

Wells SR, Jennings MH, Rome C, Hadjivassiliou V, Papas KA, Alexander JS. **alpha-, gamma and delta-tocopherols reduce inflammatory angiogenesis in human microvascular endothelial cells.** J Nutr Biochem. 2009 May 13. [Epub ahead of print]

Vitamin E, a micronutrient (comprising alpha-, beta-, gamma- and delta-tocopherols, alpha-, beta-, gamma- and delta-tocotrienols), has documented antioxidant and non-antioxidant effects, some of which inhibit inflammation and angiogenesis. We compared the abilities of alpha-, gamma- and delta-tocopherols to regulate human blood cytotoxicity (BEC) and lymphatic endothelial cytotoxicity (LEC), proliferation, invasiveness, permeability, capillary formation and suppression of TNF-alpha-induced VCAM-1 as in vitro models of inflammatory angiogenesis. alpha-, gamma- and delta-tocopherols were not toxic to either cell type up to 40 muM. In BEC, confluent cell density was decreased by all concentrations of delta- and gamma-tocopherol (10-40 muM) but not by alpha-tocopherol. LEC showed no change in cell density in response to tocopherols. delta-Tocopherol (40 muM), but not other isomers, decreased BEC invasiveness. In LEC, all doses of gamma-tocopherol, as well as the highest dose of alpha-tocopherol (40 muM), decreased cell invasiveness. delta-Tocopherol had no effect on LEC invasiveness at any molarity. delta-Tocopherol dose dependently increased cell permeability at 48 h in BEC and LEC; alpha- and gamma-tocopherols showed slight effects. Capillary tube formation was decreased by high dose (40 muM) concentrations of alpha-, gamma- and delta-tocopherol, but showed no effects with smaller doses (10-20 muM) in BEC. gamma-Tocopherol (10-20 muM) and alpha-tocopherol (10 muM), but not delta-tocopherol, increased LEC capillary tube formation. Lastly, in BEC, alpha-, gamma- and delta-tocopherol each dose-dependently reduced TNF-alpha-induced expression of VCAM-1. In LEC, there was no significant change to TNF-alpha-induced VCAM-1 expression with any concentration of alpha-, gamma- or delta-tocopherol. These data demonstrate that physiological levels (0-40 muM) of alpha-, gamma- and delta-tocopherols are nontoxic and dietary tocopherols, especially delta-tocopherol, can limit several BEC and LEC endothelial behaviors associated with angiogenesis. Tocopherols may therefore represent important nutrient-signals that limit cell behaviors related to inflammation/angiogenesis, which when deficient, may predispose individuals to risks associated with elevated angiogenesis such as inflammation and cancer; further differences seen from the tocopherols may be due to their blood or lymphatic cell origin.