DIOXOAPORPHINE ALKALOID AND FLAVONE from piper manausense YUNK.

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RESUMEN

1,2-Metilendioxi-6-metil-4H-dibenzo [de,g] quinolina -4,5(6H)-diona; 5-hidroxi-4',7-dimetoxiflavona; β-sitosterol; estigmasterol y ésteres de los ácidos láurico y esteárico, fueron aislados del tallo de *Piper manausense* Yunk (Piperaceae).

ABSTRACT

1,2Methylenedioxy-6-methyl-4H-dibenzo [de,g] quinoline -4,5(6H)-dione together with 5-hydroxy-4',7-dimethoxyflavone; β-sitosterol, stigmasterol and esters from the lauric and stearic acids, were isolated from the stem of *Piper manausense* Yunk (Piperaceae).

INTRODUCCION

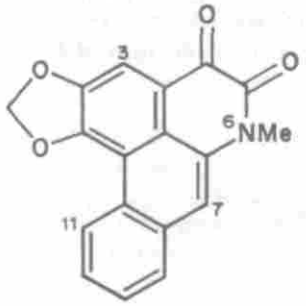
Aporphine alkaloids have been studied extensively because these compounds are of pharmacological significant importance (1). The presence of these constituents in the Piperaceae family has been reported in *Piper longum, P. auritum* and *P. sanctum* (2). In the present study, an investigation of the benzene extract of the stem of *Piper manausense* Yunk (Piperaceae) yielded 1,2-methylenedioxy-6-methyl-4H-dibenzo [de, g] quinoline-4,5(6H)-dione (Cepharadione-A) **1**, together with 5-hydroxy-4',7-dimethoxyflavone **2**, β-sitosterol, stigmasterol and esters from lauric and stearic acids.

RESULTS AND DISCUSSION

Cepharadione-A **1** was obtained from *P. manausense* as orange needles. Its EI-MS showed a molecular ion peak at am/z 305 and fragments at m/z 277(M^+-CO) and 249(M^+-2CO). The IR absorption bands at 1660 and 1595 cm^{-1} and the UV (237,

278, 285 sh, 302, 314 and 432) absorptions are similars to that 4,5-dioxoaphorphines (3). The ^{1}H NMR spectrum revealed the presence of one N-nethyl and one methylenedioxy group with the singlets at δ 3.85 and δ 6.46 respectively; two singlets at δ 8.14 and δ 7.51 were attributed to unusually poorly shielded hydrogen atoms placed at C-3 and C-7, respectively; this fact suggested that the **B** ring of the alkaloid was highly strained as expected for 4,5-dioxoaporphines (3). The other coupled aromatic protons in **1** cause three groups of PMR bands at δ 8.99-9.01 (m, H-11), δ 7.90-7.92 (m, H-8) and δ 7.66-7.73 (m, H-9 and H-10). Irradiation experiments of the most downfield aromatic absorption at δ 8.99-9.01, led to a 25% enhancement of the proton signal at δ 7.51 indicating the transannular coupling between H-11 and H-7, which confirmed the assignment for **1** (4). Cepharadione-A was previously isolated from *Piper longum* (2) and *P. sanctum* (5) in the Piperaceae family.

5-Hydroxy-4',7-dimethoxyflavone**2** is a known constituent of *Piper peepuloides* Roxb (6). This compound exhibited UV maxima at 328 and 270 nm, and IR absorption bands at 3400 cm^{-1} (OH) and 1630 cm^{-1}(CO). This information together with a study of its ^{1}H NMR spectrum indicated it to be a flavone. The signal at δ 3.85 was assigned to OMe-7 and OMe-4'. The two doublets (J = 3.0 Hz) at δ 6,36 and δ 6.48 were attributed to H-6 and H-8, respecitvely; the singlet at δ 6.00 corresponds to H-3. The pesence of an AA'BB' system was suggested by the two doublets (J = 8.0 Hz) at δ 7.00 and δ 7.85. This structure was confirmed by comparison with published spectral data (7) and by MS, which exhibited the molecular ion peak at m/z 298 in accord with a flavone containing one hydroxyl and two methoxyl groups. The retro-Diels Alder fragments (m/z 132 and m/z 166) showed the presence of one methoxyl group on **B** ring.



