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STRYCHNOS - ASPIDOSPERMA ALKALOIDS AND A NOVEL HYDROXYDILACTAM ARTEFACT FROM LEUCONOTIS GRIFFITHII (APOCYNACEAE)

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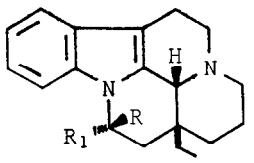
SUMMARY: The alkaloidal fraction of Leuconotis griffithii (Apocynaceae) extracts contains Strychnos-Aspidosperma alkaloids including eburnamine, methyl eburnamine, methyl isoeburnamine, norfluorocurarine, norfluorocurarine N-oxide and leuconolam (a hydroxydilactam artefact) as deduced from spectral and X-ray diffraction analysis.

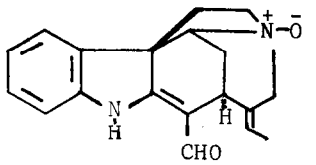
Leuconotis griffithii (Apocynaceae), a woody climber collected from Kepong Forest Reserve, Malaysia, was dried and extracted by methanol. Silica gel chromatography of the alkaloidal fraction provided a number of Strychnos-Aspidosperma alkaloids (300 mg/Kg) including eburnamine (1a)[1], methyl eburnamine (1b)[2], methyl isoeburnamine (1c)[2], norfluorocurarine[3] and norfluorocurarine N-oxide (2) as deduced from their spectral (UV, IR, MS, ^{1}HNMR and ^{13}CNMR) data. Norfluorocurarine N-oxide (2), a new natural product, showed similar 90 MHz-HNMR characteristics as norfluorocurarine (2) and both had similar 25 MHz-^{13}CNMR spectra except that the resonances at 56, 56.5 and 61 ppm due to carbons 21, 5 and 3 bonded to tertiary nitrogen in norfluorocurarine were shifted downfield to 70, 75, and 79 ppm respectively in 2 due to the N-oxide function.

1a : R=OH, R_1=H

1b : R=OMe, R_1=H

1c : R=H, R_1=OMe,





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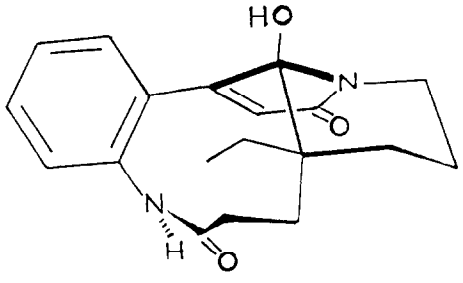
Significant amounts of a crystalline compound, leuconolam (m.p. 263-264° from aqueous ethanol), were also isolated. The e.i.-mass spectrum showed a molecular ion 326 ($C_{19}H_{22}N_2O_3$) as the base peak with other important fragments at 308 (6, M-H_2O), 297 (7, M-C_2H_5), 279 (4, M-H_2O-C_2H_5), 251 (3, M-H_2O-C_2H_5-CO), 186 (26), 172 (16), and 145 (34). Found, M^+; 326.1629. Calcd. for $C_{19}H_{22}N_2O_3$; 326.1630. The IR spectrum showed ν_{max}(KBr) 3460 (OH), 3190 (NH), 1690 (C=ON), 1650 (C=ON) and 1600 cm^{-1} (C=C). The 90 MHz-^{1}HNMR ($CDCl_3$) spectrum showed absorptions at 8.1 (1H, s, C=ONH, exchanged by D_2O), 7.9 (1H, br.d, ArH), 7.1-7.4 (3H, m, ArH),

5.82 (1H, s, =CH), 5.1 (1H, s, OH, exchanged by D_2O), 3.96 (1H, br.d, CHHN), 2.9 (1H, unresolved ddd, CHHN), 1.1-2.3 (10H, overlapping m, $5xCH_2$) and 0.54 (3H, t, CH_3). The ^{13}CHMR spectrum showed seven quaternary carbons at δ 177.8, 166.5, 155.7, 135, 133.1, 93.6, and 44.9, five methine carbons at 129.4, 129.3, 128.1, 126.6 and 126.1, six methylenes at 35.3, 32.1, 27.3, 25.4, 24.1, and 19.7 and one methyl at 6.9 ppm.

The spectral data seem to support an "indole-type" alkaloid or derivative containing C=CH-C=O, -C=ON, $-CH_2CH_3$ and C-OH functionalities. However, the UV spectrum λ_{max}(ethanol) 205 (ε 8960), 218 (9060), and ca 292 (sh, 1390) nm, is not typical and apparently excludes most indole-type structures or acylated o-substituted anilines. Single crystals of leuconolam $C_{19}H_{22}N_2O_3.2EtOH$ were obtained and the X-ray diffraction analysis[5] performed showed the structure to be 3 with the perspective drawing shown in Figure 1.



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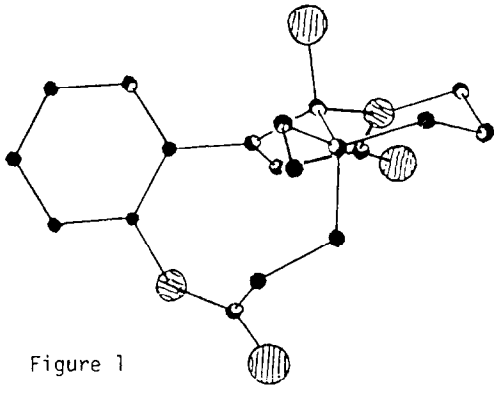

Figure 1

As shown, leuconolam has the unusual structural feature that the two N-C=O planes are out-of-plane with the benzene ring and this affects the spectral data particularly the UV spectrum. This skeletal type is similar to rhazinilam, an artefact previously isolated from Rhazya stricta[4]. Although present in fresh extracts of dried plant materials, leuconolam was absent in freshly collected plant material, showing that it was also an artefact from the oxidative transformation of an aspidosperma-alkaloid precursor.

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2. M.P. Cawa, S.K. Talapatra, K. Nomura, J.A. Weisbach, B. Douglas, and E.C. Shoop, Chem. Ind., 1242 (1963).
3. B. Pyuskyulev, I. Ognyanov and P. Panov, Tetrahedron Lett., 46, 4559 (1967).
4. K.T. De Silva, A.H. Ratcliffe, G.F. Smith and G.N. Smith, Tetrahedron Lett., 10, 913 (1972).
5. The crystals of 3 belong to the space group $P2_12_12_1$, with a=8.07, b=11.38 and c=20.46Å.

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