SYNTHESIS AND ANTI-INFLAMMATORY EFFECT OF FOUR RUTAECARPINE METABOLITES

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Rutaecarpine is a main quinazolinocarboline alkaloid isolated from Evodia rutaecarpa. In our previous studies, rutaecarpine was metabolized by liver microsomal enzymes to yield four rutaecarpine metabolites, 3-, 10-, 11-, and 12-hydroxyrutaecarpine. In this report, we described the detailed synthesis of these four metabolites and evaluated their anti-inflammatory effect on lipopolysaccharide-induced NO production in RAW264.7 macrophages. Among them, 3-hydroxyrutaecarpine showed the most potent anti-inflammatory activity with EC₅₀ value 27.1 μM.

Key words: Evodia rutaecarpa, rutaecarpine, hydroxyrutaecarpine, anti-inflammatory activity

Introduction

The dried fruit of Evodia rutaecarpa, called Wu-Chu-Yu in Chinese, is a commonly used traditional Chinese medicine (TCM) in the treatment of headache, gastrointestinal disorders, postpartum haemorrhage, amenorrhea, and hypertension. Rutaecarpine (Fig. 1) is a main quinazolinocarboline alkaloid isolated from Evodia rutaecarpa, which has shown a variety of pharmacological effects such as anti-inflammatory, antiplatelet aggregatory, anticancer and vasodilator effects.

Our previous report demonstrated that rutaecarpine was metabolized by liver microsomal enzymes and yielded four rutaecarpine metabolites, 3-, 10-, 11-, and 12-hydroxyrutaecarpine (Fig. 1) which were identified by using high-performance liquid chromatography (HPLC) with UV and ¹H NMR comparison. In this report, the detailed synthesis of these four metabolites was described, and their anti-inflammatory activity to repress lipopolysaccharide (LPS)-induced nitric oxide (NO) production in RAW264.7 macrophages was also evaluated.

Materials and Methods

I. General experimental procedures

Melting points were determined on a Yanaco MP-13 micro-melting point apparatus and are uncorrected. IR spectra were obtained on a Nicolet Avatar