavones, lignans, and coumestans can bind to estrogen receptors and produce both estrogenic and antiestrogenic effects to mediate hormonal imbalances. Research into the estrogen-like effects of black cohosh has yielded conflicting results. One study identified the isoflavone formononetin in a black cohosh preparation, whereas another study found no traceable amount. One study concluded that black cohosh could bind to estrogen receptors, whereas another study concluded that black cohosh did not increase the proliferation of breast cancer that would have resulted from binding to estrogen sites. The authors attributed inconsistencies in research findings to the lack of controlled, randomized studies with women of homogenous hormonal status.

Keywords: Cancer, chemical constituents, phytoestrogens, research reviews, safety.

**Warnecke, G.** 1985. Influence of a phytopharmaceutical on climacteric complaints. *Medizinische Welt*. 36: 871-874.

Evaluates the effectiveness of black cohosh, hormone replacement therapy, and a psychopharmaceutical drug for treating various symptoms of menopause in an open, controlled, comparative study. Sixty menopausal female patients were divided into three groups and received either Remifemin® (40 drops twice daily), estrogens (0.625 mg daily), or Diazepam (2 mg daily) for a 12-week duration. The Kupperman Menopausal Index, Clinical Global Impression Scale, and Profile of Mood States were used to evaluate the effectiveness of each treatment. All therapies were deemed comparatively good, and both Remifemin® and estrogens similarly stimulated vaginal mucosa with an increase in cytological indices. Because it lacked any negative side effects and performed as well as the estrogens in treating neurovegetative menopausal

symptoms and as well as the psychopharmaceutical for treating depression, black cohosh was considered an excellent choice for treating mild to moderate menopausal symptoms.

Keywords: Assessment scales, clinical studies, hormone replacement therapy, medicinal uses, menopause, Remifemin®.

**Watanabe, K.; Mimaki, Y.; Sakagami, H.; Sashida, Y.** 2002. Cycloartane glycosides from the rhizomes of *Cimicifuga racemosa* and their cytotoxic activities. *Chemical and Pharmaceutical Bulletin*. 50(1): 121-125.

Analyzes the chemical constituents in rhizomes of black cohosh. Twelve cycloartane glycosides are identified. Four of these compounds are new discoveries; their structures, activities, and cytotoxic potential were evaluated.

Keywords: Chemical constituents.

**Wende, K.; Mugge, C.; Thurow, K. [and others].** 2001. Actaeapoxide 3-O-β-D-xylopyranoside, a new cycloartane glycoside from the rhizomes of *Actaea racemosa* (*Cimicifuga racemosa*). *Journal of Natural Products*. 64: 986-989.

Identifies a new cycloartane glycoside from a triterpene fraction of an extract of black cohosh.

Keywords: Chemical constituents.

**Whiting, P.W.; Clouston, A.; Kerlin, P.** 2002. Black cohosh and other herbal remedies associated with acute hepatitis. *Medical Journal of Australia*. 177(8): 440-443.

Reports on six cases of hepatotoxicity believed to be caused by various herbal remedies. The herbal products were not analyzed or evaluated in any of the cases presented, yet were assumed to have caused the illness, as no other causes were identified. One patient took black cohosh alone for 1 week before symptoms appeared, whereas other patients used various herbal combinations. A list of herbs believed to cause hepatotoxicity is included.

Keywords: Toxicity.

**Winterhoff, H.; Butterweck, V.; Jarry, H.; Wuttke, W.** 2002. Pharmacological and clinical studies using *Cimicifuga racemosa* for



climacteric complaints. *Wien Med Wochenschr.* 152(15-16): 360-363. In German.

Presents the results of clinical studies on the medicinal properties of black cohosh.

Keywords: Clinical studies, medicinal uses.

**Winterhoff, H.; Spengler, B.; Christoffel, V. [and others].** 2003.

*Cimicifuga* extract BNO 1055: reduction of hot flushes and hints of antidepressant activity. *Maturitas.* 44(Suppl. 1): S51-S58.

Shows a significant reduction in hot flushes and antidepressant activity in rats administered the ethanolic black cohosh extract BNO 1055 contained in Klimadynon<sup>®</sup>/Menofem<sup>®</sup>.

Keywords: Clinical studies, Klimadynon<sup>®</sup>/Menofem<sup>®</sup>, medicinal uses.

**Woo, K.C.; Park, Y.S.; Jun, D.J. [and others].** 2004. Phytoestrogen cimicifugoside-mediated inhibition of catecholamine secretion by blocking nicotinic acetylcholine receptor in bovine adrenal chromaffin cell. *Journal of Pharmacology and Experimental Therapeutics.* 309: 641-649.

Investigates the effects of cimicifugoside, a pharmacologically active compound found in the roots of black cohosh.

Keywords: Clinical studies, physiological actions, phytoestrogens.

**Wuttke, W.; Jarry, H.; Heiden, I. [and others].** 2000. Selective estrogen receptor modulator (SERM) activity of the *Cimicifuga racemosa* extract BNO 1055: pharmacology and mechanisms of action [Abstract]. *Phytomedicine.* 7(Suppl. 2): 12.

Tests the estrogenic effects of the black cohosh extract BNO 1055. Ovariectomized rats were treated with either estradiol or black cohosh for 6 hours, 7 days, or 3 months. Estradiol stimulated the uterus, yet black cohosh did not. Both estradiol and black cohosh prevented the development of osteoporosis. Black cohosh also showed beneficial effects on hepatic and lipid metabolism and on the central nervous system, which may account for its ability to reduce hot flashes. The authors concluded that black cohosh contains phyto-selective estrogen receptor modulators that have no effect on the uterus but showed desirable effects on other organs.

