APIGENIN: CHEMOPREVENTIVE AND CHEMOTHERAPEUTIC POTENTIAL FOR PROGESTIN-DEPENDENT BREAST CANCER

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ABSTRACT

Use of estrogen-progestin hormone replacement therapy (HRT) has been linked to increased risk of breast cancer, an effect that has been attributed to the progestin component. Commonly available antiprogestins are associated with adverse side-effects and their use is therefore limited in humans. In the studies described herein we examined the capacity of apigenin to both prevent the onset, and treat already existing progestin-dependent breast tumors. Using ELISA we assessed the in vitro suppression of progestin-dependent induction of vascular endothelial growth factor (VEGF) by apigenin in human breast cancer cells. In order to determine the therapeutic potential of apigenin we used a progestin-dependent breast cancer model previously described by Liang et al (2007). We further examined the preventive effects of apigenin using a progestin accelerated dimethylbenz (a) anthracene (DMBA)-induced mammary tumor rat model. Apigenin suppressed VEGF induction by both progesterone and other synthetic progestins. Immunohistochemical analysis showed that apigenin dramatically induced apoptosis, suppressed VEGF and Her-2/neu expression and, and partially suppressed MPA-induced proliferation of xenograft tumors. In addition, intraperitoneal administration of apigenin delayed significantly the occurrence of MPA-accelerated DMBA-induced mammary tumors, as well as decreasing their incidence, in a dose-dependent manner. These studies suggest that apigenin has both chemopreventive and chemotherapeutic properties against hormone-dependent breast cancers.