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[Planta Med.](#) 2007 Apr;73(4):318-22. Epub 2007 Mar 12.

Coadministration of the aromatase inhibitor formestane and an isopropanolic extract of black cohosh in a rat model of chemically induced mammary carcinoma.

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Abstract

Non-steroidal as well as steroidal **aromatase** inhibitors are currently being discussed as alternatives to tamoxifen in the first-line treatment of patients with hormone-dependent breast cancer. Many of these women are in a postmenopausal state and additionally troubled by climacteric complaints. Naturally occurring symptoms like hot flushes and night sweats can be triggered or augmented by anti-hormonal drugs. At the **aromatase** molecule, steroidal inhibitors like exemestane and formestane compete with the hormonal precursors for the substrate binding site and inactivate the enzyme irreversibly. An isopropanolic extract of the rootstock of **black cohosh** (iCR), which is a common comedication of **aromatase** inhibitors in breast cancer patients suffering from climacteric symptoms, contains triterpene glycosides and cinnamic acid esters, both of which possess structural similarities to steroids. We therefore tested a high dose of iCR, guaranteeing an effective uptake of 60 mg herbal substance per kg body weight and shown to influence rat bone and uterus, for putative interactions with two low dosing regimens of 3.5 mg or 5.0 mg formestane per animal and day. We chose a rat model of chemically induced breast cancer and evaluated tumor growth and serum estrogen levels. Compared to a tumor area of 1400 mm² after 21 days of unopposed tumor growth, formestane treatment, irrespective of concomitant **black cohosh** application, significantly reduced neoplastic growth by 50%. Formestane also significantly reduced serum estrogen levels, an effect which was also not abolished by iCR. Therefore, in this experimental setting, when challenging two low doses of formestane with a high dose of iCR, our data do not raise concerns against combining **aromatase** inhibitors with **black cohosh**.

PMID: 17354167 [PubMed - indexed for MEDLINE]

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