Keywords: Clinical studies, physiological actions.

**Wuttke, W.; Seidlová-Wuttke, D.; Gorkow, C.** 2003. The *Cimicifuga* preparation BNO 1055 vs. conjugated estrogens in a double-blind placebo-controlled study: effects on menopause symptoms and bone markers. *Maturitas*. 44(Suppl. 1): S67-S77.

Compares the selective estrogen receptor modulator (SERM) effects of the black cohosh extract BNO 1055 (Klimadynon<sup>®</sup>/Menofem<sup>®</sup>) to those of conjugated estrogens or a placebo in a randomized, double-blind clinical trial with postmenopausal women. Black cohosh showed similar results to estrogen in reducing hot flashes and bone loss and increasing vaginal superficial cells. Black cohosh did not show any effect on endometrial thickness. These results suggested that black cohosh had constituents with SERM activity that affected the brain/hypothalamus, bones, and vagina, but did not affect the uterus.

Keywords: Clinical studies, Klimadynon<sup>®</sup>/Menofem<sup>®</sup>, medicinal uses, physiological actions.

**Xu, H.; Fabricant, D.S.; Johnson, H.E. [and others].** 2001. Using random amplified polymorphic DNA (RAPD) markers to identify plant species and variants. [Abstract]. In: *Botanical dietary supplements: natural products at a crossroads*; 2001 Nov 8-11; Asilomar, CA. Washington, DC: American Society of Pharmacognosy and Council for Responsible Nutrition: p. 32.

Reports on the use of random amplified polymorphic DNA markers to identify plant species, confirming the use of the technique to discern black cohosh from other medicinal plant species.

Keywords: Chemical constituents, research.

**Zerega, N.J.C.; Mori, S.; Lindqvist, C. [and others].** 2002. Using amplified fragment length polymorphisms (AFLP) to identify black cohosh (*Actaea racemosa*). *Economic Botany*. 56(2): 154-164.

Reports on the use of DNA fingerprinting to analyze and identify rhizomes of black cohosh and related species (*Actaea pachypoda*, *A. cordifolia*, and *A. podocarpa*). Two black cohosh products were evaluated by amplified fragment length polymorphisms (AFLP) analysis and found to contain only black cohosh. AFLP was found to be a successful method to evaluate product quality. Wild populations of black cohosh in Virginia and North Carolina were also evaluated, but did not contain sufficient genetic markers

to distinguish different populations of the same species. Results of this research supported the classification of the species under the genus *Actaea*.

Keywords: Chemical constituents, products, related species, research.

**Zierau, O.; Bodinet, C.; Kolba, S. [and others].** 2002. Antiestrogenic activities of *Cimicifuga racemosa* extracts. Journal of Steroid Biochemistry and Molecular Biology. 80: 125-130.

Determines that black cohosh contains compounds with antiestrogenic properties. The effects of ethanolic and isopropanolic extracts of black cohosh were tested on MCF-7 cancer cells and gene expression. Results showed that black cohosh did not bind to estrogen receptors. The authors noted that the exact mechanism of action of the herb remains unknown, though it is believed that either there are several active constituents that work synergistically, or the components have selective estrogen receptor modulator-like capabilities.

Keywords: Cancer, clinical studies, physiological actions.

## Popular Press

**Blumenthal, M.** 1999. Herb market levels after five years of boom: 1999 sales in mainstream market up only 11% in first half of 1999 after 55% increase in 1998. HerbalGram. 47: 64-65.

Discusses trends in the market for herbal supplements. In 1999, the largest gain in sales for any single herb was for black cohosh. In the first 8 months of 1999, sales increased 477 percent, most likely due to publicity of research documenting the beneficial effects of black cohosh for treating menopause symptoms. In 1998, retail sales for black cohosh totaled \$586,468, and in 1999 sales were up to \$3,385,393.

Keywords: Market, retail sales.

**Blumenthal, M.** 2002. Herb sales down in mainstream market, up in natural food stores. HerbalGram. 55: 60.

Discusses trends in sales of herbal products. In 2001, total sales of herbal dietary supplements were down 21 percent in food stores, drug stores, and mass market retailers. Black cohosh sales increased by 106 percent in the same year; ranking tenth on the list of 20 top-selling herbs, with sales of 901,512 units at \$9,639,506.

Keywords: Market, retail sales.

**Botany.com.** 2004. *Cimicifuga*. <http://www.botany.com/Cimicifuga.html>. [Date accessed: September 13].

Provides information on *Cimicifuga* botany, nomenclature, and propagation. The genus name *Cimicifuga* comes from the Latin words ‘cimex’ for bug and ‘fugare’ to flee. Bugbanes can be found growing in Europe, North America, China, Japan, and Mongolia. Plants prefer moist, fertile soil in full to partial shade. Supportive staking may be necessary. Propagation is done by seed and root division. Species and varieties are listed.

Keywords: Botanical description, nomenclature, propagation.

**Brown, D.** 2002. Women taking another look at ways to treat menopause: problems with hormone therapy may boost other remedies. The Washington Post. August 29, 2002: A3.

Discusses the potential increase in the use of black cohosh to treat menopausal symptoms in response to growing concerns about the negative side effects of hormone replacement therapy.

Keywords: Medicinal uses.

**Decker, A.** 2003. Black cohosh – the real story. PRWEB Newswire press release. <http://www.prweb.com/releases/2003/7/prweb73024.htm>. [Date accessed: September 13, 2004].

