Immunomodulatory and Anti-Inflammatory Activity of Selected Osthole Derivatives

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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 synthetized 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 Ű 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 Ű (rat cells), whereas compound **2** stimulated the production of both cytokines. Compounds **1**, **2** and **3** were also strongly inhibitory on tumour necrosis factor Ű production in human blood cells (73, 78 and 80% inhibition at 10 Ôg/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