Oroxylin A inhibition of lipopolysaccharide-induced iNOS and COX-2 gene expression via suppression of nuclear factor-kappaB activation

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Abstract

Polyphenols are major components of many traditional herbal remedies, which exhibit several beneficial effects including anti-inflammation. The exact mechanism of the anti-inflammatory action of polyphenols, however, has not been determined. In the present study, we examined the effects of eight different polyphenols isolated from Chinese herbs, including two flavonoids (myricitrin and oroxylin A), four ellagitannins (penta-O-galloyl-beta-glucopyranose, woodfordin C, oenothein B, and cuphiin D1), and two anthraquinones (emodin and physcion), on lipopolysaccharide (LPS)-induced nitric oxide (NO) production, and inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) gene expression in RAW264.7 macrophages. The results indicated that only oroxylin A and emodin concentration-dependently inhibited LPS-induced NO production. The remaining compounds slightly inhibited LPS-induced NO production only at the highest concentration examined. Furthermore, oroxylin A inhibited the expression of LPS-induced iNOS and COX-2 proteins and mRNAs without an appreciable cytotoxic effect on RAW264.7 cells. Emodin also inhibited LPS-induced iNOS protein as potently as oroxylin A, but it inhibited LPS-induced iNOS mRNA expression only slightly and did not affect COX-2 mRNA and proteins. This was consistent with the findings that oroxylin A but not emodin or physcion inhibited prostaglandin E(2) synthesis induced by LPS. The inhibitory effects of oroxylin A on LPS-induced iNOS and COX-2 gene expression were also demonstrated in Bcl-2-overexpressing RAW264.7 macrophages, suggesting that oroxylin A inhibition of iNOS and COX-2 expression was not due to its antioxidant effect. Furthermore, oroxylin A but not emodin blocked nuclear factor-kappaB (NF-kappaB) binding and transcriptional activation associated with decreased p65 proteins in the nucleus induced by LPS. These results indicated that oroxylin A, an active component in Huang Qin, inhibited LPS-induced iNOS and COX-2 gene expression by blocking NF-kappaB activation, whereas emodin inhibition of LPS-induced iNOS expression may be mediated by a different transcription factor.