Outlines history, research, and examples of the safety of black cohosh in response to a research article by Davis and others (2003) suggesting a link between black cohosh and the metastasization of breast cancer.

Keywords: Cancer, research reviews, safety.

**Fern, K.** 1997–2000. Plants for a future: the species database. [http://www.triblio.org/pfaf/cgi-bin/find\\_lat?LAT=&COM=black+cohosh&FAM=&RATING=1](http://www.triblio.org/pfaf/cgi-bin/find_lat?LAT=&COM=black+cohosh&FAM=&RATING=1). [Date accessed: September 13, 2004].

Provides details on black cohosh habitat, medicinal uses, cultivation, and propagation. Black cohosh is hardy to zone 4. Blooms last from July to October, with seeds ripening from August to October. Flowers have a slightly unpleasant odor. Plants can grow in a variety of soils, but prefer moist, semishaded sites. Medicinal actions reported include alterative,

antidote, anti-inflammatory, antirheumatic, antispasmodic, astringent, birthing aid, cardiotoxic, diaphoretic, diuretic, emmenagogue, expectorant, homeopathic, hypnotic, hypoglycemic, sedative, tonic, and vasodilative. Roots are harvested in fall after leaves die down. The most common commercial uses are for feminine complaints related to menstruation and menopause. Reports other medicinal indications, including rheumatism, tinnitus, high blood pressure, and inflammation. The dried plant can be used to repel insects. Plants are well suited for use in the garden. Propagation is done by seed or by division of the rhizomes. Seed is sown in a cold frame or in the garden as soon as it is ripe. Stored seeds do not germinate as well. Root division is done in spring or fall.

Keywords: Cultivation, flowers, habitat, hardiness range, harvest, insect deterrent, medicinal uses, propagation.

**Grieve, M.** 1931. A modern herbal. Hypertext version by Botanical.com. 1995-2002. <http://www.botanical.com/botanical/mgmh/c/cohbla83.html>. [Date accessed: September 13, 2004].

Presents a plant description and information on medicinal uses, preparations, and chemical constituents. Common names include black snake root, rattle root, squaw root, and bugbane. Details are provided on root characteristics and preparations.

Keywords: Botanical description, chemical constituents, common names, medicinal uses, preparations, rhizomes.

**HeartSpring.net.** 2003. Perimenopause symptoms – black cohosh. [http://www.heartspring.net/perimenopause\\_symptoms.html](http://www.heartspring.net/perimenopause_symptoms.html). [Date accessed: September 13, 2004].

Provides detailed information on menopause and black cohosh from the National Institutes of Health and the National Center of Complementary and Alternative Medicine.

Keywords: Medicinal uses, menopause.

**Jackson, D.; Shelton, K.** 1997–2001. Alternative nature online herbal. [http://altnature.com/gallery/Black\\_Cohosh.htm](http://altnature.com/gallery/Black_Cohosh.htm). [Date accessed: September 13, 2004]

Provides information on black cohosh habitat, chemical constituents, medicinal properties, and folklore. Also serves as a retail venue for

tinctures. Native Americans used the roots to treat snakebite, rheumatism, and female ailments.

Keywords: Habitat, medicinal uses, Native American uses, vendors.

**Kliger, B.** 2003. Black cohosh. *American Family Physician*. 68(1): 114-116.

Summarizes information on the use of black cohosh to treat menopausal symptoms. Includes information on chemical constituents, physiological actions, adverse reactions, as well as a review of clinical studies.

Keywords: Medicinal uses, research reviews.

**Missouri Botanical Garden.** 2002. *Actaea racemosa*. <http://www.mobot.org/gardeninghelp/plantfinder/Plant.asp?code=J790>. [Date accessed: September 13, 2004].

Presents information for cultivation and gardening. Black cohosh grows in hardiness zones 3 to 8. It is an herbaceous perennial in the Ranunculaceae family, growing four to six feet in height with a two to four feet spread. Plants prefer average, moist, rich, well-drained soil in partial to full shade. Flowers resemble those of bottlebrush (*Callistemon* spp.) and grow on long terminal racemes, with no petals but numerous white stamens. Leaves are deeply cut and compound. The name bugbane comes from the plant's unpleasant smell, which repels insects. No serious pest or disease problems are known, though occasionally rust and leaf spot may appear. If soils dry out, leaves will turn brown at the margins. Best suited for woodland gardens or naturalized areas.

Keywords: Cultivation, flowers, habitat, hardiness range, insect deterrent, light requirements, pests and disease, Ranunculaceae family, soil requirements.

**National Center for Complementary and Alternative Medicine.**

2003. Questions and answers about black cohosh and the symptoms of menopause. <http://ods.od.nih.gov/factsheets/blackcohosh.html>. [Date accessed: September 13, 2004].

Summarizes black cohosh medicinal uses in a question and answer format. Includes information about preparations, historical uses, reviews of significant clinical studies, physiological effects, regulatory status, and side effects.

Keywords: History, medicinal uses, physiological actions, preparations, research reviews, side effects.

**Perry, L.** 2001. *Cimicifuga*. PSS 123 garden flowers. Plant and Soil Science, University of Vermont. <http://pss.uvm.edu/pss123/percimic.html>. [Date accessed: September 13, 2004].

Summarizes black cohosh cultivation information. Black cohosh is a member of the buttercup (Ranunculaceae) family. Plants flower after three to four years of growth. Leaves are ternately compound, with a dark green to blackish color. Flowers are long white racemes, with a distinct number of pistils for each species in the genus. For cultivation, soil should be moist and acidic. There are few pest and disease problems associated with cultivated plants. Propagation is done by seed and by division of roots. Stratified seeds have erratic germination, and roots of mature plants can be difficult to divide. In the landscape, plants are best suited for woodlands, borders, and native plantings. Common species and cultivars are listed.

