

# ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

*Science-based Information for Clinicians*

American Health Consultants Home Page—<http://www.ahcpub.com>

CME for Physicians—<http://www.cmeweb.com>

## EDITORIAL ADVISORY BOARD

**Judith Balk, MD,  
FACOG**  
Assistant Research  
Professor  
University of Pittsburgh  
Pittsburgh, PA

**Kay Ball, RN, MSA,  
CNOR, FAAN**  
Perioperative  
Consultant/Educator  
K & D Medical  
Lewis Center, OH

**Mary Hardy, MD**  
Medical Director  
Cedars-Sinai Integrative  
Medicine Medical Group  
Los Angeles, CA

**Lynn Keegan, RN,  
PhD, HNC, FAAN**  
Director,  
Holistic Nursing  
Consultants  
Port Angeles, WA

**Felise B. Milan, MD**  
Associate Professor  
Clinical Medicine  
Albert Einstein  
College of Medicine  
Montefiore Medical  
Center  
Bronx, NY

**Dónal P. O'Mathúna,  
BS (Pharm), MA, PhD**  
Professor of Bioethics  
and Chemistry  
Mount Carmel College  
of Nursing  
Columbus, OH

## Black Cohosh: The “Hot” Treatment for Hot Flashes

*By Melinda Ring, MD*

THE TOP PRESCRIPTION HORMONE REPLACEMENT THERAPY (HRT), Prempro (medroxyprogesterone/conjugated estrogen), suffered a marked decline in popularity following the July 9, 2002, Women's Health Initiative (WHI) announcement that HRT increased the relative risk of breast cancer and cardiovascular disease. The early halt to the Prempro arm of the WHI study dropped the number of Prempro prescriptions filled weekly from 379,581 to 211,249 in just the first two months.<sup>1</sup>

This abrupt loss of confidence in HRT stimulated tremendous interest in the already fashionable field of “natural” alternatives for the management of climacteric symptoms. More than any other herbal remedy, black cohosh (*Cimicifuga racemosa*) shows promise in being an effective and acceptable treatment for vasomotor symptoms.

### Historical Perspective

Black cohosh is an indigenous herb of the buttercup (Ranunculaceae) family that produces 3- to 8-foot spikes of bright white flowers. Many of its synonyms refer to its insect-repellent characteristics. (See Table 1.)

Native Americans used the herbal roots to assist in labor/parturition and for musculoskeletal complaints and respiratory problems. It was adopted rapidly by early settlers for its sedative and muscle-relaxant effects. In the 1800s the Eclectic medical practitioners, major players in the medical world of their era, endorsed its use for many conditions, especially those related to women's health.

In the late 19th century, Lydia E. Pinkham's Vegetable Compound, which contained black cohosh, unicorn root, and fenugreek, was a best-seller for, as the label proclaimed, “all those painful complaints and weaknesses so common to our best female population.” Lydia's family made a fortune with her concoction, peaking in 1925 with annual revenues of \$3.8 million. Although black cohosh was the chief “active” ingredient of the vegetable compound, the 36-

## INSIDE

*Table:  
Synonyms for  
black cohosh  
page 18*

*Table:  
Studies  
on the  
estrogenicity  
of black  
cohosh  
page 19*

*Is black  
cohosh  
estrogenic?  
page 21*

*CAM center  
profile  
page 24*

*Alternative Therapies in  
Women's Health is now  
available on-line. For more  
information, go to  
[www.ahcpub.com/online.html](http://www.ahcpub.com/online.html)  
or call (800) 688-2421.*

proof alcohol content may have accounted for some of its renowned “therapeutic” properties, especially during Prohibition.

In the 1930s, herbal use abated in America; however, black cohosh was developed and investigated further in Europe, primarily Germany.

### Pharmacology/Mechanism of Action

The black cohosh root contains many substances believed to play an active therapeutic role. Of primary importance are the triterpene glycosides, including actein, 27-deoxyactein, and cimifugoside. The most often studied preparation, Remifemin, is standardized to the 27-deoxyactein content. Other compounds include resins (cimicifugin), caffeic and isoferulic acids, and fukinolic acid.

