

The dietary supplement genistein can undermine breast cancer treatment

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Many supplements sold without a prescription and marketed to post-menopausal women include plant compounds, such as genistein, that can block the effectiveness of Letrozole, a breast cancer drug. Credit: Photo by L. Brian Stauffer, U. of I. News Bureau

Women taking aromatase inhibitors to treat breast cancer or prevent its recurrence should think twice before also taking a soy-based dietary supplement, researchers report.

Genistein, a soy isoflavone that mimics the effects of estrogen in the body, can negate the effectiveness of aromatase inhibitors, which are

designed to reduce the levels of estrogens that can promote tumor growth in some types of breast cancer.

The new study, which included researchers from the University of Illinois, Virginia Polytechnic and State University and the National Center for Toxicological Research, appears in the journal *Carcinogenesis*.

Aromatase inhibitors are a mainstay of breast cancer treatment in post-menopausal women. These drugs work by interfering with the enzyme aromatase, which catalyzes a crucial step in converting precursor molecules to estradiol, the main estrogen in the body.

About two-thirds of all cases of breast cancer diagnosed in the U.S. are estrogen dependent or estrogen sensitive, which means that the tumors grow more rapidly in the presence of estrogen.

Most women diagnosed with breast cancer are post-menopausal, so their ovaries are no longer producing normal levels of estrogen. Other tissues, however, produce a steroid hormone, androstenedione (AD), which – with the help of aromatases – is converted to testosterone and estrogens. The estrogens produced from AD can stimulate the growth of some types of breast cancer tumors.

The researchers conducted several trials in a mouse model of estrogen-dependent post-menopausal breast cancer. First, they gave the mice AD, which was converted to estrogen and created a high estrogen environment.

This helped the researchers determine the maximum growth rate of the breast cancer tumors.

Next, they added Letrozole, an aromatase inhibitor widely prescribed to

post-menopausal women with estrogen-dependent breast cancer. This treatment (Letrozole) effectively blocked the effects of AD and the breast cancer tumors stopped growing.

But when they added genistein (a plant estrogen or "phytoestrogen" present in many dietary supplements) to the mix, the researchers observed a dose-dependent reduction in the effectiveness of the breast cancer drug. Specifically, the tumors began to grow again. They grew fastest at the highest dietary doses of genistein.

"To think that a dietary supplement could actually reverse the effects of a very effective drug is contrary to much of the perceived benefits of soy isoflavones, and unsettling," said William Helferich a professor of food science and human nutrition at Illinois and principal investigator on the study. "You have women who are taking these supplements to ameliorate post-menopausal symptoms and assuming that they are as safe as consuming a calcium pill or a B vitamin."

Many women take genistein supplements to control hot flashes and other symptoms of menopause. The researchers found that the doses commonly available in dietary supplements were potent enough to negate the effectiveness of aromatase inhibitors.

"These compounds have complex biological activities that are not fully understood," Helferich said. "Dietary supplements containing soy-based phytoestrogens provide high enough dosages that it could be a significant issue to breast cancer patients and survivors."

Plant estrogens from soy are not the only ones of concern, Helferich said. In a recent study, he and his colleagues found that certain mixtures of estrogenic botanical components and extracts marketed as supplements to assist "female libido enhancement" and sold without a prescription appeared to spur breast cancer tumor growth at low doses,

while having no effect on tumors at high doses.

That study appeared last year in *Food and Chemical Toxicology*.

"We are just starting to understand the complex effects of the dietary supplements that contain phytoestrogens," Helferich said. "There is an ongoing human experiment in which the outcome is unknown. These findings raise serious concerns about the potential interaction of the estrogenic dietary supplements with current breast cancer therapies."

Source: University of Illinois at Urbana-Champaign

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