Keywords: Cultivation, flowers, habitat, landscape uses, pests and disease, propagation, Ranunculaceae family.

**Plyler, S.C.** 2001–2002. Black cohosh (*Cimifuga racemosa*). Indian spring herbal encyclopedia. <http://www.indianspringherbs.com/BlackCohosh.htm>. [Date accessed: September 13, 2004].

Provides general information, including nomenclature, history, medicinal uses, preparations, and dosage. The name cohosh comes from the Algonquian word for “rough,” which describes the physical characteristics of the roots. Other common names describe characteristics and properties of the plant, such as “snakeroot,” denoting its use as an antidote, and “rattleroot,” which describes the sound of the dried seeds in their pods. Medicinal properties attributed to black cohosh are antispasmodic, antitussive, sedative, emmenagogue, astringent, diuretic, and expectorant. Roots are collected in autumn and made into tinctures with alcohol. The chemical constituents are not soluble in water.

Keywords: Chemical constituents, common names, dosage, harvest, history, medicinal uses, nomenclature, preparations.

**Sievers, A.F.** 1930. Cohosh bugbane. The herb hunters guide. Misc. Publ. No. 77. Washington, DC: U.S. Department of Agriculture. Washington, DC. Hypertext version 8 Apr. 1998. <http://www.hort.purdue.edu/newcrop/herbhunters/cohoshbugbane.html>. [Date accessed: September 13, 2004].

Offers information on black cohosh common names, habitat, botanical characteristics, and harvest. Common names include cohosh bugbane, black snakeroot, bugwort, rattlesnakeroot, rattleroot, rattleweed, rattletop, richweed, and squawroot. Plants prefer shaded woodlands, but occasionally will grow in fencerows, pasturelands, and open fields. The plant's range is centered around the Ohio Valley, extending north to Maine and Wisconsin and south to Georgia and Missouri. Plants can grow to 8 feet in height. Leaves are divided into three toothed, multiply-divided leaflets. Flower spikes are six inches to two feet in length, with small white feathery blooms. Buds, flowers, and seeds appear along the spike at the same time. Seedpods ripen in the fall and rattle in the wind. Flowers have an offensive smell. Roots consist of a horizontal knotted rhizome with long fleshy rootlets. Roots are collected in the fall after seeds are ripe.

Keywords: Botanical description, common names, flowers, habitat, harvest, odor, range, rhizomes.

**Stelling, K.** 1994. Native botanical profile: *Cimicifuga racemosa*. Canadian Journal of Herbalism. April: 21-25.

Provides a profile of black cohosh. Includes botanical and common names, name origins, botany, habitat and harvest, pharmacognosy, constituents, actions, pharmacology, therapeutics (cardiovascular, genito-sexual, oncology, musculo-skeletal, respiratory, gastrointestinal, and neurological), pharmacy, toxicity, folklore, and references.

Keywords: Chemical constituents, common names, habitat, harvest, medicinal uses, physiological actions, research reviews.

**Stolberg, S.G.** 2001. The estrogen alternative – black cohosh. <http://www.mercola.com/2001/may/19/estrogen.htm>. [Date accessed: September 13, 2004].

Discusses the history of herbal medicine, the growing popularity of herbal remedies, and modern clinical research. Black cohosh is a popular remedy for the symptoms of menopause, with a substantial market in Germany and growing demand in the United States.

Keywords: History, market demand, medicinal uses, research reviews.

**Strauch, B.** 1995. An herb to know – black cohosh. The Herb Companion. October/November: 24-25.



Presents a general overview of black cohosh. Includes botanical description, nomenclature, medicinal uses, landscape uses, and cultivation.

Keywords: Botanical description, cultivation, landscape uses, medicinal uses, nomenclature.

**SusanLoveMD.org.** 2003. Black cohosh hits the headlines. <http://www.susanlovemd.org/community/flashes/hotflash030725.htm>. [Date accessed: September 13, 2004].

Discusses research by Davis and others (2003) that suggests black cohosh may cause breast cancer to metastasize. The author points out that research done on mice that are bred to develop breast cancer may not apply to women.

Keywords: Research reviews, toxicity.

## Other Information Sources

**Anon.** 2003. *Cimicifuga racemosa* monograph. *Alternative Medicine Review*. 8(2): 186-189.

Summarizes clinical studies on the medicinal applications of black cohosh. Includes nomenclature, constituents, and physiological actions. Most commonly used to treat symptoms of menopause, black cohosh is also beneficial for reducing menstrual migraines and tinnitus. The herb has been shown by various studies to be safe and effective when hormone replacement therapy is contraindicated due to the risk of developing breast cancer. Occasional cases of transient, mild gastrointestinal upset have been reported. No serious side effects are known.

Keywords: Chemical constituents, hormone replacement therapy, medicinal uses, migraines, nomenclature, research reviews, side effects.

**American Botanical Council.** 2002. Black cohosh monograph. *The ABC clinical guide to herbs*. [http://www.herbalgram.org/default.asp?c=Black\\_Cohosh\\_Monograph](http://www.herbalgram.org/default.asp?c=Black_Cohosh_Monograph). [Date accessed: September 13, 2004].

Presents the latest information on black cohosh, summarizing results from clinical studies. This well-documented and fully referenced monograph includes sections on medicinal uses, dosage and administration, pharmacological actions, chemistry, mechanisms of action, contraindications, drug interactions, regulatory status, and commercial products.