The mechanism of action remains a mystery. There has been considerable debate about whether black cohosh is a true phytoestrogen: a plant-derived substance exhibiting estrogenic activity. In vitro and in vivo studies to assess estrogenic properties have yielded contradictory results. Sample studies on the estrogenicity of black cohosh, with their rationales and pros and cons are detailed in Table 2.<sup>2,4</sup>

Table 1 Synonyms for black cohosh	
<i>Cimicifuga racemosa</i>	<i>Actaea racemosa</i>
Bugbane	Bugwort
Black snakeroot	Rattle snakeroot
Rattletop	Macrotys

### Clinical Trials

Studies on vasomotor symptoms uniformly have recorded improvements in response to placebo in 30-50% of women, calling into question any study that supplies treatment response rates without a control group for comparison. For a study on hot flashes to be truly meaningful, it should include a lead-in period prior to therapy, double-blind and crossover designs, a placebo control, and stringent measures of frequency and severity of hot flashes.<sup>3</sup>

Kronenberg and Fugh-Berman recently published a review limited to randomized controlled trials (RCTs) for menopausal symptoms.<sup>4</sup> Searches of the MEDLINE and AMED (allied and complementary medicine database) yielded four RCTs on black cohosh performed between 1985 and 2001.<sup>5-8</sup> (See Table 3.)

The first three trials were performed in Germany in the 1980s.<sup>5-7</sup> Each trial studied 60-80 women with climacteric symptoms, and used validated outcome measures. These scales assess both somatic and psychometric complaints, and include the Kupperman menopausal index, the Self-assessment Depression Scale (SDS), the Hamilton Anxiety Scale (HAM-A), and the Clinical Global Impression Scale (CGI). Significant improvement was noted in all three trials. All studies employed black cohosh extracts standardized to 27-deoxyactein, although there was some variation in formulation and dosing. (See Table 3.) The results of the most rigorous of these trials, the Stoll trial, have been questioned because standard estrogen doses did not show an effect on hot flashes over that of placebo (both showed similar reductions).

The most recent study, and the only RCT published in an English language journal, involved a different population.<sup>8</sup> Eighty-five women (69 completed the trial) who were breast cancer survivors with daily hot flashes took either placebo or black cohosh for two months. No significant difference in frequency or duration of hot flashes was noted between the two groups. The findings of this study are compromised by the brief duration of the study, and may not apply to menopausal women without breast cancer. The fact that 59 of the women were taking the anti-estrogen tamoxifen also clouds the results.

**Alternative Therapies in Women's Health**, ISSN 1522-3396, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.  
**VICE PRESIDENT/PUBLISHER:** Brenda L. Mooney.  
**EDITORIAL GROUP HEAD:** Lee Landenberger.  
**MANAGING EDITOR:** Paula L. Cousins.  
**EDITOR:** Leslie G. Coplin.  
**GST Registration Number:** R128870672.  
 Periodical rate postage pending at Atlanta, GA.  
**POSTMASTER:** Send address changes to *Alternative Therapies in Women's Health*, P.O. Box 740059, Atlanta, GA 30374.

Copyright © 2003 by American Health Consultants. All rights reserved. No part of this newsletter may be reproduced in any form or incorporated into any information-retrieval system without the written permission of the copyright owner.

**Back issues:** \$42. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.



### Statement of Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Education guidelines, physicians have reported the following relationships with companies related to the field of study covered by this CME program. Dr. Hardy is on the Scientific Advisory Board of Pharmavite Corp. Dr. Balk, Ms. Ball, Dr. Keegan, Dr. Milan, and Dr. O'Mathúna have no relationships with companies related to the field of study covered by this continuing education program.

