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DATURILINOL - A NEW WITHANOLIDE FROM THE LEAVES OF DATURA METEL

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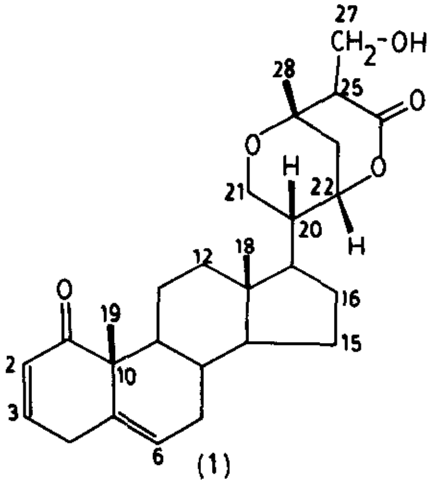
Abstract - A withanolide daturilinol (1) has been isolated from the fresh leaves of Datura metel and its structure elucidated through spectral studies.

Datura is the genera belongs to the family solonaceae, that are known for various tropane alkaloids[1,2] and C-28 steroidal lactones, related to ergostane-nucleus[3]. In an earlier communication we have reported the isolation and characterization of a withanolide daturilin from Datura metel[4]. A thorough research for the steroidal consitituents of the leaves of Datura metel has now led to the isolation of a new withanolide which is named as daturilinol (**1**) and its structure was established through spectroscopic studies.



(1)

Compound **1** was obtained as a white crystalline solid which on recrystallization from ethyl acetate-methanol (8:2) formed prismatic rods melted at 145-146°C, $[\alpha]_D^{20}$ -80° (c=0.09, $CHCl_3$). It has molecular formula $C_{28}H_{38}O_5$, determined through high resolution mass m/z 454.2791 (calcd. for $C_{28}H_{38}O_5$ 454.2719). Its uv spectrum showed band at 212 nm, indicating α,β-unsaturated chromophore without extended conjugation. The ir spectrum exhibited a band at 3450 cm^{-1} indicating the presence of hydroxyl group in the molecule and two bands at 1680 and 1710 cm^{-1}, represented α,β-unsaturated carbonyl and lactone respectively, which are characteristic of withanolides[5].

Apart from the molecular ion, the mass spectrum showed a fragment at m/z 436.2609, representing the loss of water molecule and a peak at m/z 365.2484 was due to the loss of C-25 to C-27 along with their oxygen functions. The prominent peaks at m/z 269.1831 and 268.1820 were indicative of M^+-side chain fragment with or without transfer of hydrogen. The ^{1}H-nmr spectrum of **1** showed two doublets of double doublets at δ 5.85 ($J_{2,3}$ = 10.0Hz, $J_{2,4a}$ = 3.2Hz, $J_{2,4b}$ = 1.2Hz) and 6.76 ($J_{3,2}$ = 10.0Hz, $J_{3,4a}$ = 4.9Hz,$J_{3,4b}$ = 2.5Hz) and a doublet of triplets at δ 5.55 (J = 6.1Hz) which have been attributed to olefinic protons H-2, H-3 and H-6 respectively. Three methyl groups H-18, H-19 and H-28 appeared as sharp singlets at δ 0.69, 1.21 and 1.31 respectively. Two double doublets of one-proton each, resonating at δ 2.82 ($J_{4a,4b}$=21.6Hz, $J_{4a,3}$ = 4.9Hz) and 3.27 ($J_{4b,4a}$ = 21.6Hz, $J_{4b,3}$ = 2.5Hz) have been assigned to H-4a and H-4b. The data recorded so far is comparable with that of daturilin[4]. However the signals of H-27a (δ 5.99, d, J_{gem} = 8.0Hz) and H-27b (δ 6.56, d, J_{gem} = 0.8Hz) of daturilin, appeared at δ 3.74 (dd, $J_{27a,27b}$ = 10.3Hz, $J_{27a,25}$ = 3.1Hz) and 3.98 (dd, $J_{27b,27a}$ = 10.3Hz, $J_{27b,25}$ = 8.1Hz) in case of **1**. Moreover, a one-proton double doublet ($J_{25,27a}$ = 3.1Hz, $J_{25,27b}$ = 8.1Hz) appeared at δ 2.45 which was assigned to H-25; and a one-proton broad singlet at δ3.56 was due to hydroxyl proton. In view of the above data which is comparable with the published data of withanolides[6-8], structure **1** has been assigned to daturilinol.

