

Note

Studies on the chemical constituents of *Nardostachys jatamansi* DC (Valerianaceae)

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A new sesquiterpene acid, nardin and a new pyranocoumarin have been isolated from the rhizomes of *Nardostachys jatamansi* and characterized as *E*-2-methyl, 3-(5,9-dimethylbicyclo[4.3.0]nonen-9-yl)-2-propenoic acid and 2',2'-dimethyl-3'-methoxy-3',4'-dihydropyranocoumarin, respectively using spectral studies and chemical correlation. The stereochemistry of nardin has been determined using X-ray crystallographic studies.

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The rhizomes and roots of *Nardostachys jatamansi* DC (locally known as Jatamansi) are used as an antistress agent in traditional medicine and marketed in India as an anti-convulsant Ayurvedic drug, Ayush 56. The occurrence of a number of sesquiterpenes, lignans, neo-lignans and coumarins has been reported¹. Previously the authors isolated a new terpenoid ester, nardostachysin², the structure and stereochemistry of which was established as 7',8'-dihydroxy-4'-methylene hexahydrocyclopenta[*c*]pyran-1'-one-8'-methyl ester of 7,9-guaiadien-14-oic acid using spectral and chemical studies.

Results and Discussion

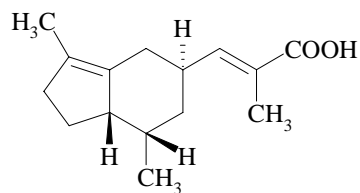
In the present investigation a new sesquiterpene acid, nardin **1** and a new pyranocoumarin **2** have been isolated from this plant, besides several known coumarins. The present communication reports in detail the structure and stereochemistry of nardin **1** and the pyranocoumarin **2**.

The hexane extract on column chromatography over silica gel afforded nardin **1**, C₁₅H₂₂O₂ (M⁺ 234), [α]_D²⁵ -123.8° (EtOH), m.p. 133-34°C, yield 0.01%

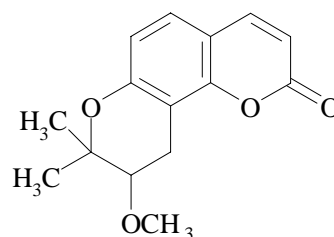
from the *n*-hexane eluent. In the infrared spectrum the peak at 1683 cm⁻¹ indicates the presence of an α,β-unsaturated carbonyl group which has been confirmed from the ¹³C NMR peak at 173.9 ppm. The ¹H NMR spectrum of the compound **1** indicates the presence of three methyl groups at δ 1.89 (3H, s, vinylic methyl), 1.63 (3H, s, vinylic methyl) and 0.79 (3H, d, *J* = 7.0 Hz). A significant peak at 7.19 (1H, d, *J* = 9.9 Hz) was observed thereby confirming the presence of an olefinic proton.

The ¹³C NMR spectrum of the compound **1**, including DEPT experiment, reveals the presence of 15 carbon atoms of which three methyl carbons appeared at δ 13.5, 12.1 and 12.0 ppm, four methylene carbons were discernible at δ 37.5, 28.8, 25.5 and 24.6 ppm and four quaternary carbons at δ 173.9, 133.3, 131.2 and 125.3 ppm. Considering the spectral properties, the structure of this new compound appeared to be **1**.

The structure of nardin **1** was firmly established by X-ray crystallographic analysis (Figure 1. ORTEP diagram). Figure 2 shows the content of the asymmetric unit as a dimer of chatnj-X molecules associated head-to-head through their carboxylic functions. The structure was found to be chiral with tetragonal space group P_{41,21,2} (solved in P₄₁); cell: *a* = *b* = 11.03 and *c* = 53.5 Å with four molecules in the asymmetric unit. The structure of the compound was thereby established as **1**.