### Subscriber Information

**Customer Service: 1-800-688-2421.**

**Customer Service E-Mail:** customerservice@ahcpub.com

**Editorial E-Mail:** paula.cousins@ahcpub.com

**World-Wide Web:** http://www.ahcpub.com

### Subscription Prices

#### United States

\$299 per year (Student/Resident rate: \$130).

#### Multiple Copies

1-9 additional copies: \$224 each; 10 or more copies: \$199 each

#### Outside the United States

\$329 per year plus GST (Student/Resident rate: \$145 plus GST).

### Accreditation

American Health Consultants (AHC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

American Health Consultants designates this continuing medical education activity for up to 20 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity. This CME activity was planned and produced in accordance with the ACCME Essentials.

American Health Consultants is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's commission on Accreditation. Provider approved by the California Board of Registered Nursing, Provider Number CEP 10864, for approximately 12 nursing contact hours.

For CME credit, add \$50.

### Questions & Comments

Please call Paula Cousins, Managing Editor, at (816) 960-3730 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

The effect of black cohosh on menopausal symptoms has been examined through clinical trials involving more than 2,000 women. The vast majority of these trials suffer from some design flaw that limits the utility of the findings, and from variations in the dosing recommendations and extraction techniques of Remifemin, the black cohosh extract used in nearly all clinical trials.

### Side Effects, Drug Interactions, and Contraindications

**Side effects.** A very low incidence of side effects has been noted in clinical trials, primarily frontal headaches and mild gastrointestinal complaints.

**Contraindications.** Given the inconsistent evidence about black cohosh and phytoestrogen activity, women with a history of estrogen-dependent breast tumors should be advised that the real risk is unclear at this time. The German Commission E and manufacturers of Remifemin do not feel a history of breast cancer is a

contraindication to black cohosh use. Black cohosh is contraindicated in pregnancy and lactation, except when used by medical professionals to assist labor.

**Drug interactions.** The combination of tamoxifen and black cohosh appears to act synergistically in pre-clinical studies to prevent proliferation of estrogen-dependent breast cancer cells. Concurrent use with HRT is not recommended due to possible potentiation of estrogen effects. No other drug interactions or interference with lab tests have been recorded.

### Dosage and Formulations

The most commonly studied formulation of black cohosh is Remifemin. The German herb company Schaper & Brümmer initially manufactured Remifemin in liquid form. Over time the extraction process changed, along with a shift to tablets. Recently, Glaxo-SmithKline has been producing the equivalent Remifemin Menopause in the United States.

**Table 2**  
**Studies on the estrogenicity of black cohosh<sup>2,4</sup>**

	Rationale	Pro	Con
Effect on luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels	Menopause leads to lower estrogen and higher LH and FSH levels	· 110 women treated with Remifemin for 8 weeks had significantly lower LH, but not FSH.	· 150 women, 6 months on Remifemin—no change in LH, FSH · Women with breast cancer—small, but insignificant changes in LH and FSH · 15 women with a hysterectomy—no change in LH or FSH
In vitro studies of estrogen receptor	Direct evidence of interaction with estrogen receptor binding		· Binding assays in endometrial and breast cancer cell lines—no activity.
In vitro effects on proliferation of breast cancer cells	Indirect evidence of interaction with estrogen receptor	· Slightly enhanced growth of ER+ breast cancer cells (cell line T47D)	· Inhibited the growth of ER+ breast cancer cells (cell lines T47D and 435)
Isolation of constituents from the three main classes of phytoestrogens (isoflavones, lignans, and coumestans)	Identification of known phytoestrogen in black cohosh implies estrogenic activity	· The isoflavone formononetin isolated from extract · The isoflavone biochanin isolated from <i>C. Racemosa</i> roots	· No formononetin in extract · No formononetin in Remifemin or extracts of black cohosh from 13 U.S. locations
Effect on vaginal cytology	Estrogen deficiency leads to microscopic changes in vaginal cells (experienced as vaginal dryness clinically)	· Placebo-controlled, double-blind trial on menopausal women showed an effect in vaginal epithelium after treatment with Remifemin	· Six months of Remifemin caused no change in vaginal cytology in peri- and post-menopausal women
Effect on endometrium	The endometrium thins after menopause due to estrogen deficiency	· Black cohosh treatment caused an increase in uterine weight in immature female mice	· No change in uterine weight noted in another study on immature mice

