TAXILAMINE, A PSEUDOBENZYLISOQUINOLINE ALKALOID

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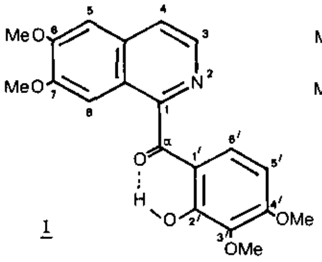
Abstract: The phenolic pseudobenzylisoquinoline taxilamine (1) has been obtained from *Berberis aristata* DC (Berberidaceae). Pseudobenzylisoquinolines are fairly widespread in nature, being found among members of the Berberidaceae, Annonaceae, Ranunculaceae and Fumariaceae.

Pseudobenzylisoquinoline alkaloids are benzylisoquinolines which incorporate three oxygenated substituents in the bottom aromatic ring. Although no *in vivo* studies using labeled precursors have as yet been conducted to ascertain their biogenesis, they most probably originate from the oxidation of protoberberinium salts. The group includes polycarpine (2) found in *Enantia polycarpa* Engl. and Diels (Annonaceae),[2,3] rugosinone (3) obtained from *Thalictrum rugosum* Ait. (Ranunculaceae),[4] and (-)-ledecorine (4) present in *Corydalis ledebouriana* K. et K. (Fumariaceae).[5] We now wish to describe the isolation and characterization of a fourth pseudobenzylisoquinoline, namely the phenolic base taxilamine (1).

Extraction with 10% acetic acid of 2 kg of the drug known in Pakistan as "rasaut", consisting of the powdered root bark of *Berberis aristata* DC (Berberidaceae), was followed by filtration of the extracts, and basification using ammonium hydroxide. The aqueous solution was then extracted with chloroform, and the organic solvent evaporated. Chromatography of the alkaloidal fraction (8 g) using neutral alumina, and elution with ethyl acetate-petroleum ether afforded berberine (5) and crude taxilamine which was further purified by silica gel TLC (ethyl acetate-petroleum ether 80:20 v/v) to give amorphous but pure taxilamine (1) (3 mg), λ_{max}^{MeOH} 238, 299 and 330 sh nm (log ε 4.48, 4.02 and 3.85), $\lambda_{max}^{MeOH\text{-}OH^-}$ 237, 292, 328 sh and 380 nm (log ε 4.53, 3.97, 3.80 and 3.77).

The 360 MHz (FT, $CDCl_3$) nmr spectrum of taxilamine shows H-5 and H-8 as singlets at δ7.15 and 7.40, respectively; H-3 and H-4 as a doublet of doublets at δ8.46 and 7.66 (J_{vic} = 5.5 Hz); and H-5' and H-6' as another doublet of doublets at δ6.44 and 7.28 (J_{vic} = 9.1 Hz). The four methoxyl signals appear as singlets at δ3.92, 3.96, 3.97 and 4.06. This spectrum bears a distinct resemblance to that reported for rugosinone (3).[4]



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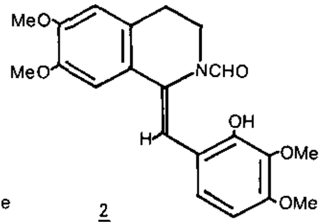

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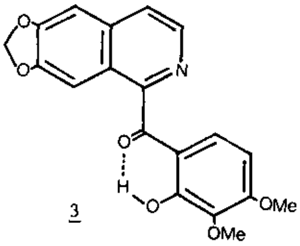

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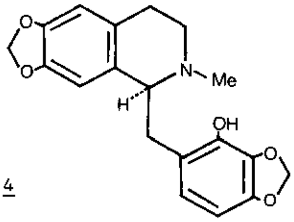

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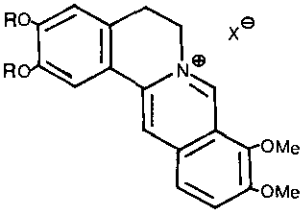

5, R + R = CH_2
6, R = CH_3

The mass spectrum of taxilamine confirms the molecular formulation $C_{20}H_{19}O_6N$, showing molecular ion m/z 369 (32). Other fragments are m/z 354 (14), 352 (15), 326 (14), 311 (16), 310 (68), 296 (33), 188 (57), 181 (13), 149 (75), 86 (50), 84 (74) and 49 (100). The m/z 181 and 188 fragments are due to cleavage of the C-1 to C-α bond.

Pseudobenzylisoquinolines are thus of fairly widespread occurrence in nature, having now been found among members of four different plant families.

Additionally, the Baeyer-Villiger oxidative rearrangement leading from protoberberinium alkaloids to pseudobenzylisoquinolines appears to be a favorite route for the catabolism of protoberberinium salts. More specifically, taxilamine (1) must probably have been formed in nature through oxidative rearrangement of palmatine (6) to supply initially polycarpine (2). Hydrolytic N-deformylation followed by further oxidation would then afford taxilamine.[3]

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References and Footnotes

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3. N. Murugesan and M. Shamma, Tetrahedron Lett., 4521 (1979). See also N. Murugesan and M. Shamma, Heterocycles, 14, 585 (1980).
4. W.-N. Wu, J.L. Beal and R.W. Doskotch, J. Nat. Prod., 43, 143 (1980).
5. I.A. Israilov, M.S. Yunusov and S. Yu. Yunusov, Khim. Prir. Soedin., 537 (1978); Chem. Natural Compounds, 465 (1979).
6. Besides taxilamine, plants of the Berberidaceae family have recently yielded an array of novel alkaloids; see S.F. Hussain, M.T. Siddiqui and M. Shamma, Tetrahedron Lett., 21, 4573 (1980); thus abundantly justifying the encomium made more than one hundred years ago: "The time is fast coming when gardens of any pretensions to beauty will be judged by their collections of Berberis, for there is not any other class of evergreen shrub which affords so many points for interesting observation." Shirley Hibbard in "The Floral World and Garden Guide", vol. v, p. 163 (1862).

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