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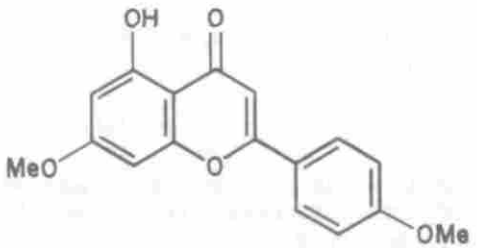

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EXPERIMENTAL

Plant material. The plant material used in this study was collected from the Ducké Forest Reserve, Manaus, Am., Brazil and identified by Dr. W. Rodrigues from the INPA, Manaus, where a voucher specimen is on deposit (INPA Herbarium No. 68227).

Extraction and isolation. Ground, dried stem (1 Kg) was extracted with benzene. The conc. extract (30g) was chromatographed on a silica gel column (200g). Elution with petrol yielded successively fatty esters (800 mg); β-sitosterol [1500 mg; mp 138-140° (MeOH); M^+ m/z 414] and stigmasterol [200 mg; mp 158-160° ($CHCl_3$); M^+ m/z 412). Elution with benzene gave 5-hydroxy-4',7-dimethoxyflavone **2** (80 mg). Next, the column was eluted with benzene-EtOAc (9:1) to obtain a mixture (75 mg) which was purified by preparative TLC on silica gel G, with $CHCl_3$-EtOAc (1:1) as eluting solvent, yielding cepharadione-A **1** (35 mg). The fatty ester fraction was transmethylated and the methyl esters analyzed by GC, using a Hewlett Packard 5700 A apparatus, a OV-275 (12%)/Chromosorb W HP column (5m x 2.5mm i. d.); the temperature was programmed from 130 to 230° at 4°/min with nitrogen as carrier gas. Identifications were achieved using methylic esters as internal standards. This analysis revealed the presence of lauric and stearic acids.

1,2-Methylenedioxy-6-methyl-4H-dibenzo [de,g] quinoline-4,5(6H)-dione. (Cepharadione-A) 1. Orange needles, mp > 300° (dec.) (EtOAc); λ_{max}^{MeOH} nm (log ξ): 237(4.00), 278(3.88), 285 sh (3.80), 302(3.94), 314(3.97), 432(4.08); ν_{max}^{KBr} cm^{-1}: 3050,2920, 2850, 1660, 1620, 1595, 1500, 1490, 1410, 1370, 1335, 1300, 1245, 1050, 940, 870; ^1H NMR (300 MHz, $CDCl_3$): δ 3.85(3H,s, N Me-6), 6.46(2H, s, CH_2O_2-1,2), 7.51(1H, s, H-7), 7.66-7.73 (2H, m, H-9, H-10), 7.90-7.92 (1H, m, H-8), 8.14(1H, s, H-3), 8.99-9.01(1H, m, H-11); MS m/z(rel. int.): 306(M^+ + 1, 17), 305(M^+, 90), 277(100), 276(18), 260(12), 249(4), 248(10).

5-Hydroxy-4',7-dimethoxyflavone. (Acacetin-7-methylether)2 Pale yellow needles, mp 168-170° ($CHCl_3$); λ_{max}^{EtOH} nm (log ξ): (270(4.23), 328 (4.30); ν_{max}^{KBr} cm^{-1}: 3400, 2860, 1630, 1500, 1440, 1350, 1250, 1190; ^1H, NMR (90 MHz, $CDCl_3$): δ 3.85(6H, s, OMe-4', OMe-7), 6.36 (1H, d, J = 3.0 Hz, H-6), 6.48(1H, d, J = 3.0 Hz, H-8), 6.00(1H, s, H-3), 7.00(2H, d, J = 8.0 Hz, H-3', H-5'), 7.85(2H, d, J = 8.0 Hz, H-2', H-6'), 12.8(1H, br s, OH-5); MS m/z (rel. int.): 298(100), 166(12), 132(20).

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