A novel antioxidant, octyl caffeate, supperssion of LPS/IFN-γ-induced inducible nitric oxide synthase gene expression in rat aortic smooth muscle cells

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摘要

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-γ (IFN-γ) in cultured primary rat aortic smooth muscle cells (RASMCs) in vitro and LPS-induced hypotension in vivo. Octyl caffeate (0.1 – 1.0 μM) exerted a concentration-dependent inhibition of iron-catalyzed lipid peroxidation in rat brain homogenates. Furthermore, octyl caffeate (20, 50, and 100 μM) concentration-dependently diminished the initial rate of superoxide-induced NBT reduction and the enzymatic activity of xanthine oxidase. It also concentration-dependently (1 – 50 μM) inhibited the NO production, iNOS protein and messenger RNA expressions upon stimulation by LPS (100 μg/mL)/IFN-γ (100 U/mL) in RASMCs. In addition, we found that octyl caffeate did not significantly affect IκBα degradation stimulated by LPS/IFN-γ in RASMCs. On the other hand, octyl caffeate (10 and 50 μM) significantly suppressed activation of c-Jun-N-terminal kinase and extracellular signal-regulated kinase. Moreover, octyl caffeate (10 mg/kg, i.v.) significantly inhibited the fall in mean arterial pressure stimulated by LPS (7.5 mg/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.