Keywords: Chemical constituents, clinical studies, dosage, medicinal uses, physiological actions, products, regulatory status, research reviews.

**Association of Natural Medicine Pharmacists. [n.d.].** Black cohosh monograph. <http://www.anmp.org/monographs/>. [Date accessed: September 13, 2004].

Summarizes current research on black cohosh. Includes sections on nomenclature, botanical data, history and traditional uses, active constituents, pharmacological activities, clinical applications, clinical data, dosage, safety, and side effects. Includes medicinal references.

Keywords: Botanical description, chemical constituents, history, nomenclature, physiological actions, research reviews, side effects.

**Beuscher, N.** 1996. *Cimicifuga racemosa* L.: black cohosh. Quarterly Review of Natural Medicine. Spring: 19-28.

Summarizes current research on black cohosh. Includes sections on history, botany and taxonomy, plant description, commercial products, chemical constituents and their identification, pharmacology, side effects, toxicity, applications and dosage, clinical trials, and references. Includes a table of information on commercial black cohosh products with product name, delivery form, effective ingredients, indications, and manufacturer (though some information has changed since the article was published).

Keywords: Botanical description, chemical constituents, history, physiological actions, products, research reviews, side effects, toxicity.

**Blumenthal, M., ed.** 1998. The complete German Commission E monographs. Austin, TX: American Botanical Council. 685 p.

Approves the use of black cohosh to treat climacteric menopause symptoms, dysmenorrhea, and premenstrual symptoms. Although there is a possible side effect of gastric discomfort, there are no known contraindications or drug interactions. Dosage is suggested at 40 mg of crude drug. Because of the lack of long-term research, it is suggested that use be stopped after 6 months.

Keywords: Contraindications, dosage, drug interactions, German Commission E, medicinal uses, menopause, side effects.

**Britton, N.L.; Brown, A.** 1913. An illustrated flora of the Northern United States, Canada, and the British Possessions. New York: Charles Scribner's Sons. Vol. 2. In: U.S. Department of Agriculture, Natural Resources Conservation Service. 2001. The PLANTS database. Version 3.1. Baton Rouge, LA: National Plant Data Center. Available at <http://plants.usda.gov>. [Date accessed: September 13, 2004].

Provides a botanical illustration of black cohosh.

Keywords: Botanical description.

**Cook, W.** 1869. The physiomedical dispensatory. <http://medherb.com/cook/home.htm>. [Date accessed: September 13, 2004]. [Scanned version by Medical Herbalism 2001]

Offers historical information on medicinal uses, properties, and preparations. Provides a description of the genus and species traits, and properties of the root as used in commerce. Black cohosh is said to have sedative powers on the nervous and circulatory systems, serous tissues, and the uterus. Instructions for making various preparations are included.

Keywords: Botanical description, eclectic physicians, history, medicinal uses, preparations.

**Council of the Pharmaceutical Society of Great Britain.** 1911. The British pharmaceutical codex. 18<sup>th</sup> ed., 3<sup>rd</sup> rev. <http://www.ibiblio.org/herbmed/eclectic/bpc1911/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by H. Kress 2001–2002].

Describes black cohosh roots, constituents, and various preparations and dosages used historically.

Keywords: Chemical constituents, dosage, history, medicinal uses, preparations.

**Ellingwood, F.** 1919. The American Materia Medica, therapeutics and pharmacognosy. <http://www.ibiblio.org/herbmed/eclectic/ellingwood/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by M. Moore 2001–2002].

Offers a historical description of black cohosh medicinal uses. Preparations, physiological actions, and constituents are presented. Treatments are included for muscular aches, hysteria, acute fevers, angina pectoris, cough, pleurisy, chorea, stomach-ache, amenorrhea, dysmenorrhea, postpartum

hemorrhage, epilepsy, smallpox, and gonorrhoea. Medicinal actions are described.

Keywords: Chemical constituents, eclectic physicians, history, medicinal uses, physiological actions, preparations.

**Felter, H.W.** 1922. The Eclectic Materia Medica, pharmacology and therapeutics. <http://www.ibiblio.org/herbmed/eclectic/felter/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by M. Moore 2001–2002].

Provides historical information on the medicinal uses of black cohosh as described by the eclectic physicians. Indications for use included muscle soreness, aching, rheumatism, lumbago, stomach-ache, pain in the ovaries or uterus, afterbirth pains, irregular menstruation, and chorea. Excessive doses have caused headache, nausea and vomiting, vertigo, vision impairments, and reduced circulation. The therapeutic effects of the drug are described in detail.

Keywords: Chemical constituents, eclectic physicians, history, medicinal uses, side effects.

**Felter, H.W.; Lloyd, J.U.** 1898. King's American dispensatory. 18<sup>th</sup> ed., 3<sup>rd</sup> rev. <http://www.ibiblio.org/herbmed/eclectic/kings/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by H. Kress 2000–2001].

Presents a thorough historical account of black cohosh, with a technical botanical description, chemical constituents, medicinal uses and actions, and preparations. Common names and their sources are discussed. Native Americans used black cohosh medicinally long before European settlement. The eclectic physician John King introduced the plant to commercial use in the 1830s. The history of research into chemical constituents is provided. Small doses of black cohosh have been found to improve the appetite and digestion, although large doses increase secretions from the kidneys and skin and decrease circulation. Excessive doses can cause nausea, vomiting, vertigo, and impaired vision, but are not fatal. The most prominent medicinal treatments include those for rheumatism, neuralgia, muscular pains, conjunctivitis, dyspepsia, dysmenorrhoea, amenorrhoea, afterpains, chorea, asthma, spasmodic afflictions, headache, and fevers.

