

DATUMELIN – A NEW WITHANOLIDE FROM *DATURA METEL L.*

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From the alcoholic extract of the fresh, undried leaves of *Datura metel*, a new withanolide datumelin has been isolated and its structure elucidated by spectroscopic studies.

**Key words:** *Datura metel*, Withanolide, Datumelin.

## INTRODUCTION

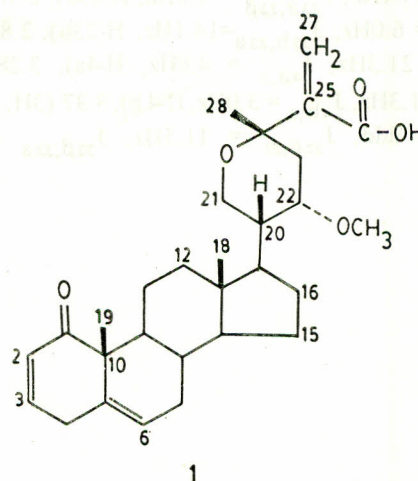
*Datura* is a genus in the family Solanaceae which is commonly known for tropane alkaloids [1], while reports on the isolation of a few withanolides and C-28 steroidal lactones from several *Datura* species are on record [2, 3]. Earlier, we have reported the isolation and characterization of a tropane alkaloid [4] and a withanolide [5] from the leaves of *Datura metel*. Extended studies in the non-alkaloidal constituents of the same plant have led to the isolation of a new withanolide datumelin and its structure has been established as 1 through spectroscopic studies.

## RESULTS AND DISCUSSION

The acetic acid insoluble fraction of the ethanolic extract of the leaves of *Datura metel* was subjected to column chromatography, affording a white crystalline solid which formed irregular plates on recrystallization from chloroform-methanol (1:1) m.p. 170-173° |  $\alpha$  |  $D_{20}^{20}$  - 21° (C=O. 6, CHCl<sub>3</sub>). Its UV spectrum showed absorption at 212 nm, indicating the presence of  $\alpha,\beta$ -unsaturated ketone without extended conjugation. The IR spectrum exhibited a band for -OH stretching at 3250 and two bands at 1740 and 1685 cm<sup>-1</sup> for acid carbonyl and  $\alpha,\beta$ -unsaturated carbonyl groups [6]. The high resolution mass spectrum gave the molecular ion peak at m/z 468.2869, corresponding to the molecular formula C<sub>29</sub>H<sub>40</sub>O<sub>5</sub>. A peak at m/z 453.2631 is due to the loss of methyl group and the peak at m/z 437.2700 represents the loss of methoxy group, whereas the peak at m/z 365.2486 showed the further loss of C<sub>25</sub>-C<sub>27</sub>. The peak at m/z 269.1838 and 268.1818 corresponds to the fragments of compositions C<sub>19</sub>H<sub>25</sub>O and C<sub>19</sub>H<sub>24</sub>O formed by the elimination of side chain, with or without hydrogen rearrangement. The <sup>1</sup>H-NMR spectrum exhibited four sharp singlets at  $\delta$  0.78, 1.24,

1.42 and 3.37 which have been assigned to H-18, H-19, H-28 and OCH<sub>3</sub> groups respectively.

Two double doublets of one proton each resonating at  $\delta$  2.82 ( $J_{4a,4b} = 21.3\text{Hz}$ ,  $J_{4a,3} = 4.8\text{Hz}$ ) and  $\delta$  3.28 ( $J_{4b,4a} = 21.3\text{Hz}$ ,  $J_{4b,3} = 3.0\text{Hz}$ ) have been attributed to H-4a and H-4b. The downfield region of <sup>1</sup>H-NMR showed two doublets of double doublets at  $\delta$  5.83 ( $J_{2,3} = 10.4\text{Hz}$ ,  $J_{2,4a} = 3.1\text{Hz}$ ,  $J_{2,4b} = 1.3\text{Hz}$ ) and 6.77 ( $J_{3,2} = 10.4\text{Hz}$ ,  $J_{3,4a} = 4.8\text{Hz}$ ,  $J_{3,4b} = 3.0\text{Hz}$ ) assigned to H-2 and H-3. H-6 appeared at  $\delta$  5.55 as doublet of triplet ( $J = 6.1\text{Hz}$ ,  $W_{1/2} = 1.6\text{Hz}$ ) and the remaining two vinylic protons as narrow doublets ( $J = 0.8\text{Hz}$ ) at  $\delta$  6.01 and 6.69 respectively whereas the acidic proton appeared at  $\delta$  10.30 as a broad singlet. These observations and comparative studies with the spectral data of other withanolides [7-10] collectively led to the assignment of structure 1 for datumelin.



