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ALTAMISIN, A NEW SESQUITERPENE LACTONE FROM AMBROSIA CUMANENSIS H.B.K.

J. Borges*, M.T. Manresa, J.L. Martín, C. Pascual y P. Vázquez
Departamento de Química Orgánica. Universidad Autónoma de Madrid.
Canto Blanco. Madrid-34. Spain.

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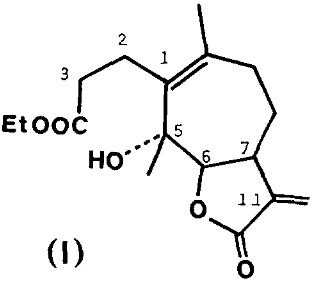
In this communication we report the isolation and structure determination of altamisin (I), a new sesquiterpene lactone whose structure is related to that of the psilostachyins[1]. Chloroform extraction of the aerial part of Ambrosia cumanensis H.B.K.[2], collected from the outskirts of San Salvador (Central America) and known locally as Altamisa, gave, after chromatography on Kieselgel 60, four crystalline products. The first, $C_{17}H_{24}O_5$, m.p. 101-102° (n-hexane), $[\alpha]_D$ +34.9°, was a new sesquiterpene lactone which we propose to name altamisin. The other three products were identified as psilostachyin, psilostachyin B and psilostachyin C [1].



(I)

Altamisin contained one α,β'-unsaturated γ-lactone (λ_{max} 212 nm, ε 12,700); IR band at 1768 cm^{-1} (Nujol). A second IR carbonyl absorption at 1725 cm^{-1} corresponded to the absorption expected for either a δ-lactone or an ester function. The presence of one tertiary hydroxyl group was indicated by an IR signal at 3530 cm^{-1} and a sharp singlet integrating for one proton at δ4.88 in the NMR spectrum in deuterated dimethylsulfoxide. As expected, the signal disappeared on the addition of D_2O to the NMR sample.

The NMR spectrum of altamisin in $CDCl_3$ provided further evidence for an α,β'-unsaturated γ-lactone system of the type found in the psilostachyins[1]; a doublet at $\delta 4.70$ (1 H, J = 9 Hz) was assigned to the C-6 lactonic proton. Moreover, doublets at $\delta 5.46$ and 6.16 (J = 3.5 Hz) were typical of the C-11 exocyclic methylene group. The NMR spectrum also exhibited signals characteristic of one tertiary methyl group (singlet, 3 H, $\delta 1.21$), which was assigned to a methyl group attached to a carbon bearing a hydroxyl group, and of a second methyl group on a double bond (slightly broadened singlet, 3 H, $\delta 1.72$). The NMR spectrum also displayed signals characteristic of an ethyl ester; a quartet (2 H, $\delta 4.10$, J = 7 Hz) and a triplet (3 H, $\delta 1.24$, J = 7 Hz).

The mass spectrum of altamisin showed a molecular ion at m/e 308 and a fragmentation pattern in accordance with the presence of the ethyl ester side chain attached to C-1 (e.g., m/e 221, 59 %, allylic cleavage of the C_2-C_3 bond).

The evidence so far described is fully in accordance with structure I for altamisin. Although the configuration at C-5 was not established, biogenetic considerations suggest that altamisin has the same configuration at C-5 as psilostachyin, since all pseudoguaianolides and psilostachyins isolated from the genus Ambrosia possess the same stereochemistry at this centre.

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