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Pterostilbene suppressed lipopolysaccharide-induced up-expression of iNOS and COX-2 in murine macrophages.

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Abstract

Pterostilbene, an active constituent of blueberries, is known to possess anti-inflammatory activity and also to induce apoptosis in various types of cancer cells. Here, we investigated the inhibitory effects of pterostilbene on the induction of NO synthase (NOS) and cyclooxygenase-2 (COX-2) in murine RAW 264.7 cells activated with lipopolysaccharide (LPS). Western blotting and real-time polymerase chain reaction (PCR) analyses demonstrated that pterostilbene significantly blocked the protein and mRNA expression of iNOS and COX-2 in LPS-induced macrophages. Treatment with pterostilbene resulted in the reduction of LPS-induced nuclear translocation of the nuclear factor-kappaB (NFkappaB) subunit and the dependent transcriptional activity of NFkappaB by blocking phosphorylation of inhibitor kappaB (IkappaB)alpha and p65 and subsequent degradation of IkappaB alpha. Transient transfection experiments using NFkappaB reporter constructs indicated that pterostilbene inhibits the transcriptional activity of NFkappaB in LPS-stimulated mouse macrophages. We found that pterostilbene also inhibited LPS-induced activation of PI3K/Akt, extracellular signal-regulated kinase 1/2 and p38 MAPK. Taken together, these results show that pterostilbene down regulates inflammatory iNOS and COX-2 gene expression in macrophages by inhibiting the activation of NFkappaB by interfering with the activation of PI3K/Akt/IKK and MAPK. These results have an important implication for using pterostilbene toward the development of an effective anti-inflammatory agent.