

Medicine for Menopause

Researchers study herbal remedies for hot flashes

By KATHLEEN FACKELMANN

Catherine L. Eagon, a physician at Allegheny General Hospital in Pittsburgh, recalls talking to a patient who had been treated for breast cancer. The woman confided that she was now taking an herbal remedy for hot flashes, one of the most disruptive symptoms of menopause. The remedy worked, she told Eagon, but was it safe?

Eagon couldn't answer that question. No one can. Although many women turn to herbal products for relief from symptoms of menopause, these natural medicines haven't been subjected to the same rigorous review that prescription drugs must undergo before being marketed to the public.

That lack of knowledge presents a particular concern for breast cancer survivors. Researchers know that the most commonly prescribed treatment for hot flashes, estrogen replacement therapy, should not be given to women who have suffered from breast cancer. Estrogen, the female sex hormone, may trigger a return of breast cancer, an event that is often fatal.

Eagon guessed that at least some of the traditional plant medicines for hot flashes contain naturally occurring compounds that mimic estrogen. If so, could they spark a recurrence of breast cancer? That question led her to begin a scientific collaboration with biochemist Patricia K. Eagon of the University of Pittsburgh, who has had a long-standing interest in estrogen. She's also Catherine Eagon's sister.

Catherine and Patricia Eagon and their colleagues have yet to find an answer to the cancer-related questions about herbal remedies, but their preliminary findings have yielded important information for women who are not at high risk of breast cancer.

In a systematic study of herbal compounds, the team found that some age-old remedies do show estrogenlike properties, suggesting that the products function like estrogen in dissipating hot flashes. Yet enthusiasts of herbal remedies say they don't provoke the nasty side effects

of estrogen replacement therapy, which include bloating, weight gain, and the resumption of a monthly menstrual cycle.

Catherine Eagon recommends herbal remedies for women who are unwilling to take prescription drugs and have no family history of breast cancer.

"Women are miserable when they are having hot flashes," she notes. "I think we should do what we can to modify their symptoms."

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Menopause, the time during which a woman's menstrual cycle stops, generally occurs in the late forties or early fifties. As the ovaries stop producing estrogen, a woman can experience a number of unwanted symptoms, including weight gain and headaches, as well as hot flashes. During a hot flash, a wave of heat sweeps through a woman's upper body, her heart beats more rapidly, and she perspires profusely. Some women suffer these spells on a regular basis for years.

The Eagons started their scientific odyssey with folk remedies long thought to relieve menopausal symptoms.

The team examined dang gui (*Angelica sinensis*), a plant used in Chinese medicine as a female tonic; hops (*Humulus lupulus*), a familiar ingredient in beer; vitex (*Vitex angus-castus*), a Mediterranean plant used to relieve menopausal symptoms; black cohosh (*Cimicifuga racemosa*), a plant that Native Americans

relied on as a cure for menopausal symptoms; blue cohosh (*Caulophyllum thalictroides*), a plant also used by Native Americans; and licorice root (*Glycyrrhiza uralensis*), the flavoring of the candy by the same name, now taken in the Netherlands as a female tonic.

To see whether extracts of these plants function like estrogen or perhaps block it, the researchers ground up cells known to contain lots of docking sites, or receptors, for estrogen. The team then mixed this material in test tubes with a radioactive estrogen. The researchers used a radiation detector to determine how successfully the plant extracts bound to the estrogen receptor.

Licorice, dang gui, and blue cohosh showed clear evidence of binding to the estrogen receptor. Licorice was "remarkably strong" at competing with the real estrogen, Patricia Eagon said. The Eagons presented their results on March 31 at an American Association for Cancer Research meeting in New Orleans.

Hops also showed estrogenlike binding, and so might mimic the hormone, a finding that fits with the folklore about hops workers, she added. Men who worked in the hops fields were said to suffer from a lackluster libido, whereas female field hands were said to be sexy. Vitex also competed for the estrogen receptor, but less robustly than the other compounds, Patricia Eagon noted. Black cohosh showed no activity in the test.

After hooking up with a receptor, estrogen tells the cell to divide—hence the concern about breast cancer. Although the plant compounds dock with the estrogen receptor, do they give cells the same message that estrogen does? The researchers tested the compounds on uterine cells. When estrogen binds with the receptor in such cells, it tells them to proliferate. So do some of the plant extracts, the Eagons learned.

For their test, the researchers relied on rats whose ovaries had been removed and who therefore did not produce much estrogen. In a female rat, as in a woman,

the cell division triggered by estrogen provides a soft cushion in case a pregnancy occurs. Without estrogen, the uterus remains small.

Licorice, hops, and blue cohosh did not promote uterine growth. After adding extracts of dang gui to the animals' chow, however, the researchers discovered an increase in uterine weight. Black cohosh and vitex also spurred uterine cells to divide. Such results raise worries about what these compounds might do to breast cells, particularly breast cancer cells.

The researchers plan to expose breast cancer cells to extracts of dang gui and some other herbal remedies. If the cells proliferate in the laboratory, it could indicate a risk for women with breast cancer.

Not all compounds that bind to a receptor trigger cell activity. For example, tamoxifen and raloxifene, drugs made in the laboratory, attach to the estrogen receptor, preventing the hormone from binding. They thus block, rather than promote, breast cell proliferation. Patricia and Catherine Eagon hope that such a compound can be found among the herbal remedies.

"The possibility that these herbs contain anti-estrogens is a wide-open question," she says, noting that such a product could be used to prevent breast cancer.

Botanist James A. Duke, an expert on herbal medicines, is no fan of the synthetic drugs. "Anything that latches onto the estrogen receptor could prevent cancer, but it could also cause cancer," says Duke, who has retired from the U.S. Department of Agriculture in Beltsville, Md., and is an author of *The Green Pharmacy* (1997, Rodale Press). He points out that tamoxifen has been linked to uterine cancer.

He says he would advise his daughter to rely on an herb-based method of blocking breast cancer rather than pop a prescription drug. Duke argues that people have evolved with plant-based medicines and that such remedies are thus gentler than synthetic alternatives.

Yet women shouldn't view herbal products as riskfree, says Patricia Eagon. "The thought is, by many people, 'Oh, these things are natural, so they must be okay,'" she says. Women using herbal remedies to combat hot flashes should think of such products as powerful medicines, she adds.

She also notes that some people take more than the intended dose of an herb or take it in combination with prescription drugs—a practice that can lead to dangerous drug interactions or overdoses.

The results of the collaboration between the sisters mean different things to different women. For women

at high risk of breast cancer, the jury is still out. "If I were a woman at very high risk of breast cancer, I would think twice about taking these [herbal remedies] for menopausal symptoms," Patricia Eagon

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says. Unfortunately, there isn't much that physicians can recommend yet for women in this situation, she adds.

For women who have ruled out prescription drugs and are not at particular risk of breast cancer, the scale may tip toward the benefits of herbal remedies.

In the Eagon study, only dang gui appeared to work like an estrogen in every test. That evidence convinced Patricia Eagon, who suffers from hot flashes, to try the herb.

She buys dang gui from a trusted herbalist, noting that many commercial preparations contain too little of the herb to do any good. She then prepares an alcohol extract of dang gui to make a foul-tasting tea.

"But it works," she says.

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