

Antiinflammatory Activity of Cinnamic Acid Esters

M. E. Godoy, A. Rotelli, L. Pelzer and C. E. Tonn

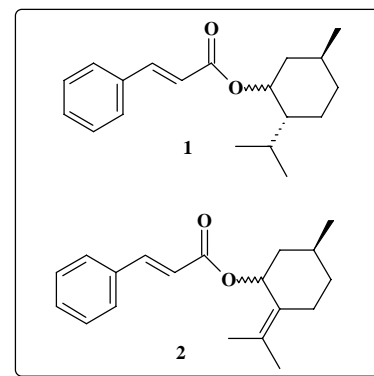
Química Orgánica. INTEQUI-CONICET. UNSL. Chacabuco y Pedernera (5700). San Luis, Argentina

E-mail: egodoy@unsl.edu.ar

Abstract: The cinnamate esters of 3-p-menthanol (trivial name, menthol) (**1**) and 4(8)-p-menthen-3-ol (trivial name, pulegol) (**2**) were prepared and their anti-inflammatory activity was measured. Some of the monoterpenoid esters displayed interesting anti-inflammatory activity.

Introduction

Natural phenylpropanes, represented by the bornyl esters of coumaric, caffeic y ferulic acid have shown effectiveness as antiinflammatory drugs [1,2]. Bearing in mind these precedents, in this work we report the results of our tests, by the carreeenan induced-edema test method, of the antiinflammatory activity of some cinnamic acid esters prepared in the laboratory.



Experimental Part

Ester Preparation

Pulegyl and menthyl cinnamates were obtained following the previously describe nmethodology [3]. The corresponding acid chloride was prepared under an inert atmosphere using thionyl chloride in refluxing anhydrous benzene. The acid chloride was added to the monoterpene alcohol dissolved in dry benzene containing a few Mg shavings and then refluxed for 8 hrs [4]. The esters were identified by their physical constants, ^1H and ^{13}C NMR and MS. Pulegol was prepared from pulegone by NaBH_4 reduction in the presence of CeCl_3 .

Carrageenan Test

Acute mouse paw edema was induced by administration of 3.5% carrageenan. Previously the animals had received an interperitoneal dose of 75 mg/kg of the compounds under study, while the reference animal received 80 mg/kg of phenylbutazone. The volumes of the mice paws were compared 1, 3,

5, and 7 hrs after administration of carrageenan to measure the anti-inflammatory effect [5,6].

Results and Discussion

All the compounds tested displayed interesting activity although the effects of pulegyl cinnamate were particularly noteworthy (Table 1).

Table 1. Carrageenan Test.

Products	Percentages of Inhibition of Acute Inflammation			
	1 hr	3 hrs	5 hrs	7 hrs
Phenylbutazone	69(i)	73(i)	73(i)	69(i)
Cinnamic acid	58(b)	45(c)	52(d)	27
Pulegol	54(g)	54(d)	45(e)	47(g)
Pulegyl cinnamate	49(a)	62(j)	56(h)	50(b)
Menthyl cinnamate	48(f)	49(j)	32	47(a)

(a) $p < 0.002$; (b) $p < 0.0002$; (c) $P < 0.0007$; (d) $p < 0.0001$; (e) $p < 0.003$;
(f) $p < 0.008$; (g) $p < 0.001$; (h) $p < 0.0003$; (i) $p < 0.000001$; (j) $p < 0.00001$.

Acknowledgements: This work was done with funding from CONICET and UNSL. We thank Dr. P.C. Rossomando and Lic. E. García for the ^1H and ^{13}C NMR spectra.

References and Notes

- Zschocke, S.; Lehner, M.; Bauer, R. *Planta Medica* **1997**, *63*, 203.
- Maldonado, E; Ramírez Apan, M. T.; Pérez-Castorena, A. L. *Planta Medica* **1998**, *64*, 660.
- Faraoni, M.B. en Tesis de Magister (Univ.Nac.del Sur). «Nuevo método para la síntesis de compuestos organoestánicos en átomo de estaño quiral» (1997).
- Gastaminza, A. E.; Ferracutti, N. N. *An. Asoc. Quím. Argent.* **1983**, *71*, 587.
- Sugishita, E.; Amagaya, S.; Ogihara, Y. *J. Pharmacobio-Dyn.* **1981**, *4*, 565.
- Favier, L.S.; Tonn, C.E.; Guerreiro, E.; Rotelli, E.; Pelzer, L. *Planta Medica* **1998**, *64*, 657.