1



2

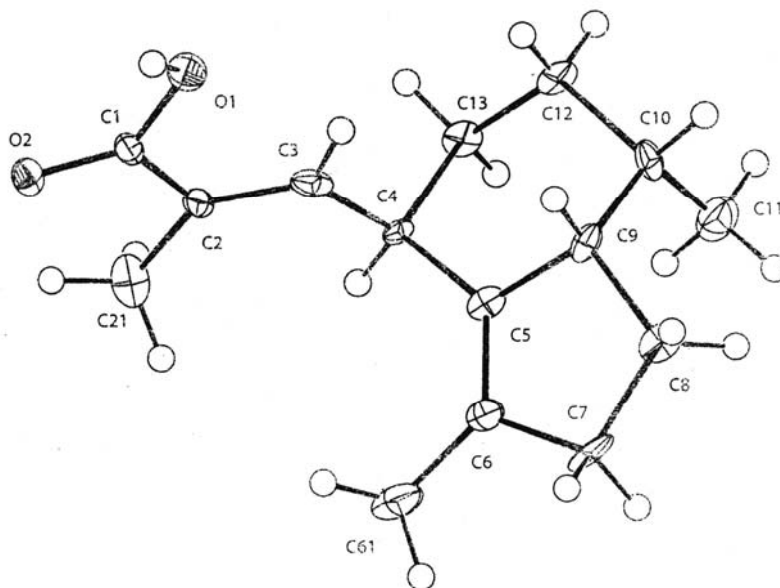


Figure 1—The ORTEP view of one monomer of the asymmetric unit with the numbering adopted in the X-ray determination. All ellipsoids are drawn at the 50% probability level except for hydrogens represented as spheres of arbitrary radii.

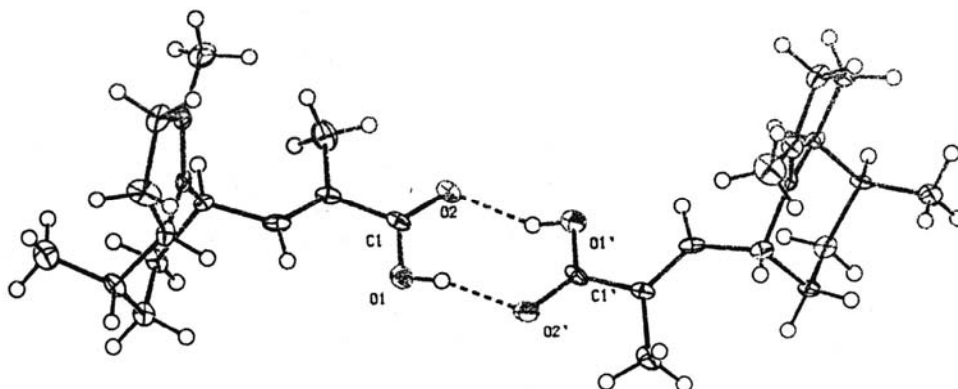


Figure 2—The content of the asymmetric unit is a dimer of *chatnj-x* molecules, associated head-to-head through their carboxylic functions.

Besides nardin **1** several furanocoumarins viz. angelicin, oroselin and pyranocoumarins viz. jatamansin, jatamansinol have been reported from this plant^{3,4}. On chromatographic resolution using 5% ethyl acetate in hexane as eluent colourless crystals of the pyranocoumarin **2**, C₁₅H₁₆O₄ (M⁺ 260), m.p. 81°C (hexane-methanol mixture) were obtained in 0.004% yield. From the spectral analysis its structure was established as 2',2'-dimethyl-3'-methoxy-3',4'-dihydropyranocoumarin **2**. The UV absorption spectrum in ethanol exhibit peaks at $\lambda_{\max}^{\text{MeOH}}$: 221 (log ϵ 3.01), 249 (log ϵ 2.80), 257 (log ϵ 2.83) and 320 (log ϵ 3.20) nm characteristic of pyranocoumarins. IR spectral band at 1721 cm⁻¹ indicates the presence of δ -lactone. The ¹H NMR spectrum of the compound indicate the

presence of four aromatic protons at δ 6.18 (1H, d, J = 9.4 Hz, H-3), 7.57 (1H, d, J = 9.4 Hz, H-4), 7.25 (1H, d, J = 8.4 Hz, H-5) and 6.80 (1H, d, J = 8.5 Hz, H-6) typical of coumarin moiety. Further, its ¹H NMR spectrum displayed signals due to two methyls at δ 1.82 (3H, s), 1.65 (3H, s) and a methoxyl at 3.9 (3H, s).

Materials and Methods

The rhizomes of *N. jatamansi* DC. were collected in June 2003, and were identified by Prof. Nanda Dulal Paria, Department of Botany, Ballygunge Science College, Calcutta University. A voucher specimen (NJ-7) has been deposited at the Centre of

Advanced Studies on Natural Products, Department of Chemistry, Calcutta University.

Air dried powdered rhizomes (2.5 kg) were extracted with *n*-hexane for 48 hr in a Soxhlet apparatus. After removal of the solvent from the extract the residue obtained (134 g) was subjected to column chromatography over silica gel using *n*-hexane, *n*-hexane-ethyl acetate and ethyl acetate-methanol as eluates.

