Inhibition of NOS Inhibitors and Lipopolysaccharide Induced Inducible Nitric Oxide Synthase and Cyclooxygenase 2 Gene Expressions by Rutin, Quercetin, and Quercetin Pentaacetate in RAW264.7 Macrophages

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Abstract

In the present study, experiments were performed to explore the action of quercetin, the most widely distributed flavonoids, and its major metabolite, quercetin-3´-sulfate, on lipopolysaccharide (LPS)- and interferon-γ (IFN-γ)-induced nitric oxide (NO) production in BV-2 microglia. Quercetin could suppress LPS- and IFN-γ-induced NO production and inducible nitric oxide synthase (iNOS) gene transcription, while quercetin-3´-sulfate had no effect. LPS-induced IκB kinase (IKK), nuclear factor-κB (NF-κB) and activating protein-1 (AP-1) activation, and IFN-γ-induced NF-κB, signal transducer and activator of transcription-1 (STAT1) and interferon regulatory factor-1 (IRF-1) activation were reduced by quercetin. Moreover quercetin was able to induce heme oxygenase-1 expression. To address the involvement of heme oxygenase-1 induction in iNOS inhibition, heme oxygenase-1 antisense oligodeoxynucleotide was used. Quercetin-mediated inhibition of NO production and iNOS protein expression were partially reversed by heme oxygenase-1 antisense oligodeoxynucleotide, but was mimicked by hemin, a heme oxygenase-1 inducer. The involvement of signal pathways in quercetin-induced heme oxygenase-1 gene expression was associated with tyrosine kinase and mitogen-activated protein kinases activation. All these results suggest quercetin should provide therapeutic benefits for suppression of inflammatory-related neuronal injury in neurodegenerative diseases.