Immunomodulatory and Anti-Inflammatory Activity of Selected Osthole Derivatives

Michał Zimecki, Jolanta Artym, Wojciech Cisowski, Irena Mażol, Maciej Włodarczyk, and Michał Gleński*

a Department of Experimental Therapy, Institute of Immunology and Experimental Therapy, R. Weigla str. 12, 53–114, Wrocław, Poland
b Department of Pharmacognosy, Wrocław Medical University, Nankiera sq. 1, 50–140 Wrocław, Poland. E-mail: michalg@farmgn.am.wroc.pl
* Author for correspondence and reprint requests

Z. Naturforsch. 64c, 361–368 (2009); received October 17/December 3, 2008

From osthole [7-methoxy-8-(3-methyl-but-2-enyl)-chromen-2-one] (I), obtained by selective extraction of Peucedanum ostruthium (L.) W. Koch roots, ostholic acid (II) was synthesized as a result of its oxidation with chromium trioxide. From ostholic acid, through its chloride, four amides were obtained: the morpholide 1, the p-chloro-benzylamide 2, the piperidine 3 and the N-methyl-piperazide 4. Except for 1, other compounds have not been described before. The amides 1–4 and their precursor osthole (I) were tested for their potential activities in selected immunological assays. The compounds showed moderate inhibitory activity in the humoral immune response to sheep erythrocytes in mice in vitro, and 4 was the most suppressive. The effects of 1 and 3 on concanavalin A- and pokeweed mitogen-induced mouse splenocyte proliferation were inhibitory and those of 4 stimulatory. The compounds were also tested for their activity on tumour necrosis factor Û and interleukin 6 production, induced by lipopolysaccharide, in cultures of rat peritoneal cells and human peripheral blood mononuclear cells. Compounds 1, 3 and 4 inhibited tumour necrosis factor Û (rat cells), whereas compound 2 stimulated the production of both cytokines. Compounds 1, 2 and 3 were also strongly inhibitory on tumour necrosis factor Û production in human blood cells (73, 78 and 80% inhibition at 10 g/ml, respectively). On the other hand, 2 and 4 stimulated the interleukin 6 production (2- to 3-fold stimulation). In addition, 2 and 4 suppressed the carrageenan-induced inflammation in mice (56.5% and 68.3% inhibition, respectively). In summary, the compounds predominantly displayed suppressive and anti-inflammatory activities in the investigated models.

Key words: Peucedanum ostruthium (L.) W. Koch, Osthole Derivatives, Humoral Immune Response, Carrageenan