

## Black Cohosh and Breast Cancer: A Review of the Research

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Human observational studies (epidemiological studies) and experimental evidence suggest that soy isoflavones, which act as phytoestrogens (plant-based estrogens) in the body, help reduce the risk of breast cancer. In Asia, where soy isoflavone intake is high, the incidence of breast cancer in women is 75 percent lower than in North America.<sup>1,2</sup> Soy isoflavones have been shown to slow the cell division rate of breast cells, an effect associated with a lower risk of developing cancerous mutations.<sup>3</sup>

The herb black cohosh also contains an isoflavone, formononetin, shown to act as a phytoestrogen in human studies.<sup>4</sup> In Europe, black cohosh has been used routinely and with great success for the past 40 years as a treatment for menopausal symptoms, PMS and other female reproductive disorders (e.g., dysmenorrhea), in place of conventional hormone replacement therapy and oral contraceptives.<sup>5</sup> Black cohosh has also been recommended or prescribed in the United States for more than 100 years, and was an official drug of the U.S. Pharmacopoeia from 1820 to 1926 (the era prior to the political movement that has allowed patented drugs, manufactured by pharmaceutical companies, to dominate the drug market, not to mention the influence pharmaceutical companies have been allowed to exert on the prescribing practices of medical practitioners).

Over the years, many studies have documented black cohosh's effectiveness and safety. Published reports from Germany, where black cohosh has been used as a primary mode of treatment for menopausal symptoms for the past 40 years, indicate that it has a high safety profile and is associated with few and infrequent side effects, including nausea, vomiting, headaches, dizziness, and breast pain (mastalgia). No drug interactions are reported in the medical literature for black cohosh, adding to the evidence that it is a safe intervention for the management of menopausal symptoms, as well as PMS, dysmenorrhea and other female reproductive complaints.<sup>5,6</sup> Throughout its documented use by millions of women over the past 40 years, there has been no indication that supplementation with black cohosh increases the risk of breast cancer or any other female reproductive cancer.<sup>7</sup> Moreover, black cohosh has a safety profile superior to that of hormone replacement therapy, is known to increase the risk of breast cancer by 2.3 percent per year, and shown to increase the risk of other conditions (heart disease and stroke), according to recently published results of the U.S. Women's Health Initiative Study.<sup>8,9</sup>

Intrigued by the physiological effects of black cohosh on female reproductive tissues, a number of researchers have designed experimental studies to examine the influence of black cohosh on breast cancer risk. As stated previously, its long historical use in Europe and the United States as an effective and natural treatment for menopausal symptoms, PMS and other female conditions, has shown that it is not associated with an increased risk of breast cancer or any other cancer.<sup>10</sup> Additionally, all of the experimental studies performed to date involving the use of human breast

cells and human breast cancer cells, have shown that standardized extracts of black cohosh actually block the development of breast cancer and/or decrease the ability of breast cancer cells to divide and multiply.

The assumption made by many investigators was that black cohosh might encourage the growth of breast cancer cells because it has a weak estrogenic effect, which is likely to promote proliferation of these cells. However, *in vitro* studies, using human breast cells and human breast cancer cells, have demonstrated the opposite effect. In these studies, black cohosh has been shown to have an antiproliferative effect on a number of human breast cancer cell lines.

Reporting in the journal *Breast Cancer Research and Treatment* (2002), C. Bodinet and J. Freudenstein showed that black cohosh extract significantly inhibited human breast cancer cells (MCF-7 breast cancer cell line) from proliferating (dividing and spreading). They also showed that black cohosh extract enhanced the effectiveness of tamoxifen (a drug given to patients with a history of estrogen-receptor-positive breast cancer, to help prevent a recurrence or spread of their condition), in its ability to suppress the proliferation of breast cancer cells. These researchers concluded that black cohosh extract treatment may be a safe, natural remedy for menopausal symptoms in patients who have had breast cancer.