Table 3

## Trials on black cohosh

Study	Randomized	Double-Blind	Placebo-Control	Treatment-Control	Subjects	Remifemin Dose	Results
Warnecke, et al (1985)	X			X	Menopausal symptomatic women, 45-60 y	Liquid 40 drops bid	Kupperman Index, HAM-A, SDS, CGI all showed "highly significant reductions" with Remifemin, diazepam, and conjugated estrogens
Stoll (1987)	X	X	X	X	> 3 hot flashes daily and psychic complaints, 46-58 y	Tablets 40 mg bid	Kupperman Index and HAM-A showed significant improvement in the Remifemin group (P < 0.001) but not the estrogen or placebo groups
Lehmann-Willenbrock, et al (1988)	X			X	Climacteric symptoms, had a hysterectomy, but still had ≥ 1 ovary, ≥ 40 y	Tablets 40 mg bid	Kupperman Index improved in Remifemin and estrogen groups (P = 0.01)
Jacobson et al (2001)	X	X	X		Breast cancer survivors with daily hot flashes, > 18 y	Tablets 20 mg bid	Both placebo and Remifemin groups had decreased frequency and intensity of hot flashes, with no significant difference between the groups; no change in global rating of health scale. Only significant improvement was decrease in sweating with treatment (P = 0.04)

Each tablet contains 20 mg of dried rhizome (underground stem) and root extract. Patients are advised to take one tablet twice daily (a change from previous manufacturer recommendations to take two equivalent tablets twice daily). Inactive ingredients include cellulose powder, lactose monohydrate, potato starch, magnesium stearate, and peppermint oil. Each 20 mg tablet is standardized to contain 1 mg of 27-deoxyactein.<sup>9</sup>

Unlike prescription HRT, the beneficial effect of black cohosh is a gradual process. The first therapeutic effects generally are seen within two weeks of treatment initiation, with maximal symptom relief occurring in most women by 8-12 weeks.

Because no long-term studies have been conducted to date, it is recommended that consumption of black cohosh not exceed six consecutive months without physician guidance. If symptoms return after a month-long cessation of therapy, treatment may be resumed for another six months.

Lydia Pinkham's herbal compound is still available,

and has been reformulated with iron, calcium, vitamins E and C, black cohosh, motherwort, dandelion, licorice, Jamaican dogwood, pleurisy root, and gentian (Numark Laboratories, NJ). It no longer has a 36-proof alcohol content.

Other dosage approaches include: dried root/rhizome (0.5-1 g 3-4 times per day); liquid extracts (1.5-3 mL/d of 1:2 extract; 3.5-7 mL/d of 1:5 extract); or tinctures (6-12 mL/d of 1:10 tincture).

### Regulatory/Professional Status

In the 1980s, black cohosh was approved by Germany's Commission E for "neurovegetative complaints of premenstrual, dysmenorrheic, or climacteric origin." In the United States, it is available over the counter as a dietary supplement, although it does not have GRAS (generally regarded as safe) status.

In 2001, the American College of Obstetricians and Gynecologists (ACOG) released a bulletin indicating that black cohosh may be helpful in short-term (less than

six months) management of vasomotor symptoms, based on general consensus and expert opinion.<sup>10</sup>

### Current Research

Currently in progress, the National Center for Complementary and Alternative Medicine-funded Phase II study at the University of Illinois College of Medicine is a year-long randomized, double-blind study of 112 women comparing HRT, black cohosh, red clover, and placebo. The Phase I single-dose pharmacokinetic study of these two herbs was implemented to assist in determining dosage requirements. Columbia University also is conducting a 12-month trial to observe the effect of black cohosh on hot flashes, bone metabolism, and cognitive function. The results of these well-designed studies will help elucidate the role black cohosh should play in symptom management of the climacteric.

