Concentration-dependent differential effects of quercetin on rat arotic smooth muscle cells.

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Abstract

Quercetin is one of the most ubiquitous bioflavonoids in foods of plant origin. Although quercetin is generally considered to provide protection against oxidative injury and inflammation, recent studies have demonstrated that its cytoprotective effects occur within a narrow concentration range. We attempted to examine the concentration-dependent effect on proliferation and inflammation in the primary culture of rat aortic smooth muscle cells. We demonstrate that quercetin inhibited [3H]thymidine incorporation into rat aortic smooth muscle cells only at concentrations ≤ 50 μM in a concentration-dependent manner. Nevertheless, quercetin, at concentrations ≥ 100 μM, reduced cell viability; this was further characterized as being due to apoptosis, which occurred through the proteolytic activation of pro-caspase-3. Additionally, the phosphorylation of c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (p38MAPK) substantially increased in rat aortic smooth muscle cells exposed to 100 μM quercetin, results which differ from observations by others and ourselves of cells exposed to ≤ 50 μM quercetin. Unlike P-JNK and P-p38, the phosphorylation of extracellular signal-regulated kinase 1/2 (ERK1/ ERK2) was not significantly affected by the concentration-dependent effects of quercetin. Surprisingly, the adverse effects of higher concentrations of quercetin could be ameliorated by adding the antioxidants, catalase, and N-acetylcysteine (NAC). Furthermore, the electrophoretic mobility shift assay (EMSA) showed that rat aortic smooth muscle cells exposed to quercetin at concentrations of ≤ 50 μM caused concentration-dependent inhibition of nuclear factor kappa B (NF-κB) activity, whereas concentrations of ≥ 100 μM resulted in increased NF-κB binding activity. We demonstrate for the first time that quercetin at low concentrations has antiproliferative and antiinflammatory effects, but at concentrations of ≥ 100 μM, is likely to induce the opposite effects on rat aortic smooth muscle cells.