THE ISOLATION AND STRUCTURE OF "HARAPPAMINE"— A NEW ALKALOID FROM *BUXUS PAPILOSA*

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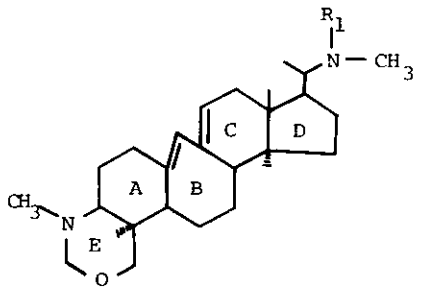
ABSTRACT— A new alkaloid "harappamine" has been isolated from the leaves of *Buxus papilosa* which has been assigned structure (1).

Buxus papilosa (Buxaceae) is a plant which grows abundantly in the northern regions of Pakistan. A number of alkaloids have previously been reported from this plant.[1-5] In the previous communication we have reported the isolation of "moenjodaramine" (2) from the leaves of this plant which was found to have a novel pentacyclic skeleton bearing both a tetrahydrooxazine ring and a 9(10→19) *abeo*-diene system.[6] We now report the structure of a new and closely related alkaloid "harappamine" (1) from the leaves of the same plant.



(1) R_1 = H
(2) R_1 = CH_3

"Harappamine" was isolated by chromatography of the crude mixture of alkaloids on a neutral alumina column. A number of alkaloidal fractions were obtained, the "harappamine" containing fraction being eluted with 50% pet-ether/60% $CHCl_3$.

The infra-red spectrum of the substance showed bands at 3400 cm^{-1} (N-H), 2840 cm^{-1} (C-H) and 1650 cm^{-1} (C=C). The U.V. spectrum showed maxima at 238 and 246 nm and shoulders at 205 and 253 nm, characteristic of the presence of a 9(10→19) *abeo*-diene system.[3] The proton NMR spectrum ($CDCl_3$) showed three singlets, corresponding to the three tertiary methyl groups at δ 1.03, δ 1.06 and δ 1.12. The secondary (C-21) methyl group resonated as a doublet at δ 0.72 (J=7.7 Hz). Two singlets at δ 2.10 and δ 2.41 were assigned to the two N(CH_3) groups at C-20 and C-3 respectively. A set of AB doublets resonating at δ 3.24 and δ 3.82 were assigned to the C-29

methylene protons (J_{AB}= 10.6 Hz), while another set of AB doublets centred at δ 3.57 and δ 4.42 (J_{AB}= 7.4 Hz) were attributed to the methylene protons α-to the C-3 nitrogen. The isolated olefinic proton at C-19 resonated as a singlet at δ 5.98, while a multiplet centred at δ 5.56 was ascribed to the C-11 olefinic proton. A comparison of the NMR spectrum of "harappamine" with that of "moenjodaramine" which has also been reported as a synthetic derivative by the French group,[8] showed the NMR spectra of the two substance were virtually identical, with "harappamine" containing one less N-methyl group than (2).

The mass spectrum of "harappamine" showed a molecular ion peak at m/z 412.3454 corresponding to the formula $C_{27}H_{44}N_2O$ (calcd. 412.3453). The substance showed a base peak at m/z 58.0660 corresponding to the composition $C_3H_8N^+$. This may be attributed to the ion $CH_3CH = \overset{+}{N}(H)-CH_3$ commonly encountered in alkaloids bearing a-$CH(CH_3)$-$NHCH_3$ grouping on ring D,[7] or to the ion $CH_2=\overset{+}{N}(CH_3)_2$ found in alkaloids bearing a-$N(CH_3)_2$ grouping on ring A.[7] Another peak at m/z 57.0625 corresponded to the fragment $CH_2=\overset{+}{N}(CH_3)\dot{C}H_2$. A peak at m/z 85.0887 was in accordance with the composition $C_5H_{11}N$ (calcd. 85.0891) corresponding to the fragment $\dot{C}H_2-CH_2-CH = \overset{+}{N}(CH_3)_2$ formed by the cleavage of ring A along with the side chain. A peak at m/z 71.0734 (C_4H_9N) was consistent with the fragment $\dot{C}H_2-CH = \overset{+}{N}(CH_3)_2$ formed by cleavage of ring A accompanied by an intramolecular proton transfer.

In the light of above studies structure (1) is proposed for "harappamine".

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