Keywords: Botanical description, chemical constituents, eclectic physicians, history, medicinal uses, physiological actions, preparations.

**Foster, S.** 1999. Black cohosh: *Cimicifuga racemosa*. A literature review. HerbalGram. 45: 35-50.

Includes thorough information on all aspects of black cohosh—etymology, botanical description, botanical history, new taxonomic twists, North American species of *Cimicifuga*, ethnobotany, medicinal history, development in eclectic medicine, chemical investigations, European experience (1743–1980), studies of the 1980s and 1990s, safety and toxicity, and cultivation. Includes extensive references, tables, and pictures.

Keywords: Botanical description, chemical constituents, cultivation, ecology, history, Native American uses, research reviews, toxicity.

**Foster, S.** 2000. Black cohosh (*Cimicifuga racemosa*). Steven Foster Group Herb Monographs. <http://www.stevenfoster.com/education/monograph/bkcohosh.html>. [Date accessed: September 13, 2004].

Presents information on historical and modern uses of black cohosh, including references and a discussion of clinical trials. Black cohosh is a member of the buttercup (Ranunculaceae) family, and is found in deciduous forests from Ontario to Georgia, and west to Wisconsin and Arkansas. Leaves are divided into threes, with another three-lobed terminal leaflet. In May, plants send up a showy spike of white flowers three to eight feet in height. Individual flowers do not have petals but numerous stamens. The name *Cimicifuga* comes from “cimex,” the Latin word for bug—specifically the bed bug *Cimex lectularius*—and the Latin “fugare,” meaning to drive away. The American species *Cimicifuga racemosa* does not possess the strong odor of the European species. Native Americans used black cohosh to treat a variety of female ailments and rheumatism. In the nineteenth century, early American physicians used black cohosh as an anti-inflammatory for rheumatism and arthritis, to relieve pain during childbirth, and to regulate abnormal menstruation. Medicinal properties of the roots are attributed to a combination of constituents. Several clinical studies on the effectiveness and safety of black cohosh are summarized. Black cohosh is listed in the German Commission E Monograph for use in treating premenstrual ailments, dysmenorrhea, and climacteric menopausal symptoms. As the negative side effects of hormone replacement therapy become more widely known, the use of black cohosh is expected to increase.

Keywords: Botanical description, chemical constituents, flowers, history, medicinal uses, nomenclature, odor, Ranunculaceae family, research reviews.

**Foster, S.; Duke, J.A.** 2000. A field guide to medicinal plants and herbs of Eastern and Central North America. 2d ed. National Audubon Society, National Wildlife Federation, and the Roger Tory Peterson Institute. New York: Houghton Mifflin Co. 411 p.

Summarizes medicinal uses of black cohosh. Black cohosh is a perennial which grows 3 to 8 feet in height, with sharply toothed, thrice-divided leaves. Long spiked flowers appear from May through September. Rhizomes were used by Native Americans for menstrual problems and childbirth. In the 19th century, black cohosh was also used as an anti-inflammatory and treatment for bronchitis, chorea, fever, nervousness, and snakebite. Medicinal actions are hypoglycemic, sedative, and anti-inflammatory. Black cohosh is a popular herb for treating menopausal symptoms such as hot flashes, with several clinical studies supporting its efficacy.

Keywords: Botanical description, medicinal uses, Native American uses, range.

**Harding, A.R.** 1936. Ginseng and other medicinal plants. <http://www.ibiblio.org/herbmed/eclectic/harding/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by M. Moore 2002].

Presents common names, habitat and range, plant description, root description, and harvest. The tall flower spikes make black cohosh a conspicuous plant. This perennial herb belongs to the the Ranunculaceae family, which also includes goldenseal. Plants reach up to eight feet in height. Leaves have three leaflets again divided into threes. Each leaflet is two inches long, toothed and sharply pointed at the apex, and is smooth, thin, and dark green. The graceful raceme of flowers grows up to two feet in length, and buds, blooms, and seeds consecutively along the same spike. Flowers are apetalous, with numerous showy white stamens. Seed pods are dry, ribbed, thick, and leathery. Seeds are in two rows, and rattle in the pods when disturbed by wind. Roots are horizontal irregular knotted rhizomes. The top of the rhizome is covered with hard stumps and scars from previous stems, and long rootlets emerge from the bottom. Roots are dark reddish brown externally, and white with rays of a woody texture internally. Dried roots are dark inside and outside, but the cross of woody rays is a lighter color and still visible. Rhizomes should be collected after the seeds have ripened in September.

Keywords: Botanical description, common names, flowers, habitat, harvest, medicinal uses, Ranunculaceae family, range, rhizomes, seeds.

**Horticopia, Inc.** 2001. Horticopia® on-line plant information. <http://www.horticopia.com/hortpix/html/pc1487.htm>. [Date accessed: September 13, 2004].

Provides useful information for cultivating black cohosh. Plants grow in hardiness zones 4A to 8A, in partial shade, and moist soil.

Keywords: Cultivation, habitat, hardiness range.

**Lloyd, J.U.; Lloyd, C.G.** 1931. *Cimicifuga racemosa*. Bulletin of the Lloyd Library of Botany, Pharmacy and Materia Medica. 9(30 pt. 2): 224-288.

Provides a thorough historical account of black cohosh. Includes botanical description, nomenclature, history, distribution, similar species descriptions, medicinal uses, pharmacological actions, chemical constituents, microscopic structure, preparations, and dosage.