### Conclusion

Although only four RCTs involving black cohosh have been published to date, the three that involved the general perimenopausal population showed significant improvement in vasomotor symptoms compared to placebo. Respected organizations such as ACOG have given a preliminary “seal of approval” for limited duration of use. The utility and safety of black cohosh for women with more complex hormonal environments, such as breast-cancer survivors (who may be taking tamoxifen), are unclear.

### Recommendation

For now, black cohosh is an herb with minimal side effects, and at least some suggestion of benefit in the management of vasomotor symptoms in menopause. Recommend it to your patients who are looking for an alternative to HRT, reminding them to use reputable brands and follow the dosing guidelines. Unlike estrogen, black cohosh has no known effect on bone or cardiovascular health. Treatment of women with a history of breast cancer should be individualized. ❖

---

*Dr. Ring is Clinical Training Attending Physician and Coordinator, CAM Curriculum, Internal Medicine Residency Training Program, St. Joseph Hospital, Chicago, IL.*

### References

1. NDCHealth: A health care information services company.
2. Questions and answers about black cohosh and the symptoms of menopause. Office of Dietary Supplements Web site. Available at: [http://ods.od.nih.gov/factsheets/blackcohosh\\_pf.html](http://ods.od.nih.gov/factsheets/blackcohosh_pf.html). Accessed Feb. 12, 2003.

3. Fitzpatrick LA, Santen RJ. Hot flashes: The old and the new, what is really true? *Mayo Clin Proc* 2002;77:1155-1158.
4. Kronenberg F, Fugh-Berman A. Complementary and alternative medicine for menopausal symptoms: A review of randomized, controlled trials. *Ann Intern Med* 2002;137:805-813.
5. Warnecke G. Beeinflussung Klimakterischer Beschwerden durch ein Phytotherapeutikum: Erfolgreiche Therapie mit Cimicifuga-Monoextrakt. *Med Welt* 1985;36:871-874.
6. Stoll W. Phytopharmakon influences atrophic vaginal epithelium—double-blind study—Cimicifuga vs. estrogenic substances [in German]. *Therapeutikon* 1987;1:23-31.
7. Lehmann-Willenbrock E, Riedel HH. Clinical and endocrinologic studies of the treatment of ovarian insufficiency manifestations following hysterectomy with intact adnexa [in German]. *Zentralbl Gynakol* 1988;110:611-618.
8. Jacobson JS, et al. Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer. *J Clin Oncol* 2001;19:2739-2745.
9. GlaxoSmithKline. Remifemin. Available at: [www.remifemin.com/professional](http://www.remifemin.com/professional). Accessed Feb. 12, 2003.
10. ACOG: Use of Botanicals for management of menopausal symptoms. *ACOG Pract Bull* 2001;28:1-11.

## Is Black Cohosh Estrogenic?

**Source:** Bodinet C, Freudenstein J. Influence of *Cimicifuga racemosa* on the proliferation of estrogen receptor-positive human breast cancer cells. *Breast Cancer Res Treat* 2002;76:1-10.

**Abstract:** Hormone replacement therapy is contraindicated in women with breast cancers due to concerns regarding the potential for breast cell proliferation. To determine the influence of black cohosh (*Cimicifuga racemosa* [CR]) on estrogen-dependent mammary cancers, these researchers conducted an in vitro investigation of the effect of an isopropanolic CR extract on the proliferation of estrogen receptor-positive breast cancer cells. The experiments were performed using the human breast adenocarcinoma (MCF-7) cell test system. The influence of CR extract on the proliferation of the MCF-7 cells was determined by measuring the incorporation of radioactively labeled thymidine. Under estrogen-deprived conditions, the CR extract significantly inhibited MCF-7 cell proliferation. Additionally, application of the CR extract inhibited estrogen-induced proliferation of MCF-7 cells. Moreover, the proliferation-inhibiting effect of tamoxifen was enhanced by the CR extract. Such data that suggest a non-estrogenic or estrogen-antagonistic effect of CR on human breast cancer cells lead to

the conclusion that CR treatment may be a safe, natural remedy for menopausal symptoms in breast cancer.

