

Women prescribed combination HRT should use caution when taking apigenin supplement, study finds

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Hormone replacement therapies, or medications containing female hormones that substitute those no longer produced by the body, are often prescribed to reduce the effects of hot flashes and other menopausal symptoms in women. Research and clinical trials on hormone replacement therapies have indicated a higher incidence of tumors, especially breast cancer, in postmenopausal women who take synthetic hormones; therefore, doctors have become more reluctant to prescribe the treatment. In 2011, studies conducted by University of Missouri researchers found that a natural compound called apigenin, which is found in celery, parsley, and apples, could reduce the incidence of tumor growth in women receiving hormone replacement therapy. Now, based on subsequent studies conducted by MU researchers, they are recommending that women not ingest pure apigenin as a supplement.

A new study shows that when the supplement apigenin is ingested in a diet at the same concentration as subjects received during IV injections in previous studies—the benefits were reversed leading to a higher incidence of cancerous tumors in subjects receiving progestin.

"Typically, hormone replacement therapies improve the lives of menopausal women and achieve very good results," said Salman Hyder, the no data to suggest that these items are harmful. Zalk Endowed Professor in Tumor Angiogenesis and professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center. "However, research has proven that in women receiving therapies that involve a combination of the natural component estrogen and the synthetic progestin, a higher incidence of breast cancer tumors can occur."

Hyder explains that many women normally have

benign lesions in breast tissue. These lesions don't typically form tumors until they receive the "trigger" that attracts blood vessels to cells essentially feeding the lesions causing them to form and expand— in this case, progestin is the trigger. Hyder's previous research focused on identifying natural supplements containing compounds that lessen the likelihood of tumor development and growth.

During the study, laboratory rats were divided into four groups. Two groups were placed on a controlled diet; the other two were given apigenin through a diet supplemented with apigenin. Researchers found that the mice that ingested apigenin through their diets were found to have a higher incidence of tumor growth.

"We know that apigenin is effective when injected directly into the bloodstream, so intravenous supplements may still be a possibility," Hyder said. "However, the mice that ingested apigenin began metabolizing it—which seemed to aggravate the situation causing very aggressive growth of mammary tumors."

"Women should continue consuming a healthy diet," Hyder said. "Fruits and vegetables most likely contain other protective compounds, and there is However, we do not recommend that women who are on hormone replacement therapy with a progestin component ingest pure apigenin as a supplement until further research proves otherwise. Until we know how apigenin is metabolized and interact with progestin effects, we cannot recommend that women supplement their hormone replacement therapy with this compound."

Researchers involved with the study included Benford Mafuvadze, post-doctoral fellow at Dalton



Cardiovascular Research Center; Matthew Cook, pre-doctoral fellow in Biomedical Sciences; Cynthia Besch-Williford, professor of veterinary pathobiology; and Xu Zhang, visiting researcher at the Dalton Cardiovascular Research Center.

The research was recently published online in the journal *Nutrition and Cancer*.

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