Keywords: Botanical description, chemical constituents, distribution, eclectic physicians, history, medicinal uses, nomenclature, preparations.

**Miller, R.A.** 1988. Native plants of commercial importance. Grants Pass, OR: OAK, Inc. 343 p.

Includes information on black cohosh ecology and growth range, botany, medicinal actions, use by Native Americans and eclectic physicians, chemistry, marketing, prices for dried roots, and demand.

Keywords: Chemical constituents, eclectic physicians, ecology, history, market, medicinal uses, Native American uses, prices, range.

**Moerman, D.** 1999. Native American ethnobotany: A database of foods, drugs, dyes, and fibers of native North American peoples, derived from plants. The University of Michigan-Dearborn. <http://herb.umd.umich.edu/>. [Date accessed: September 13, 2004].

Provides ethnobotanical information on medicinal plants. Native Americans used black cohosh as a tonic, cold remedy, antirheumatic, blood purifier, and treatment for irregular menstruation and kidney problems.

Keywords: History, medicinal uses, Native American uses.

**NatureServe Explorer.** 2002. An online encyclopedia of life [Web application]. Version 1.6. Arlington, VA: NatureServe. <http://www.natureserve.org/explorer>. [Date accessed: September 13, 2004].

Summarizes the conservation status of black cohosh. Includes heritage status, range, habitat, distribution, global trends, threats, economics, and references. Black cohosh has a secure global heritage status rank, though increasing commercial demand and a lack of cultivated sources are putting pressure on wild populations. Permit sales have been increasing for the National Forests in North Carolina.

Keywords: Conservation, distribution, habitat, market demand, permits, prices, range.

**Newall, C.A.; Anderson, L.A.; Phillipson, J.D., eds.** 1996. Cohosh, black. In: *Herbal medicines: a guide for health-care professionals*. London: Pharmaceutical Press: 80-81.

Provides a guide to the use of black cohosh, including information on chemical constituents, the U.S. Food and Drug Administration (FDA) listing, medicinal uses, dosages for various preparations, pharmacological actions proven by clinical research on both animals and humans, side effects and toxicity, contraindications, and warnings. Chemical constituents include the alkaloids N-methylcytisine and other unidentified compounds, unspecified tannins, a mixture of terpenoids including 12-acetylactein and cimigoside, acetic acid, butyric acid, formic acid, isoferulic acid, oleic acid, palmitic acid, salicylic acid, racemosin, formononetin, phytosterols, cimicifugin, the resinous mixture acteina, and volatile oil. Herbal uses include treatments for myalgia, sciatica, whooping cough, chorea, tinnitus, dysmenorrhea, uterine colic, muscular rheumatism, and rheumatoid arthritis. Doses for various preparations are given. Several clinical studies are summarized, indicating a hypotensive effect in rabbits and cats, competitive estrogen receptor activity, hypocholesterolaemic activity, and antibacterial activity toward both gram-positive and gram-negative organisms. High doses may be toxic, resulting in nausea, vomiting, dizziness, visual impairments, nervousness, reduced pulse, and increased perspiration. Black cohosh should not be used during pregnancy.

Keywords: Chemical constituents, contraindications, dosage, medicinal uses, physiological actions, preparations, research reviews, side effects, toxicity.



**Pengelly, A.** [n.d.]. Black cohosh (*Cimicifuga racemosa* Nutt). <http://www.ibiblio.org/herbmed/neat-stuff/cohosh.html>. [Date accessed: September 13, 2004].

Provides details on various medicinal uses of black cohosh. Includes chemical constituents; medicinal use by Native Americans, early European Americans, eclectic physicians, and physiomedical physicians; and medicinal actions and therapeutics on the nervous system, musculoskeletal system, female reproductive system, and respiratory tract.

Keywords: Chemical constituents, eclectic physicians, medicinal uses, Native American uses, physiological actions, research reviews.

**Petersen, F.** 1905. *Materia Medica and clinical therapeutics*. <http://www.ibiblio.org/herbmed/eclectic/petersen/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by M. Moore 2002].

Provides a historical summary of usage. Black cohosh has been used to relieve muscle contractions, regulate menstruation, and as a treatment for rheumatism, chorea, afterpains, and uterine diseases.

Keywords: Eclectic physicians, history, medicinal uses.

**PIERS Exports (U.S. Ports).** 2003. *Journal of Commerce*. <http://library.dialog.com/bluesheets/html/bl0571.html>. [Date accessed: September 13, 2004].

Offers complete information on cargo exported from seaports in the United States.

Keywords: Export.

**Potter, S.O.L.** 1902. *A compend of Materia Medica, therapeutics, and prescription writing*. <http://www.ibiblio.org/herbmed/eclectic/potter-comp/Cimicifuga.html>. [Date accessed: September 13, 2004]. [Scanned version by H. Kress 2000–2002].

Summarizes historical medicinal use of black cohosh. Attributed actions are antispasmodic, aphrodisiac, diaphoretic, diuretic, and expectorant. The herb has been used to treat cardiac disease, chorea, bronchitis, rheumatism, neuralgia, uterine disorders, impotence, and childbirth afterpains.

Keywords: Eclectic physicians, history, medicinal uses, physiological actions.

**Tetherow, H.** 2001. Black cohosh [Website]. <http://altmed.creighton.edu/blackcohosh>. [Date accessed: September 13, 2004].

Provides information on a variety of medicinal matters—chemistry, pharmacology, usage, dosage, side effects, and interactions. Various studies on the clinical applications and effectiveness of black cohosh are summarized, and references provided.

