Abstracts

**Alpha lipoic acid inhibits human T-cell migration: Implications for multiple sclerosis.**


We have demonstrated previously the ability of the antioxidant alpha lipoic acid (ALA) to suppress and treat a model of multiple sclerosis (MS), relapsing experimental autoimmune encephalomyelitis (EAE). We describe the effects of ALA and its reduced form, dihydrolipoic acid (DHLA), on the transmigration of human Jurkat T cells across a fibronectin barrier in a transwell system. ALA and DHLA inhibited migration of Jurkat cells in a dose-dependent fashion by 16-75%. ALA and DHLA reduced matrix metalloproteinase-9 (MMP-9) activity by 18-90% in Jurkat cell supernatants. GM6001, a synthetic inhibitor of MMP, reduced Jurkat cell migration, but not as effectively as ALA and DHLA did. Both ALA and DHLA downmodulated the surface expression of the alpha4beta1 integrin (very late activation-4 antigen; VLA-4), which binds fibronectin and its endothelial cell ligand vascular cell adhesion molecule-1 (VCAM-1). Moreover, ALA, but not DHLA, reduced MMP-9-specific mRNA and extracellular MMP-9 from Jurkat cells in their culture supernatants as detected by relative reverse transcriptase-polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA), respectively. ALA and DHLA inhibited Jurkat cell migration and have different mechanisms for inhibiting MMP-9 activity. These data, coupled with its ability to treat relapsing EAE, suggest that ALA warrants investigation as a therapy for MS.

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**Green tea (Camellia sinensis) extract does not alter cytochrome p450 3A4 or 2D6 activity in healthy volunteers.**


Green tea extract is a widely used dietary supplement. The objective of this study was to assess the influence of a decaffeinated green tea (DGT; Camellia sinensis) extract on the activity of the drug-metabolizing enzymes cytochrome P-450 2D6 and 3A4. Probe drugs dextromethorphan (30 mg, CYP2D6 activity) and alprazolam (ALPZ; 2 mg, CYP3A4 activity) were administered orally to healthy volunteers (n = 11) at baseline, and again after treatment with four DGT capsules/day for 14 days. Each DGT capsule contained 211 +/- 25 mg of green tea catechins and <1 mg of caffeine. Dextromethorphan metabolic ratios (DMRs) and alprazolam pharmacokinetics were determined at baseline and after DGT treatment. There were no significant differences in ALPZ pharmacokinetics at baseline and after DGT treatment (all P values >/= 0.05; maximum concentration in plasma, 33 +/- 8 versus 34 +/- 13 ng/ml; time to reach maximum concentration in plasma, 1.4 +/- 1.2 versus 1.4 +/- 1.2 h; area under the plasma concentration versus time curve, 480 +/- 119 versus 510 +/- 107 h. ng. ml(-1); half-life of elimination, 12.3 +/- 1.7 versus 13.1 +/- 3.4 h). The DMR was 0.053 +/- 0.045 at baseline and 0.041 +/- 0.032 after DGT supplementation (P > 0.05). The plasma concentration of the green tea flavonoid, (-)-epigallocatechin gallate, reached 1.3 +/- 1.8 microM 2 h after DGT treatment. Our results indicate that DGT is unlikely to alter the disposition of medications primarily dependent on the CYP2D6 or CYP3A4 pathways of metabolism.