

**A051 Anti-inflammatory activity of triterpenes from *Schinus molle* fruit**

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*Schinus molle* L. (Anacardiaceae) is a pepper tree used against different diseases including inflammatory pathologies (1). In a previous screening, the anti-inflammatory activity of methanol extract of *S. molle* fruits was demonstrated. The aim of this study is to isolate the active compounds of this extract and study its pharmacological effect in a chronic model of inflammation.

Two triterpenes (**1**: 300 mg, **2**: 485 mg) were isolated from the MeOH extract (91 g obtained from 298 g of fruits) by gel-filtration chromatography (Sephadex LH-20) using methanol as a mobile phase and the fractions were re-chromatographed using VLC (SiO<sub>2</sub>) and dichloromethane / ethyl acetate mixtures. In addition, one flavonoid (**3**: 300 mg) was isolated using VLC (SiO<sub>2</sub>) and different dichloromethane / methanol mixtures. Compounds were analysed using spectroscopy (MS, <sup>1</sup>H- and <sup>13</sup>C-NMR) and were identified as: (13 $\alpha$ ,14 $\beta$ ,17 $\alpha$ ,20S,24Z)-3 $\alpha$ -hydroxy-21-oxolanosta-8,24-dien-26-oic acid (**1**), a closely related 3 $\alpha$ -hydroxylanosta-8,24-dien-26-oic acid (**2**) and chamaejasmin (**3**).

In the chronic model of inflammation (**2**), all compounds showed significant activity (Dunnett's t-test) at doses of 0.25 mg/ear X 7 applications. Compounds **1** and **2** showed 39% and 48% of inhibition respectively, whereas **3** showed only 26% of inhibition. Dexamethasone was used as a positive control (85% of inhibition at 0.05 mg/ear - 7 doses).

Compounds **1** and **2** are structurally related to the lanostanoids isolated from *Schinus terebinthifolius*, which are anti-inflammatory and inhibit phospholipase A<sub>2</sub>. For that, the inhibition of this enzyme could be hypothesised as the possible mechanism of action of lanostanes from *Schinus molle*.

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**References:** **1.** Duke, J.A. (1985) CRC Handbook of Medicinal Herbs, CRC Press, Boca Raton, pp. 434. **2.** Stanley, P.L. et al. (1991). Skin Pharmacol. 4: 262-271.

**A052 Effect of Asteraceae species on two models of cell-mediated allergy**

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Following our investigations on the Mediterranean anti-inflammatory Asteraceae, we undertook a study of *Inula viscosa*, *Pallenis spinosa* and *Santolina chamaecyparissus*. Methanolic extracts were tested on a contact hypersensitivity (CHS) model induced by 2,4-dinitro-1-fluorobenzene (DNFB) and a tuberculinic-type delayed hypersensitivity (DTH) model provoked by sheep red blood cells (SRBC) (1).

The CHS sensitisation phase was induced by topical application of 0.2% DNFB in acetone onto the shaved abdomen on days 0 and 1. To elicit an allergic reaction, the animals were challenged 5 days later with DNFB on the ear surface. Ear swelling was assessed 24 h and 96 h after challenge by measuring ear thickness with a micrometer. Plant extracts were applied topically in pre- and post-challenge treatments. For DTH study, mice were sensitised on day 0 by injecting s.c. 2x10<sup>7</sup> SRBC in 0.1 mL of PBS into the back. Five days later, these mice were challenged by injecting 1x10<sup>8</sup> SRBC in 0.025 mL of PBS into the right hind paw. The paw thickness was measured with a micrometer 18 h and 24 h after challenge. Plant extracts were administered i.p. immediately before and 16 h after challenge. Statistical significance was assessed using the Dunnett's t-test.

In the CHS test, pre-challenge treatment with *P. spinosa* extract inhibited the early elicitation phase by 40 %, while *I. viscosa* reduced the swelling to a lesser extent. Of the three extracts, only that of *S. chamaecyparissus* was active following post-challenge treatment. When the extracts were assayed in the SRBC test, *S. chamaecyparissus* was the most effective of the three species, inhibiting the reaction by 41% at the time of maximum swelling (18 h).

According to these results, *P. spinosa* is preventative while *S. chamaecyparissus* exerts its anti-inflammatory activity, demonstrated prior to this study (2), following reaction.

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**References:** **1.** Góngora L. et al. (2000) Life Sci. 66, 183-188. **2.** Sala A. et al. (2000) Life Sci. 66, PL35-40.