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FILE: ▪ Green Tea (*Camellia sinensis*)
▪ Epigallocatechin-3-Gallate
▪ Prostate Cancer
▪ Breast Cancer

HC 070185-365

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RE: Review of the Potential Efficacy of Epigallocatechin-3-Gallate in the Treatment of Breast and Prostate Cancers

Stuart EC, Scandlyn MJ, Rosengren RJ. Role of epigallocatechin gallate (EGCG) in the treatment of breast and prostate cancer. *Life Sci.* 2006;79:2329–2336.

Epigallocatechin-3-gallate (EGCG), a major constituent of green tea (*Camellia sinensis*), has been studied extensively as a potential treatment for many diseases, including various cancers. EGCG has been shown to have beneficial effects on Parkinson's disease, Alzheimer's disease, stroke, and diabetes. Epidemiologic data suggest that EGCG may protect against hormone-related cancers, such as breast and prostate cancers. The potential efficacy of EGCG in the treatment of breast and prostate cancers is reviewed and the possible mechanisms of action involved are discussed.

Several in vitro studies have shown a decrease in the number of both androgen-dependent (LNCaP) and androgen-independent prostate (DU145) cancer cells in response to treatment with EGCG. Apoptosis has been identified as the mechanism responsible for this effect, and the degree of apoptosis after EGCG treatment appears to be similar in DU145 and LNCaP cells. This finding suggests that the cytotoxic effects of EGCG are not influenced by the presence or absence of the androgen receptor. EGCG has also been shown to inhibit the activity of the epidermal growth factor receptor (EGFR) and to reduce the nuclear localization of nuclear factor κB (NF-κB) in prostate cancer cells. EGFR is known to activate intracellular enzymatic pathways that play a role in anti-apoptotic and growth stimulatory signaling. NF-κB is vital for tumor growth because it promotes and represses the expression of genes involved in survival and apoptosis. EGCG also inhibits various processes required for angiogenesis and metastasis in prostate cancer cells.

Increases in insulin-like growth factor-I (IGF-I) and decreases in IGF-binding protein-3 (IGFB-3) are associated with the progression of prostate cancer and with poor outcomes in

prostate cancer patients. Animal studies have shown that the consumption of a green tea mixture containing EGCG decreased IGF-I and increased IGFBP-3 levels. Thus, the modulation of these two molecules may represent a mechanism for chemoprevention via green tea consumption. Relatively few epidemiologic studies of the association between green tea consumption and prostate cancer risk have been conducted, and those that have been conducted have yielded conflicting results. Several clinical trials have been conducted to determine the ability of green tea extracts to prevent the development and progression of prostate cancer. The results of these trials to date indicate that green tea has little antineoplastic ability. The use of caffeinated preparations in trials has limited ability of subjects to complete the experimental treatments. Future trials should employ decaffeinated green tea extract preparations or purified EGCG.

In vitro studies have shown that EGCG is cytotoxic to breast cancer cells, regardless of estrogen receptor status; although, few studies have evaluated the mechanism responsible for this cytotoxicity. However, on the basis of a comprehensive literature review, it is thought likely that EGCG induces apoptosis in most, if not all, breast cancer cell lines by modulating intracellular signaling pathways that control cell cycle progression. Most in vivo studies of the beneficial effects of green tea extracts on breast cancer chemoprevention have used polyphenol mixtures rather than individual catechins. However, both studies of polyphenol mixtures and of EGCG alone have shown beneficial effects on tumor growth and metastases, which suggests that EGCG is predominantly responsible for the chemopreventative effect. Epidemiologic studies of the association between green tea consumption and breast cancer risk have also yielded conflicting results, i.e., some have shown no association and some chemopreventative effects. For example, different studies have shown chemopreventative effects of green tea consumption in specific groups of women, such as those with the low-activity catechol-*O*-methyltransferase allele, high-activity angiotensin-converting enzyme, or low levels of estrones.

The authors conclude that "EGCG induces apoptosis in both breast and prostate cancer cells in vitro." It appears that the cytotoxic effect of EGCG is not influenced by the hormone receptor status of the cell lines of either of these cancers. The cell cycle of both of these cancer cell lines has been shown to be arrested in the G_1 phase after treatment with EGCG. This likely results from a decrease in the auto-phosphorylative capacity of EGFR and the subsequent decrease in activity of intracellular signaling cascades, which are activated by EGFR. Although the authors consider these results to be "promising," they have yet to be duplicated in in vivo models or in cancer patients.

—Brenda Milot, ELS

The American Botanical Council has chosen not to include the original article.