**Source:** Kennelly EJ, et al. Analysis of thirteen populations of black cohosh for formononetin. *Phytomedicine* 2002;9:461-467.

**Abstract:** Black cohosh (*Actaea racemosa* L. syn. *Cimicifuga racemosa* L. Nutt.) is a promising natural alternative to hormone replacement therapy for treating menopausal symptoms, but the mechanism of action is not understood. The clinical actions of this plant have been attributed to the isoflavonone formononetin since 1985, when its presence was reported in a black cohosh extract. Others have since looked for formononetin, but have not detected it. These researchers looked for formononetin in extracts of black cohosh roots and rhizomes collected in 13 U.S. locations. The rhizome samples were extracted using 80% methanol, and the extracts were partially purified using solid-phase extraction to concentrate any isoflavonoids that might be present. The researchers tested for formononetin using thin-layer chromatography and high-performance liquid chromatography with a photodiode array detector and a mass spectrometer. Formononetin was not detected in any of the plant populations examined. Remifemin and CimiPure also were analyzed, and no formononetin or ononin (formononetin-7-glucoside) was found. Therefore, the clinically observed estrogen-like actions of black cohosh, such as reduction of hot flashes, likely are due to a compound, or combination of compounds, other than formononetin.

#### ■ COMMENTS BY MARY L. HARDY, MD

Clinicians interested in using black cohosh want to know one thing: Is this herb estrogenic or not? The presence or absence of estrogenic activity has implications for both safety and efficacy, especially for patients who either do not want or are advised not to take estrogen. The confusion over the status of black cohosh began during its development as a modern phytomedicine in Germany. Because of the observed clinical effects on menopausal women, estrogenic activity was assumed. Since then, black cohosh routinely has been referred to as a phytoestrogen (a plant-based product that acts like an estrogen) and has even been called a SERM (selective estrogen receptor mediator). Earlier literature reported the presence of formononetin, a weak phytoestrogenic constituent, in the root of black cohosh. This was perplexing to botanists and other herbal experts who did not expect to find constituents common to the Fabaceae or bean family (the plant family of both soy and red clover) in such an unrelated species. Black cohosh belongs to the buttercup or Ranunculaceae family. So, in order to clarify this question we have to examine the evidence for three things: Does black cohosh contain a known phytoestrogen? Do black cohosh extracts (BCE) bind to estrogen receptors? Do BCEs demonstrate evidence of growth promotion generally associated with estrogen—especial-

ly in breast cancer cells? The abstracts selected for review this month address these issues.

Kennelly and colleagues in New York have done a rigorous analysis of multiple samples of black cohosh collected from the wild in 13 U.S. locations. The chemical methods were extracting and the results are consistent. No formononetin was found in any of the wild samples or in two commercial extracts tested. This should put to rest the mistaken data reported in 1985. This work was performed by the botanical research unit headed by Fredi Kronenberg, PhD, and is independent of any commercial sponsorship. There is no known phytoestrogen in black cohosh.

Estrogen receptor binding of BCEs has not been reported, although several investigators have checked for such activity. This lack of binding has been demonstrated for both the alpha and beta estrogen receptors.

