

Does Tea Prevent Cancer? An Update on Laboratory and Clinical Studies.

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Tea (*Camellia sinensis*, Theaceae) is the second most commonly consumed beverage in the world and is consumed as one of three processed types- green, oolong, and black, which differ in terms of their sensory qualities as well as their chemical composition. Studies have focused on both tea extracts as well as purified compounds. (-)-Epigallocatechin-3-gallate (EGCG), the most abundant polyphenol in green tea; theaflavins, the characteristic polyphenols in black tea; and caffeine have been the most extensively studied. \

Laboratory studies have shown that tea and tea constituents, both polyphenols and to a lesser extent caffeine, have cancer preventive activity in a number of animal models and at different stages of the carcinogenic process. For example dietary administration of green tea extract inhibits 4-(methylnitrosamino)- 1-(3-pyridyl)-1-butanone (NNK)-induced lung tumorigenesis in mice. In most studies that have examined the issue, the polyphenols have been reported to be the major active constituents in tea, although in some models, for example ultraviolet light-induced skin carcinogenesis, caffeine has been shown to exert potent cancer preventive activity. Recent animal model studies have focused on the potentiation of the cancer preventive effects of tea by other dietary compounds or pharmaceutical agents. For example, dietary administration of green tea polyphenols in combination with atorvastatin resulted in a greater than additive reduction in tumor number and volume in NNK-treated mice compared to either treatment alone. Our laboratory has observed that treatment of mice with EGCG in combination with inhibitors of catechol-o-methyltransferase enhances the *in vitro* bioactivity of EGCG and improves the bioavailability of unmethylated EGCG in mice.

A number of potential mechanisms have been proposed for the cancer preventive activities of tea and tea components based on *in vitro* studies. These mechanisms remain largely untested *in vivo*, although there are some exceptions including induction of phase II drug metabolizing enzymes and modulation of insulin-like growth factor signaling. Interestingly, there is increasing evidence to suggest that polyphenol-induced oxidative stress may play a role in the anticancer activity of EGCG. Our laboratory and others have demonstrated that EGCG-induced oxidative stress is critical for inhibition of cell growth and induction of apoptosis: inclusion of exogenous antioxidants such as superoxide dismutase stabilize EGCG and reduce its growth inhibitory effects under cell culture conditions. More recently, it has been reported that orally-administered EGCG can induce oxidative stress in human lung cancer xenografts in mice without affecting the liver or small intestine. These results suggest some selectivity for the pro-oxidant effects of tea: selectively that likely depends on molecular differences between tumor cells and normal cells. Further study is needed to fully elucidate the role of oxidative stress and other potential mechanisms in mediating the cancer preventive effects of tea.

Whereas tea has been widely studied in the laboratory for its cancer preventive activity, there is limited data with regard to hard cancer endpoints. Most human studies have focused on the modulatory effects of tea on biomarkers related to cancer (e.g. induction of endogenous antioxidant systems). A pilot study in Italy reported that daily supplementation with 600 mg green tea polyphenols reduced the progression prostate intraepithelial neoplasia to prostate

cancer in 30 subjects by 90% compared to placebo. Similar and larger studies are needed to effectively test the cancer preventive efficacy of tea and tea constituents in human subjects.

In conclusion, although there is ample laboratory data demonstrating the preclinical cancer preventive activity of tea and tea constituents, the underlying mechanism(s) of action remain unclear and the efficacy of tea for cancer prevention in humans remains to be conclusively demonstrated.