## EXPERIMENTAL

The melting point was recorded in a glass capillary tube and is uncorrected. The UV and IR spectra were recorded on Shimadzu UV-240 and JASCO A-302 spectrometers



respectively. The  $^1\text{H-NMR}$  spectrum was recorded on a Bruker AM-300 spectrometer and the mass spectra on Varian MAT 112 and MAT-312 double focusing mass spectrometers connected to a PDP 11/34 computer system.

*Isolation.* The fresh undried leaves of *Datura metel* were ground in ultra-turrax and repeatedly extracted with ethanol at room temperature. The combined extracts were concentrated under reduced pressure to a viscous gummy mass, which was partitioned between 10% acetic acid and ethyl acetate. The darkish green ethyl acetate phase was charcoaled, freed of the solvent under reduced pressure and treated with petroleum ether to remove the fatty material. The remaining residue was subjected to column chromatography (silica gel, 70-230 mesh, E. Merck). The petroleum ether-ether (1:1) eluate was purified by thin layer chromatography (chloroform-methanol 99:1), affording a white crystalline solid which formed irregular plates m.p. 170-173 $^{\circ}$  on recrystallization from chloroform-methanol (1:1),  $n_D^{20} = 1.4721$  (C=0.6,  $\text{CHCl}_3$ ) UV  $\lambda_{\text{max}}$  (MeOH) : 212 nm, IR  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) : 3250, 1740 and 1685  $\text{cm}^{-1}$ , HRMS m/z (rel. int. %): 468.2869 ( $\text{M}^+$ , calcd. for  $\text{C}_{29}\text{H}_{40}\text{O}_5$ , 468.2875, 22), 453.2631 ( $\text{C}_{28}\text{H}_{37}\text{O}_5$ , 24), 437.2700 ( $\text{C}_{28}\text{H}_{37}\text{O}_4$ , 30), 365.2486 ( $\text{C}_{25}\text{H}_{33}\text{O}_2$ , 10), 269.1838 ( $\text{C}_{19}\text{H}_{25}\text{O}$ , 12), 268.1818 ( $\text{C}_{19}\text{H}_{24}\text{O}$ , 18), 253.1601 ( $\text{C}_{18}\text{H}_{21}\text{O}$ , 8), 225.1275 ( $\text{C}_{16}\text{H}_{17}\text{O}$ , 32), 185.0971 ( $\text{C}_{13}\text{H}_{13}\text{O}$ , 22) and 171.0825 ( $\text{C}_{12}\text{H}_{11}\text{O}$ , 42).  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 0.78 (3H, s, H-18), 1.24 (3H, s, H-19), 1.42 (3H, s, H-28), 1.71 (1H, m, H-20), 1.94 (1H, dd,  $J_{23a,23b} = 14.1\text{Hz}$ ,  $J_{23a,22\beta} = 1.5\text{Hz}$ , H-23a), 2.18 (1H, dd,  $J_{23b,22\beta} = 6.0\text{Hz}$ ,  $J_{23b,23a} = 14.1\text{Hz}$ , H-23b), 2.82 (1H, dd,  $J_{4a,4b} = 21.3\text{Hz}$ ,  $J_{4a,3} = 4.8\text{Hz}$ , H-4a), 3.28 (1H, dd,  $J_{4b,4a} = 21.3\text{Hz}$ ,  $J_{4b,3} = 3.0\text{Hz}$ , H-4b), 3.37 (3H, s,  $\text{OCH}_3$ ), 3.78 (1H, ddd,  $J_{22\beta,20} = 11.5\text{Hz}$ ,  $J_{22\beta,23a} = 1.5\text{Hz}$ ,

$J_{22\beta,23b} = 6.0\text{Hz}$ , H-22 $\beta$ ), 4.14 (1H, dd,  $J_{21\alpha,21\beta} = 10.6\text{Hz}$ ,  $J_{21\alpha,20} = 1.8\text{Hz}$ , H-21 $\alpha$ ), 4.27 (1H, dd,  $J_{21\beta,21\alpha} = 10.6\text{Hz}$ ,  $J_{21\beta,20} = 3.5\text{Hz}$ , H-21 $\beta$ ), 5.55 (1H, dt,  $J = 6.1\text{Hz}$ ,  $W_{1/2} = 1.6\text{Hz}$ , H-6), 5.83 (1H, ddd,  $J_{2,3} = 10.4\text{Hz}$ ,  $J_{2,4a} = 3.1\text{Hz}$ ,  $J_{2,4b} = 1.3\text{Hz}$ , H-2), 6.01 (1H, d,  $J = 0.8\text{Hz}$ , H-27a), 6.69 (1H, d,  $J = 0.8\text{Hz}$ , H-27b), 6.77 (1H, ddd,  $J_{3,2} = 10.4\text{Hz}$ ,  $J_{3,4a} = 4.8\text{Hz}$ ,  $J_{3,4b} = 3.0\text{Hz}$ , H-3) and 10.30 (br s, COOH).

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