A novel antioxidant, octyl caffeate, suppressed LPS/IFN-g-induced iNOS gene expression in rat aortic smooth muscle cells.

Hsaio G;Shen MY;Chang WC;Cheng YW;Pan SL;Kuo YH;*Sheu JR

Abstract

In the present study, we investigated the effects and mechanisms of a novel potent antioxidant, octyl caffeate, on the induction of iNOS expression by lipopolysaccharide (LPS) and interferon-gamma (IFN-gamma) in cultured primary rat aortic smooth muscle cells (RASMCs) in vitro and LPS-induced hypotension in vivo. Octyl caffeate (0.1-1.0 microM) exerted a concentration-dependent inhibition of iron-catalyzed lipid peroxidation in rat brain homogenates. Furthermore, octyl caffeate (20, 50, and 100microM) concentration-dependently diminished the initial rate of superoxide-induced NBT reduction and the enzymatic activity of xanthine oxidase. It also concentration-dependently (1-50 microM) inhibited the NO production, iNOS protein and messengerRNA expressions upon stimulation by LPS (100 microg/mL)/IFN-gamma (100U/mL) in RASMCs. In addition, we found that octyl caffeate did not significantly affect IkappaBalpha degradation stimulated by LPS/IFN-gamma in RASMCs. On the other hand, octyl caffeate (10 and 50 microM) significantly suppressed activation of c-Jun-N-terminal kinase and extracellular signal-regulated kinase. Moreover, octyl caffeate (10mg/kg, i.v.) significantly inhibited the fall in mean arterial pressure stimulated by LPS (7.5mg/kg) in rats. In conclusion, we demonstrate that a novel potent antioxidant, octyl caffeate, significantly ameliorates circulatory failure of endotoxemia in vivo by a mechanism involving suppression of iNOS expression through inactivation of mitogen-activated protein kinases in RASMCs.