

Tolcapone inhibits catechol-*O*-methyl transferase-mediated methylation of (-)-epigallocatechin-3-gallate *in vivo*

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Green tea polyphenols (GTP) have been shown to exert anti-cancer effects *in vitro* and *in vivo*. Studies suggest that (-)-epigallocatechin-3-gallate (EGCG) is largely responsible for these anti-cancer effects. EGCG reduces lung cancer cell viability *in vitro* and reduces tumor incidence, multiplicity, and size *in vivo*. EGCG, however, is rapidly methylated by catechol-*O*-methyl transferase (COMT), a transformation that may limit its effectiveness in lung cancer prevention. The nitrocatechol drug tolcapone is a potent inhibitor of COMT and is used to mitigate the symptoms of Parkinson's disease. In this study, we examined the effect of tolcapone on the bioavailability of EGCG in male CF-1 mice (IACUC # 28962). Plasma and tissue levels of EGCG and its major methyl metabolites in mice (n = 6) were determined by LC-MS following oral administration of EGCG (100 mg/kg b.w.), tolcapone (30 mg/kg b.w.), or the combination (100 mg/kg b.w. + 30 mg/kg b.w., respectively). In mice treated with EGCG for 720 min, tolcapone inhibited methylation of plasma EGCG by 66 %. Similar effects were observed in the urine and organ samples. In conclusion, tolcapone effectively increased the bioavailability of unmethylated EGCG *in vivo*. The combination may therefore increase the cancer preventive effects of EGCG. Future work will test the effect of tolcapone on the bioavailability of other GTP, and also determine the effect of tolcapone/GTP combination in animal models of cancer.

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