Experimental Section

Melting points were determined in an electrically heated chamber and are uncorrected. The specific rotation was measured in a Perkin-Elmer 241 polarimeter in ethanol. The UV (in EtOH) and IR (KBr) spectra were recorded using a Hitachi U-2000, and Perkin-Elmer RX I FT-IR spectrophotometers. The ^1H and ^{13}C NMR spectra were run on Bruker AM-300L spectrometer and mass spectra were recorded on a Finnigan MAT-H-SQ-30 mass spectrometer.

Column chromatographic analysis was carried out using silica gel (60-120, S.D. FINE-CHEM Ltd., India). TLC analysis was carried out using silica gel G (Spectrochem, India). The spots were detected with iodine vapour. Analytical samples were routinely dried *in vacuo* over P_2O_5 for 24 hr. Anhydrous sodium sulphate was used for drying the organic solvents.

Nardin 1: The hexane fraction afforded the compound **1** as colourless crystals which were crystallized from hexane-methanol mixture, $[\alpha]_{\text{D}}^{25}$ -123.8° (c, 0.1042 g/100 mL, EtOH); m.p. 133-34°C; yield 0.01%, (M^+ 234); Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.92; H, 9.40. Found: C, 76.71; H, 9.34; IR (KBr): 2934, 1683, 1424 and 1299 cm^{-1} ; UV (EtOH): 224.5 (log ϵ : 3.04); ^1H NMR (300 MHz, CDCl_3): δ 7.19 (1H, d, $J = 9.9$ Hz), 3.55 (1H, m), 2.94 (1H, m), 2.20 (2H, m), 2.17 (1H, m), 1.89 (3H, s), 1.85-1.75 (4H, m), 1.43 (2H, m), 1.63 (3H, s), 0.79, (3H, d, $J = 7.0$ Hz); ^{13}C NMR (75.5 MHz, CDCl_3): δ 173.9 (C-1), 146.3 (C-3), 133.3 (C-2), 131.2 (C-1'), 125.3 (C-9'), 47.5 (C-3'), 37.5 (C-2'), 34.6 (C-6'), 33.1 (C-5'), 28.8 (C-8'), 25.4 (C-4'), 24.6 (C-7'), 13.5 (C-2'-Me), 12.1 (C-9'-Me), 12.0 (C-5'-Me).

Crystal data

Nardin 1: Tetragonal, space group $\text{P4}_1 2_1 2$ (or $\text{P4}_3 2_1 2$). The system was chiral (optically active). All parameters have been given: $a = b = 11.030$ (3) and $c = 43.350$ (5) Å, $Z = 16$ (2 molecules/a.u.). The data

were recorded at 100 K with a MARRESEARCH Image Plate detector (345 mm). Data consists of 100 frames, 4-degree rotation each (more than 360° rotation). They were processed using the DENZO/SCALEPACK computer programmes⁵. The initial number of reflection was 15057 and reduced to a number of 2427 equivalent reflections with a R_{sym} factor of 0.031 (completeness: 98.7%).

The structure was solved by direct methods and refined with the SHELX97 suite of programmes⁶. The final structure has been depicted in **Figures 1** and **2**, final R factor: 0.065 (for all 2399 accepted reflections), $R = 0.064$ (for 2335 observed reflections). The coordinates were deposited as a cif file with the CCDC under the n° CCDC 212288.

Pyranocoumarin 2: Elution with 5% ethyl acetate in hexane afforded the compound as colourless crystals which were crystallized from hexane-methanol mixture. Yield 0.004%; m.p. 81°C (M^+ 260); Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4$: C, 69.23; H, 6.15. Found: C, 69.01; H, 6.11; UV (EtOH): 221 (log ϵ 3.01), 249 (log ϵ 2.80), 257 (log ϵ 2.83) and 320 (log ϵ 3.20) nm; IR (KBr): 1721, 1605, 1250, 1120, 1089, 826 and 698 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 7.57 (1H, d, $J = 9.4$ Hz), 7.25 (1H, d, $J = 8.4$ Hz), 6.80 (1H, d, $J = 8.4$ Hz), 6.18 (1H, d, $J = 9.4$ Hz), 5.21 (1H, m), 3.9 (3H, s), 3.52 (2H, m), 1.82 (3H, s), 1.65 (3H, s); ^{13}C NMR (75.5 MHz, CDCl_3): δ 161.06 (C-2), 160.3 (C-7), 152.97 (C-8a), 143.72 (C-4), 132.4 (C-8), 126.22 (C-5), 121 (C-3'), 118.2 (C-2'), 113.06 (C-4a), 112.95 (C-3), 107 (C-6), 56.04 (C-3'-OMe), 25.75 (C-2'-Me), 21.94 (C-4'), 17.91 (C-2'-Me).

Acknowledgement

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