The theoretical concern still remains, however, that extracts could affect the growth of estrogen-dependent cells, such as breast cancer cells, despite the lack of demonstrated estrogen receptor binding or activation. The work presented by Bodinet and Freudenstein addresses this concern directly. A common breast cancer cell line (MCF-7) was exposed to BCE in the absence of estrogen, in the presence of estrogen, and in the presence of tamoxifen, a SERM used in the treatment of breast cancer. BCE given alone inhibited cell growth. When estrogen was added, BCE blunted the growth usually seen with estrogen stimulation. The normal inhibitory effect of tamoxifen on breast cancer cell growth was enhanced by the addition of BCE. Although this work was performed by the German manufacturer that produces the main commercially available extract of black cohosh, the observation that BCE impedes cell growth of breast cancer cells in vitro has been confirmed by other observers. For example, a study by Amato confirms the lack of stimulation of MCF-7 cell lines by BCE as well as the lack of effect on a gene expression assay system and in intact mice.<sup>1</sup> Similar lack of response was seen by Liu and colleagues using an in vitro system with a different breast cancer cell line (S30) and in an endometrial cell line.<sup>2</sup> Finally, two other research groups have shown similar results with MCF-7 cells as well as another breast cancer cell line (T-47D).<sup>3,4</sup> The in vitro data are robust and have been duplicated in multiple labs. BCEs do not promote growth in human breast cancer cell lines.

Human clinical trials, although limited, have not demonstrated estrogenic activity with one exception. Early uncontrolled clinical studies reported some effects on vaginal epithelium. Two recent clinical trials do not support the presence of an estrogen effect in patients. A study of breast cancer survivors, the majority of whom

were taking tamoxifen, was conducted by Jacobson et al.<sup>5</sup> The BCE was not statistically more effective than placebo in controlling hot flashes in this very difficult population. Notably, there was no change in FSH or LH levels. The largest clinical trial of BCE by uncomplicated menopause patients was conducted by Liske, from the German manufacturer.<sup>6</sup> However, the trial recently was published in a peer-reviewed journal and showed no estrogenic effects of their BCE, marketed as Remifemin. Vaginal cytology and a number of hormone levels were measured. A statistically significant decrease in hot flashes was shown. So, the limited clinical data follow the in vitro data and do not show an estrogenic effect for BCE.

In summary, a robust body of in vitro data supports the notion that BCE is not a classical phytoestrogen because it does not bind to estrogen receptors and does not promote growth in estrogen-sensitive assay systems. Clinically, although effect on menopausal symptoms has been reported, no estrogen effects can be demonstrated in human subjects either. So, although we don't know the mechanism of action for black cohosh, it appears that BCE does not act through classic estrogen pathways. Clinicians can use this information to guide patients to effective therapy in the wake of the termination of the hormone replacement arm of the Women's Health Initiative study. Because black cohosh does not appear to be estrogenic, it would be a reasonable option to consider in women who cannot or should not take conventional hormone replacement therapy. ❖

## References

1. Amato P, et al. Estrogenic activity of herbs commonly used as remedies for menopausal symptoms. *Menopause* 2002;9:145-150.
2. Liu J, et al. Evaluation of estrogenic activity of plant extracts for the potential treatment of menopausal symptoms. *J Agric Food Chem* 2001;49:2472-2479.
3. Dixon-Shanies D, Shaikh N. Growth inhibition of human breast cancer cells by herbs and phytoestrogens. *Oncol Rep* 1999;6:1383-1387.
4. Zierau O, et al. Antiestrogenic activities of *Cimicifuga racemosa* extracts. *J Steroid Biochem Mol Biol* 2002;80:125-130.
5. Jacobson JS, et al. Randomized trial of black cohosh for the treatment of hot flashes among women with a history of breast cancer. *J Clin Oncol* 2001;19:2739-2745.
6. Liske E, et al. Physiological investigation of a unique extract of black cohosh (*Cimicifugae racemosae* rhizoma): A 6-month clinical study demonstrates no systemic estrogen effect. *J Womens Health Gen Based Med* 2002;11:163-174.

## CE Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients; and
4. offer guidance to patients based on the latest science and clinical studies regarding alternative and complementary therapies.

## CE/CME Instructions

Physicians and nurses participate in this continuing medical education/continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

## CME Questions

9. **Black cohosh is among the most well-studied herbs in women's health.**
  - a. True
  - b. False
10. **Remifemin, the proprietary formula most often used in clinical trials, is standardized to:**
  - a. alcohol content.
  - b. isoflavone content.
  - c. 27-deoxyactein content.
  - d. buttercup content.
11. **Three of the four randomized controlled trials published on black cohosh to date showed:**
  - a. no significant improvement in menopausal symptoms.
  - b. a significant improvement in menopausal symptoms.
12. **Black cohosh extracts do not promote growth in human breast cancer cell lines.**
  - a. True
  - b. False

Answers: 9. a, 10. c, 11. b, 12. a.

