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ORIGINAL PAPER

Novel quercetin derivatives: synthesis and screening for anti-oxidant activity and aldose reductase inhibition

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Dedicated to Professor Štefan Toma on the occasion of his 75th birthday

The direct acylation of quercetin (*I*) with 3-chloro-2,2-dimethylpropanoyl chloride (*II*) gives a complex reaction mixture. The synthesis of different acylated quercetin with from mono- to tetra-*O*-substituted functions was achieved in a simple procedure wherein the yield of isomers depended on the stoichiometric ratio of reagents. The crude reaction mixtures were analysed (LC-MS) and compared with the isolated products. Unambiguous structural characterisation of isomeric quercetin derivatives was confirmed by NMR analysis. In addition, the quercetin dimer can be obtained in a high yield in the simple procedure. The anti-oxidant activity and aldose reductase inhibition of the compounds were screened with the aim of providing bi-functional remedies to treat diabetic complications and other diseases where oxidative stress and the polyol pathway are key etiological factors.

Keywords: quercetin, acylation, naphthoquinone, quercetin dimer, LC-MS, aldose reductase

Introduction

Flavonoids attract considerable attention due to their potential beneficial biochemical and anti-oxidant effects on human health. Most of the experimental results demonstrate that flavonoid compounds have a number of biological activities including radical scavenging, anti-inflammatory, anti-mutagenic, anti-cancer, anti-HIV, anti-allergic, anti-platelet, and anti-oxidant activities (Harborne & Williams, 2000). Of these compounds, quercetin (*I*) and quercetin *O*-glycosides are among the most ubiquitous structures of all plant phenolics (Materska, 2008). Acyl derivatives of *I* include aliphatic acids, such as acetic, malonic, and 2-hydroxypropionic acid, or aromatic acids, including benzoic, gallic, caffeic, and ferulic acid, which are frequently used in the modification of glycoside moieties (Harborne, 1994). Acylated quercetin (Qc) derivatives and pro-drugs represent useful active principles for cosmetic, dermatopharmaceutical, pharmaceutical, or dietetic compositions (Perrier et al., 2001; Golding et al., 2001). It is important to selectively modify those hydroxyls that are not equivalent in terms of chemical reactivity

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