In vitro and in vivo inhibitory activities of rutin, wogonin, and quercetin on lipopolysaccharide-induced nitric oxide and prostaglandin E(2) production

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Abstract

Flavonoids are widely distributed in plants, but their biological functions are still unclear. In the present study, in vitro and in vivo experiments were performed to demonstrate the inhibitory activities of rutin, wogonin, and quercetin on lipopolysaccharide-induced nitric oxide (NO) and prostaglandin E(2) production in RAW 264.7 macrophages, primary peritoneal macrophages, and Balb/c mice, respectively. In vitro results showed that wogonin and quercetin dose-dependently suppressed lipopolysaccharide-induced NO production in RAW 264.7 macrophages and primary peritoneal macrophages without a notable cytotoxic effect on either cell types associated with a decrease in inducible nitric oxide synthase (iNOS) protein expression in both cells. Rutin, at 80 microM only, had a slight but obvious inhibitory effect on lipopolysaccharide-induced NO production in primary peritoneal macrophages. Both wogonin and quercetin attenuated lipopolysaccharide-induced prostaglandin E(2) production in vitro. Intravenous injection of lipopolysaccharide (10 mg/kg, i.v.) resulted in a time-dependent induction of NO production in serum, and pretreatment with the L-arginine analog N-nitro-L-arginine methyl ester (L-NAME) blocked this induction. Intravenous pretreatment of Balb/c mice with rutin, wogonin or quercetin for 1 h followed by lipopolysaccharide treatment significantly inhibited lipopolysaccharide-induced NO production, but no inhibition of prostaglandin E(2) production was found. A decrease in iNOS protein, but not cyclooxygenase-2 protein, was detected in liver and lung specimens of lipopolysaccharide-treated Balb/c mice in the presence of rutin, wogonin or quercetin. In conclusion, data obtained both in vitro and in vivo suggest that wogonin and quercetin exert inhibitory activity on lipopolysaccharide-induced NO production through suppression of iNOS expression.