Public Abstract

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Title:Inhibition of progestin-induced VEGF in mammary cancer by curcumin and 2-methoxyestradiol and their potential role as anti-angiogenic & chemopreventive compounds

Hormone replacement therapy (HRT) with estrogen and progestin is commonly prescribed to alleviate the symptoms of menopause in women. However, clinical studies indicate that progestins, though not estrogens, increase the risk of breast cancer. It is known that progestins cause breast cancer cells to synthesize and release high levels of a growth factor (VEGF) that promotes the formation of new blood vessels essential for tumor nourishment and growth. Consequently, efforts are directed towards identifying compounds that will effectively inhibit progestin-induced VEGF secretion from breast cancer cells.
In this study several naturally occurring compounds were screened to evaluate their ability to inhibit progestin-induced VEGF from human breast cancer cells. Curcumin and 2-methoxyestradiol (2ME2) appeared most promising in this respect. Curcumin, a turmeric root derivative, inhibited progestin-induced VEGF secretion from human breast cancer cells and delayed chemically-induced progestin-accelerated tumor formation in rats. Curcumin may therefore prove beneficial to post-menopausal women who are prescribed combined HRT.
2ME2, an estrogen metabolite, targeted a specific protein known as hypoxia-inducible factor (HIF) which, together with progesterone receptors, appears to be essential for VEGF release from tumor cells. Blocking HIF directly caused both rat and human progestin-dependent breast tumors to regress, leading us to conclude that HIF is a potential therapeutic target through which to prevent and treat progestin-dependent breast tumors. We propose that both curcumin and 2ME2 show promise as compounds that can be used to treat, or prevent the emergence of progestin-dependent tumors and that both compounds should be tested in women consuming HRT.