

# Abstract

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## **$\alpha$ -Tocopherol modulates human umbilical vein endothelial cell expression of Cu/Zn superoxide dismutase and catalase and lipid peroxidation**

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**BACKGROUND:** Recent studies suggest the potential of  $\alpha$ -tocopherol as a gene regulator, possibly through peroxisome proliferator-activated receptor  $\gamma$  (PPAR $\gamma$ ) activation due to the structural similarity of  $\alpha$ -tocopherol to a PPAR $\gamma$  ligand, troglitazone. Other investigators have suggested that a link exists between induction of the antioxidant enzymes Cu/Zn superoxide dismutase (SOD) and catalase and PPAR $\gamma$  activation.

**OBJECTIVE AND METHODS:** This study was designed to examine whether  $\alpha$ -tocopherol modulates expression of Cu/Zn SOD and catalase in human umbilical vein endothelial cells through redox-sensitive transcription factors, PPAR $\gamma$ , and nuclear factor- $\kappa$ B (NF- $\kappa$ B).

**RESULTS:**  $\alpha$ -Tocopherol treatments showed significant increases in both PPAR $\gamma$  (1.4- to 2.2-fold,  $P < .01$ ) and NF- $\kappa$ B p50 (1.3- to 1.5-fold,  $P < .005$ ) DNA binding activities compared with vehicle control. Significant increases in Cu/Zn SOD mRNA levels (6.0-fold,  $P < .005$ ) and catalase mRNA (8.0-fold,  $P < .005$ ) and its protein levels (2.3-fold,  $P < .005$ ) and lipid peroxidation levels (5.3-fold,  $P < .005$ ) were observed at the lowest concentration (10  $\mu$ mol/L) of  $\alpha$ -tocopherol treatments. Both mRNA and protein levels of these 2 antioxidant enzymes were positively associated with lipid peroxidation ( $P < .05$ ).

**CONCLUSIONS:**  $\alpha$ -Tocopherol may play a role not only in preventing against oxidative damage as an exogenous antioxidant by scavenging free radicals and superoxide but also in modulating the expression of the endogenous antioxidant enzymes as a gene regulator through PPAR $\gamma$  and NF- $\kappa$ B in the vascular cells. The  $\alpha$ -tocopherol-mediated gene expression is either stimulatory or inhibitory, depending on its oxidative status or its concentrations.