EXPERIMENTAL

Melting point was recorded in glass capillary tube and is uncorrected. The uv spectrum was recorded on Shimadzu uv-240 ultraviolet spectrometer and ir spectrum on JASCO A-302 infrared spectrometer. The ^{1}H-nmr spectrum was run on Bruker AM-300 spectrometer operating at 300 MHz and mass spectra on Varian MAT-112 and MAT-312 double focussing mass spectrometer connected to PDP 11/34 computer system.

Plant Material: The leaves of Datura metel (5 kg) collected from Karachi, Pakistan in Feb. 1987 were identified by Dr. S.I. Ali, Department of Botany, University of Karachi and voucher specimen has been deposited in the herbarium of that department.

Isolation: The fresh undried leaves were grinded with ultra-trrax and repeatedly percolated with ethylalcohol at room temperature. The combined extract was concentrated in vacuum at

45°C and the viscous concentrated extract was partitioned between 10% acetic acid and ethyl acetate. On evaporation of the ethyl acetate fraction a gummy mass was obtained which was defatted by repeated extraction with petroleum ether and remaining residue was redissolved in ethyl acetate and charcoaled. The clear solution was concentrated under reduced pressure and subjected to column chromatography (silica gel, 70-230 mesh, E.Merck). Purification of the petroleum ether-ether (1:1) eluate by thin layer chromatography (silica gel, chloroform) afforded a white crystalline solid which on recrystallization from ethyl acetate-methanol (8:2) formed prismatic rods, mp 145-146°C $[\alpha]_D^{20}$ - 80° (c = 0.09, $CHCl_3$), uv λ_{max}(MeOH) nm : 212, Ir ν_{max}($CHCl_3$) cm^{-1}: 3450, 1710 and 1680. Hrms m/z (rel.int. %) : 454.2791 (M^+, calcd. for $C_{28}H_{38}O_5$: 454.2719, 64), 436.2609 (M^+-H_2O, $C_{28}H_{36}O_4$, 22), 365.2484 ($C_{25}H_{33}O_2$, 18), 354.2208 ($C_{23}H_{30}O$,5), 269.1831 ($C_{19}H_{25}O$, 25), 268.1820 ($C_{19}H_{24}O$, 18), 253.1590 ($C_{18}H_{21}O$, 15), 225.1278 ($C_{16}H_{17}O$, 22), 185.0968 ($C_{13}H_{13}O$, 25) and 171.0816 ($C_{12}H_{11}O$, 42). ^{1}H-Nmr ($CDCl_3$) δ: 0.69 (3H, s, H-18), 1.21 (3H, s, H-19), 1.31 (3H, s, H-28), 1.72 (1H, m, H-20), 1.84 (1H, dd, $J_{23a'23b}$ = 13.3Hz, $J_{23a,22}$ = 4.1Hz, H-23a), 1.97 (1H, dd, $J_{23b,23a}$ = 13.3Hz, $J_{23b,22}$ = 1.8Hz, H-23b), 2.45 (1H, dd, $J_{25,27a}$ = 3.1Hz, $J_{25,27b}$ = 8.1Hz, H-25), 2.82 (1H, dd, $J_{4a,4b}$ = 21.6Hz, $J_{4a,3}$=4.9Hz, H-4a), 3.27 (1H, dd, $J_{4b,4a}$ = 21.6Hz, $J_{4b,3}$ = 2.5Hz, H-4b), 3.56 (1H, br s, OH), 3.64 (1H, dd, $J_{21\alpha,21\beta}$= 13.8Hz, $J_{21\alpha,20}$ = 3.1Hz, H-21α) 3.74 (1H, dd, $J_{27a,27b}$ = 10.3Hz, $J_{27a,25}$ = 3.1Hz, H-27a), 3.90 (1H, d, $J_{21\beta,21\alpha}$= 13.8Hz, H-21β), 3.98 (1H, dd, $J_{27b,25}$ = 8.1Hz, $J_{27b,27a}$ = 10.3Hz, H-27b), 4.67 (1H, brs, $w_{\frac{1}{2}}$ = 2.9Hz, H-22), 5.55 (1H, dt, J = 6.1Hz, H-6), 5.85 (1H, ddd, $J_{2,3}$ = 10.0Hz, $J_{2,4a}$ = 3.2Hz, $J_{2,4b}$ = 1.2Hz, H-2) and 6.76 (1H, ddd, $J_{3,2}$ = 10.0Hz, $J_{3,4a}$ = 4.9Hz, $J_{3,4b}$ = 2.5Hz, H-3).

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