## CAM Center Profile

*Editor's Note: Periodically, we will publish profiles of complementary and alternative medicine centers in the United States. Please contact us with feedback about this new feature or if you would like to see a particular facility profiled in future issues of the newsletter.*

### Center for Integrative Medicine

The Center for Integrative Medicine (CIM) was developed as a program of O'Connor Hospital, which is affiliated with the Daughters of Charity Health System, in San Jose, CA. After about two and one-half years, CIM became independent and no longer was subsidized by the hospital. The center has been freestanding since October 2000.

The center began not as the project of one individual, but of a group of practitioners in the hospital, says administrator Janet Keeley. Most of the practitioners at CIM are complementary or alternative therapists. Three physicians also are associated with the center. One is a homeopath. Another, the previous medical director, does consultations and integrated medicine. A third physician recently joined the center and is a gynecologist with a focus on menopause and perimenopause.

CIM no longer has a medical director but has a "peer-support relationship" between the practitioners, Keeley says. The practitioner group acts as the governing body.

As evident in its statement of philosophy of care, CIM places a high emphasis on the credentials and education of its practitioners: "At the Center for Integrative Medicine, our expert multidisciplinary team of health care professionals provides individual evaluations, plus a variety of therapies intended to facilitate your personal healing process. All practitioners meet high credentialing standards, and provide treatments, care, education, and resources, encouraging you to take responsibility for your own self-care and to make appropriate choices regarding your health."

Several of the practitioners are registered nurses; others hold PhD or master's degrees. Many have completed training certification programs in their specialties.

### Services and Classes

At CIM, patients can access services in a variety of ways. A physician can refer patients for a specific modal-

ity or the patients can call and self-refer. CIM offers the following services: acupuncture, aromatherapy, Ayurveda (a system of medicine using natural therapies practiced in India for thousands of years), energy healing, holistic nursing, homeopathy, hypnotherapy and guided imagery, LifeLong weight loss program (a year-long holistic program), massage therapy, meditation, naturopathy, nutritional counseling and classes, physician consultations in integrative medicine, plant spirit medicine, preparation for surgery using guided imagery and mindfulness, professional renewal for health care professionals, psychotherapy and spiritual counseling, sound and music therapy, yoga, tai chi, and qi gong.

CIM also offers different kinds of classes, many of which are taught by the therapists themselves. These classes either teach patients about the services or give them a more in-depth view. Recent classes offered at CIM include: holistic nutrition from Ayurveda, self-hypnosis, aromatherapy, body rolling, and T'ai chi chih.

### Funding

To fund the center, patients pay for the classes and therapy themselves. CIM avoids the difficulty of trying to bill for third-party reimbursement, Keeley says. "We do not participate in any insurance. We will provide superbills to patients, and they may seek reimbursement, but we do not participate in that program." Although some patients may struggle to pay the out-of-pocket costs, many are highly motivated for this approach to their medical care because they pay for it themselves, she says.

CIM is an affiliate of The Foundation for Mind-Being Research (FMBR) in Los Altos, CA. FMBR was established in 1980 to assist in the evolution of consciousness studies and to help bring this new field into wider recognition as a legitimate science.

CIM also encourages its patients to become free members of the PlaneTree Library in San Jose, so they can become more educated about their health needs. PlaneTree is a consumer health and medical library that is free and open to the public.

For more information about CIM, call (408) 286-4325 or visit its web site at [www.fmbr.org/CIM/CIM.htm](http://www.fmbr.org/CIM/CIM.htm). ❖

**In Future Issues:**

**Reiki for Relaxation and Pain Relief  
Acupuncture for Labor**