Isolation and Structure of Rosamine — a New Pseudoindoxyl Alkaloid from *Catharanthus roseus*

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The isolation and structure of a new pseudoindoxyl alkaloid from _Catharanthus roseus_ leaves is described.

We have recently reported the isolation and structure of a number of new alkaloids from the leaves of _Catharanthus roseus_ (L) G. Don [1—3]. Our continuing studies on the same plant have resulted in the isolation of a new pseudoindoxyl alkaloid, "rosamine", to which structure 1 has been assigned.

**Experimental**

Leaves of _Catharanthus roseus_ (L) G. Don (72 kg) were collected from a field grown in the Karachi University campus. The crude alkaloids (134 g) obtained from the alcoholic extract of the air-dried leaves (24 kg) of the plant, were dissolved in chloroform (450 ml) and extracted with pH 3 phosphate buffer (1 l). The chloroform layer was dried (anhydrous Na₂SO₄), concentrated to 1/3 of its original volume and petroleum ether (320 ml) added to the chloroform solution which caused some of the alkaloids to precipitate out. The precipitates were filtered, and the filtrate was again concentrated to a gum (40 g). The gum was dissolved in ethyl acetate (200 ml) and extracted with pH 2 phosphate buffer (1 l). The aqueous layer was separated, washed with chloroform, basified with ammonia to pH 10 and again extracted with chloroform (1.5 l) to afford fraction F1 (22 g). This fraction was chromatographed on an alumina column (220 g) elution being carried out with ethyl acetate (5 l). The eluates were concentrated (12 g) and again loaded an another column of t.l.c. grade silica (36 g). The column was eluted with increasing polarities of petroleum ether, ethyl acetate, and ethyl acetate-methanol. Elution with ethyl acetate-methanol (9:1) afforded an alkaloid-containing fraction, which was concentrated and subjected to preparative t.l.c. (alumina) in acetone-petroleum ether (3:1) to afford the pure alkaloid, named "rosamine".

**Results and Discussion**

Rosamine was isolated as an amorphous material by differential pH extraction, column chromatography and preparative TLC. The alkaloid possessed an intense yellow fluorescence, [α]₀ = +100° (CHCl₃). The UV absorption maxima appeared at 228, 255 and 390 nm, while the minima appeared at 246, 280 and 340 nm, characteristic of the pseudoindoxyl system and strikingly similar to the UV spectra of the Iboga type pseudoindoxyl alkaloids iboluteine [4], demethoxyiboluteine [5], rupicoline and montanine [6].

The infrared spectrum of rosamine afforded a strong absorption at 1720 cm⁻¹ indicating the presence of an ester carbonyl group. Another absorption at 1690 cm⁻¹ suggested the presence of a conjugated carbonyl group.

The mass spectrum of rosamine showed the molecular ion at m/z = 352.1779 (C₂₁H₂₄N₂O₃, Calcd for C₂₁H₂₆N₂O₃, 352.1789) with other major peaks at 335 (5%), 293 (5%), 267 (8%), 216 (3%), 184 (7%), 158 (20%), 135 (100%) and 107 (50%). The fragmentation pattern of rosamine, given in the Scheme (1), is similar to that of the other four members of this series. The base peak at m/z = 135.1047 (C₁₀H₁₃N, Calcd for C₁₀H₁₃N, 135.1047), was attributed to the fragment 1 commonly found in the Iboga and Aspidosperma alkaloids bearing a double bond in the piperidine ring.

From its color, UV, IR and mass spectrum, it was apparent that rosamine was a pseudoindoxyl alkaloid while the strong resemblance of the mass spectrum to that of catharanthine suggested that rosamine may be derived from the catharanthine system. Further support to the presence of a pseudoindoxyl system came from the presence of a fragment at m/z = 158.0600 (C₁₀H₁₄NO, Calcd for C₁₀H₁₄NO, 158.0605) to which structure 2 was assigned.

The proton NMR of rosamine bore a distinct resemblance to the NMR of catharanthine except that some peaks were found to be shifted slightly upfield.
A three proton triplet resonated at $\delta$ 1.0 (7.3 Hz) corresponding to the methyl group of the ethyl side chain. A striking difference in the NMR spectrum of rosamine as compared to that of catharanthine was the upfield shift of the ester methyl group in rosamine, which resonates at $\delta$ 3.19 while in catharanthine it appears at $\delta$ 3.78. This upfield shift is due to the shielding of the ester methyl protons by the indole nucleus. A similar situation is encountered in the pseudoindoxyl of voacangine when compared to voacangine itself [7]. A one-proton doublet at $\delta$ 4.55 (4.4 Hz) was assigned to the C-21 proton $\alpha$-to the nitrogen. Structure 1 is assigned to rosamine on the basis of these data.