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VINCAPUSINE, A MINOR INDOLE ALKALOID OF *VINCA PUSILLA*

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INTRODUCTION

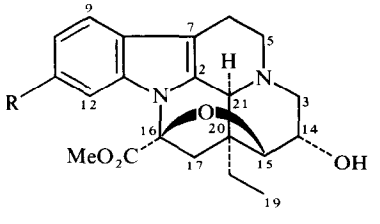
The genus *Vinca* of the family Apocynaceae is well reported for producing biologically active indole bases having novel structural patterns [1]. Although extensive work has been done on other *Vinca* species, very little work has so far been carried out on the chemical constituents of *Vinca pusilla* [2]. This plant is distributed throughout the Western Himalayas, upper Gangetic plain, Bihar, Orissa extending south towards Karnatak in India and is well known for its medicinal values [3]. In this paper we report the isolation of a new minor indole alkaloid, designated vincapusine (**1**), from both the roots and leaves of *V. pusilla*.

RESULTS AND DISCUSSION

The basic fractions of the ethanolic extracts of the leaves and roots of *V. pusilla* yielded a new minor indole alkaloid, vincapusine (**1**), besides the alkaloids lochnericine, vindorosine and venoterpine [4].

The M^+ peak of *m/e* 368.1746 proved that vincapusine (**1**) possesses the molecular formula $C_{21}H_{24}N_2O_4$ (calc. for $C_{21}H_{24}N_2O_4$ 368.1735). The UV spectrum of **1** exhibiting λ_{max} (EtOH) at 228 (log ε 4.40), 271 (3.89), 280 (sh 3.82) and 292 nm (sh 3.56) with no shift of maxima in acid or base indicated the presence of an indolic chromophore. The absorption maxima were similar to those of vincine, cuanzine, vincarodine and criocerine, indicating its structural similarity [5–8].

In the mass spectrum a strong peak at *m/e* 170 indicated the presence of a tetrahydro-β-carboline moiety [9]. The presence of a carbomethoxy and of a hydroxyl group was secured by IR absorptions (KBr) at 1758 and 3500 – 3150 cm^{-1} (broad), ^1H NMR signals at δ 4.02 (3H, *s*) and 1.83 (1H), the latter signal disappearing upon deuteration, and by the peak at *m/e* 309 due to the loss of CO_2Me. The ^1H NMR spectrum also indicated the presence of an ethyl group (δ 1.02, *t*, J = 7.4 Hz), an unsubstituted indole ring (δ 6.8–7.5, 4H, *m*) and signals at δ 2.35 and 2.74 (J = 12 Hz, one proton each for CH_2, AB system) and a one proton singlet at δ 4.14 characteristic of a *cis*-quinolizidine ring system [10]. Other proton signals in the region at δ 1–4 ppm and mass fragments at *m/e* 339, 280, 267 and 184 of vincapusine were similar to those of vincarodine (**2**) [7] in all respects except for the absence of an aromatic methoxy group. The foregoing evidence was thus in conformity with the structure **1** for vincapusine.



1 R = H
2 R = OMe

EXPERIMENTAL

The powdered air dried and defatted leaves (5 kg) of *V. pusilla* Murr. (supplied by United Chemicals and Allied Products, Calcutta and identified by National Botanical Gardens, Howrah, West Bengal) were extracted exhaustively with EtOH. The EtOH extract was concd under red. pres. and then mixed with 5% citric acid. The aq. layer was made alkaline with dil. NH_4OH and then extracted with Et_2O. The Et_2O layer was dried and the residue, after removal of solvent, was absorbed onto a column of Al_2O_3. The C_6H_6 and $CHCl_3$ eluates yielded vindorosine and venoterpine respectively [4]. Further elution of the column with $CHCl_3$–MeOH (19:1) yielded a white crystalline alkaloid (15 mg), vincapusine (**1**), mp 263° (EtOAc–petrol), $C_{21}H_{24}N_2O_4$ (M^+ 368.1746), $[\alpha]_D$ = −122° ($CHCl_3$, *c* 0.04), exhibited the following spectral data: UV (EtOH) maxima at 228 (log ε 4.40), 271 (3.89), 280 (*sh* 3.82) and 292 nm (*sh* 3.56); IR (KBr): 3500–3150 (m), 1758 (*vs*), 1620 (*w*) 1450 (*s*) and 945 cm^{-1} (*s*); ^1H NMR ($CDCl_3$): δ 1.02 (3H, *t*, J = 7.4 Hz, H-19), 1.85 (1H, *br*, −OH), 1.77 and 2.05 (2H, *m*, J = 14.4 and 7.4 Hz, H-18), 2.13 and 2.25 (2H, *m*, H-3), 2.35 and 2.74 (1H each, *d*, J = 12 Hz, H-17), 2.67 and 2.82 (2H, *m*, H-6), 3.15 and 3.33 (2H, *m*, H-5), 3.71 (1H, *m*, H-14), 3.93 (1H, *d*, J = 2.6 Hz, H-15), 4.02 (3H, *s*, $-CO_2Me$), 4.14 (1H, *s*, H-21) and 6.8–7.5 ppm (4H, *m*, aromatic). MS (% rel. intensity): 368 (57, M^+), 339 (3), 309 (8), 280 (4), 267 (93), 266 (100), 252 (13), 238 (23), 208 (27), 193 (10), 184 (12) and 170 (43).

The basic portion of the EtOH extract of the roots (7 kg) of *V. pusilla* on chromatographic separation over Al_2O_3 resulted in the isolation of lochnericine in the C_6H_6 eluted fractions [4]. Further elution of the same chromatogram with $CHCl_3$–MeOH (19:1) furnished a white crystalline compound (10 mg) identical with vincapusine (**1**).

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