Quercetin Inhibits Lipopolysaccharide-Induced Expression of Endothelial Cell Intracellular Adhesion Molecule-1

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Key Words

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Introduction

Adhesion molecules are essentially involved in the pathogenesis of inflammation. Their presence and activity on vascular endothelial and circulating leukocytes is required to initiate and perpetuate an inflammatory process. Down-regulation of an inflammatory response can be achieved by limiting the expression or function of appropriate endothelial cell or leukocyte adhesion molecules.

Quercetin is a common, naturally occurring, low-molecular-weight dietary plant flavonoid, structurally related to the antiallergic drugs cromolyn and nedocromil. It can inhibit tetradecanoylphorbol acetate-induced mononuclear cell aggregation [1] as well as cytotoxic lymphocyte (CTL) generation in murine mixed lymphocyte culture [2]. In addition, the cytotoxic activity of the CTL against P815 mastocytoma target cells is also inhibited. Each of these quercetin-sensitive processes is adhesion molecule dependent.

Materials and Methods

We investigated the effect of quercetin on (1) the attachment of peripheral blood lymphocytes (PBLs) to lipopolysaccharide (LPS)-stimulated human umbilical vein endothelial cells (HUVECs) utilizing ⁵¹Cr-labelled PBLs, and (2) the attachment of a fluorescein-labelled monoclonal antibody against intercellular adhesion molecule-1 (ICAM-1) on LPS-stimulated HUVECs.

Results

The results showed that quercetin (1) inhibited the attachment of labelled PBLs to LPS-stimulated HUVECs but did not affect the control level of attachment of PBLs to HUVECs, and (2) inhibited the expression of ICAM-1 on the surface of LPS-stimulated HUVEC. In both processes, the quercetin effect was concentration dependent (IC₅₀ = 4 µg/ml, 1-3 µM). Taxifolin (dihydroquercetin) had a negligible effect, indicating important structure-activity rela-

tionships. Thus quercetin possesses anti-inflammatory activity through its effect on the expression of adhesion molecules.

Quercetin could be acting at three potential loci; (1) at the level of transcription with decreased synthesis of ICAM-1 mRNA; (2) at the level of translation with decreased synthesis of ICAM-1 protein, or (3) on the insertion of ICAM-1 into the HUVEC plasma membrane. One or more of these mechanisms could apply, but the end result would be the same, i.e. decreased cell surface expression of ICAM-1.

If quercetin acts on HUVECs, then it (and other flavo-noids) could act on the adhesion-molecule-expressing machinery of other cells and thereby profoundly affect the initiation and perpetuation of inflammatory and other adhesion-molecule-dependent processes.

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Quercetin and Cell Adhesion