Keywords: Chemical constituents, dosage, medicinal uses, physiological actions, research reviews, side effects.

**United Plant Savers.** [n.d.]. “At-Risk” plants. <http://www.plantsavers.org/>. [Date accessed: September 13, 2004].

Provides information on the conservation status of several plants. Black cohosh is on the “At-Risk” plant list. Plants on this list are considered to be significantly declining in number due to overharvest, loss of habitat, or innate sensitivity and rareness.

Keywords: Conservation, United Plant Savers.

**U.S. Department of Agriculture Forest Service.** 1993. Income opportunities in special forest products: self-help suggestions for rural enterprises. Agric. Inf. Bull. 666. Washington, DC. 206 p.

Estimates the domestic market for black cohosh at under 50 tons, with some export to Germany.

Keywords: Export, market.

**U.S. Department of Agriculture, Natural Resources Conservation Service.** 2001. The PLANTS database. Version 3.1. Baton Rouge, LA: National Plant Data Center. <http://plants.usda.gov>. [Date accessed: September 13, 2004].

Provides information on range and distribution, conservation status, and scientific classification, with photographs. The native range within the United States includes Alabama, Arkansas, Connecticut, Delaware, Georgia, Illinois, Indiana, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, Mississippi, Missouri, New Jersey, New York, North Carolina, Ohio, Pennsylvania, South Carolina, Tennessee, Virginia, and West Virginia. Black cohosh is listed as endangered in Illinois and Massachusetts.

Keywords: Classification, conservation, distribution, range.

**Upton, R., ed.** 2002. Black cohosh rhizome: standards of analysis, quality control, and therapeutics. Santa Cruz, CA: American Herbal Pharmacopoeia. 36 p.

Provides a detailed, thorough overview of black cohosh. Includes nomenclature, history, botany, macroscopic and microscopic identification, harvest, cultivation, adulterants, preparations, chemical constituents, chemical analysis methods, medicinal uses, physiological actions, clinical research reviews, dosage, side effects, precautions, toxicity, and regulatory status.

Keywords: Chemical constituents, harvest, identification, medicinal uses, physiological actions, research reviews, side effects, toxicity.

## **Vendors**

Note: The following list of vendors is included to provide access to current information about availability and prices. The authors do not intend to recommend these vendors over others not listed, or to recommend the products they feature for medical purposes.

**Cefakliman.** [n.d.]. Black cohosh product. [http://www.zink-info.de/e/kliman\\_mono1\\_e.html](http://www.zink-info.de/e/kliman_mono1_e.html). [Date accessed: September 13, 2004].

Vendor of black cohosh for medicinal uses.

Keywords: Medicinal uses, vendors.

**EstroGentle.** [n.d.]. Black cohosh product. <http://www.thehormoneshop.com/estrogentle.htm>. [Date accessed: September 13, 2004].

Vendor of black cohosh for medicinal uses.

Keywords: Medicinal uses, vendors.

**Green Canyon Inc.** [n.d.]. Black cohosh product. <http://www.greencanyon.com/products/c100036.htm>. [Date accessed: September 13, 2004].

Vendor of black cohosh for medicinal uses.

Keywords: Medicinal uses, vendors.

**Nature's Way Herbs.** [n.d.]. Black cohosh product. [http://www.naturesway.com/products\\_catalog/](http://www.naturesway.com/products_catalog/). [Date accessed: January 10, 2005].

Vendor of black cohosh for medicinal uses.

Keywords: Medicinal uses, vendors.

**Remifemin®.** [n.d.]. Black cohosh product. <http://www.remifemin.com/>. [Date accessed: September 13, 2004].

Vendor of black cohosh for medicinal uses.

Keywords: Medicinal uses, vendors.

**RippleCreek.com.** [n.d.]. Black cohosh product. <http://www.ripplecreek.com/item-rc10.html>. [Date accessed: September 13, 2004].

Vendor of black cohosh for medicinal uses.

Keywords: Medicinal uses, vendors.

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**Predny, Mary L.; De Angelis, Patricia; Chamberlain, James L.** 2006. Black cohosh (*Actaea racemosa*): an annotated bibliography. Gen. Tech. Rep. SRS-97. Asheville, NC: U.S. Department of Agriculture Forest Service, Southern Research Station. 99 p.

Black cohosh (*Actaea racemosa*, Syn.: *Cimicifuga racemosa*), a member of the buttercup family (Ranunculaceae), is an erect perennial found in rich cove forests of Eastern North America from Georgia to Ontario. Native Americans used black cohosh for a variety of ailments including rheumatism, malaria, sore throats, and complications associated with childbirth. Europeans have used this important medicinal plant to treat menopausal symptoms for over 40 years. Recent clinical evidence supports the efficacy and safety of black cohosh for these symptoms. Recent decisions by the U.S. Food and Drug Administration on hormone replacement therapy have increased the demand for black cohosh. In a 1-year period ending in 1998, retail sales increased more than 500 percent. In 2001, when retail sales in other segments of the herbal products industry were down, black cohosh sales increased about 2 percent to an estimated value of \$6.2 million. Nearly 100 percent of black cohosh raw materials are wild harvested. Though it has received an “apparently secure” ecological ranking on the global and national scales, conservation groups list the species as “at risk” in the United States and endangered in Illinois and Massachusetts. Research is underway to determine sustainable harvest levels and to establish suitable cultivation methods.

**Keywords:** Conservation, medicinal plants, menopause, nontimber forest products, phytoestrogens, poaching.



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