Experimental data suggest that black cohosh should be considered as a component of the treatment protocol when tamoxifen is administered to patients who have had breast cancer in the past, and may further help prevent the recurrence of breast cancer in patients who previously had breast cancer cells displaying estrogen-receptor-positive phenotype.<sup>11</sup> One study concluded that extracts of black cohosh can be taken safely by patients susceptible to breast cancer (and possibly should be used as a means of chemoprevention).<sup>12</sup>

Another study demonstrated that black cohosh extract blocks the growth of human breast cancer cells (T-47D human breast cancer cell line), and these researchers noted that *in vitro* studies suggest that certain herbs, such as black cohosh extract and soy (particularly the genistein isoflavone), may have potential utility in the prevention of breast cancer.<sup>13</sup>

As one in nine women in the U.S. develops this disease, some experts suggest it may be prudent for North American women to use a well-designed black cohosh-and-soy-isoflavone-containing supplement as a preventive measure throughout adult life (unless contraindications are present), as a means to discourage the development or spread of breast cancer. Theoretically, the antiproliferative effects of these natural herbal agents, acting on breast cells, would give the immune system a better chance to destroy any cancer cell before it has an opportunity to thrive; at least this is the current thinking.

A recent study funded by Susan G. Komen Foundation showed that a specific strain of mice, bred to be more susceptible to the development of spontaneous breast cancer (transgenic mouse model of breast cancer), was no more likely to develop breast cancer during one full year of supplementation with black cohosh, at a dosage comparable to that used in women. This study showed that even mice at high risk for breast cancer development, due to genetic reasons, are no more likely to develop breast cancer during black cohosh supplementation than mice not supplemented with the herb. This study did show, however, that there was an increase in lung metastasis in mice that developed breast cancer in the black cohosh group (27 percent), compared to the nonsupplemented mice (11 percent). Whether this is an incidental or significant finding needs to be confirmed by further studies.<sup>14</sup>

Studies in humans and experimental studies, using human breast cancer cells (not breast cells

from mice), suggest that in humans, black cohosh does not increase breast cancer risk and may, in fact, reduce risk of this disease, and may provide additional protection against the recurrence of breast cancer (while managing the hot flashes induced by tamoxifen) in patients with previous histories of breast cancer.<sup>11-13</sup> In fact, researchers<sup>11</sup> concluded that extracts of black cohosh can be taken safely by patients who are susceptible to breast cancer.<sup>12</sup> Additionally, a recent study by JE Burdett, et al., demonstrated that many natural ingredients present within black cohosh extract inhibit free radical damage (mutations) to the DNA of human breast cancer cells (S30 breast cancer cell line), following exposure to a potent free radical source (menadione). In the study, many substances contained within black cohosh (methyl caffeate, caffeic acid, ferulic acid, cimiracemate A, fukinolic acid) exhibited powerful antioxidant effects, significantly reducing free radical damage and mutations within the DNA of human breast cells. The researchers state that this data suggest black cohosh can protect against cellular DNA damage caused by reactive oxygen species (free radicals) by acting as antioxidants.<sup>15</sup>

The standardized grade of black cohosh extract that demonstrates clinical efficacy provides 2.5 percent triterpene content. Standard daily dosage for menopausal women and younger women experiencing PMS or dysmenorrhea (painful menstruation) is 40 mg to 80 mg, twice per day.<sup>7</sup> Active ingredients in black cohosh extract also exhibit antispasmodic effects on smooth muscle, which may account for its ability to relieve menstrual cramps. The triterpene glycosides found in this herb are also the only known precursors (building blocks) from which the body can increase synthesis of progesterone, a factor that likely contributes to the success of this herb in the management of PMS, in which *corpus luteum* failure, resulting in low secretions of progesterone, has been shown to be a contributing factor.<sup>16</sup>

A century of cumulative human evidence and experimental investigative studies strongly suggest that black cohosh does not promote the development of breast cancer. According to studies using human breast cells and human breast cancer cells, black cohosh extract may reduce the risk of breast cancer development, and may be a consideration to help reduce hot flashes in women on tamoxifen who have had a previous history of breast cancer.<sup>11-13</sup>

Studies examining the toxicity of black cohosh (using high dosages in rats for long periods of time) suggest it is nontoxic and can be used safely long terms. However, it should not be taken during pregnancy.<sup>17</sup>

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