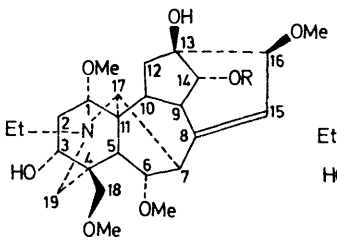
Structures of Falaconitine and Mithaconitine, Two Novel Diterpenoid Alkaloids from *Aconitum falconeri* Stapf.

By S. WILLIAM PELLETIER* and NARESH V. MODY
(*Institute for Natural Products Research and the Department of Chemistry, University of Georgia, Athens, Georgia* 30602)
and H. S. PURI
(*Pharmacognosy Research Unit, Department of Botany, Panjab University, Chandigarh*-160014, *India*)

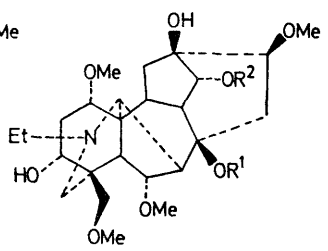
Summary The structures of two novel C_{19}-diterpenoid alkaloids, falaconitine and mithaconitine, have been determined; these are the first naturally occurring members of the diterpenoid alkaloids group which contain a C-8—C-15 double bond.

IN 1966, Singh, Bajwa, and Singh[1] reported the isolation and preliminary study of two new diterpenoid alkaloids designated as bishatisine and bishaconitine from the indigenous crude drug known as *Bish*, *Bikh*, or *Mitha telia* (*Aconitum falconeri* Stapf.). Since then no further work on either these alkaloids or this plant has been reported. We report the isolation and structure determination of two new C_{19}-diterpenoid alkaloids, falaconitine (**1**) and mithaconitine (**2**), from the roots of *Aconitum falconeri* Stapf. We also have isolated the known C_{19}-diterpenoid alkaloids, pseudaconitine (**3**), indaconitine (**4**), and veratroylpseudaconine (**5**) from this plant.[2] We find now that Singh's data for 'bishaconitine' is consistent with it being a mixture of several closely related alkaloids with the alkaloid falaconitine (**1**) predominating. Furthermore, we did not encounter either any atisine-type alkaloids or the 'bishatisine' which was reported by Singh and his co-workers.[1]

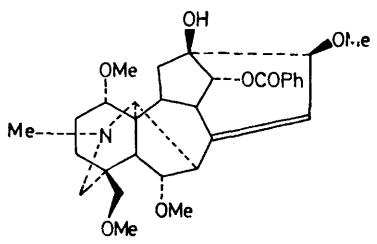
Falaconitine, a major constituent of the methanolic extract of the roots of *A. falconeri*, was isolated as an amorphous compound by a combination of pH gradient, thin layer, and column chromatrographic techniques. Falaconitine, $C_{34}H_{47}NO_{10}$, $[\alpha]_D^{28}$ + 111·5° (*c* 1·0, abs. EtOH) shows broad i.r. absorptions at 3460 (OH), 1710 (ester), 1630 (double bond), 1610 (aromatic), and 780 (trisubstituted aromatic ring) cm^{-1}. The 100 MHz ^1H n.m.r. spectrum shows absorption for an NCH_2Me group (3H, t, *J* 7 Hz) centred at δ 1·10, 4 aliphatic OMe groups (3H, s at δ 3·25,



(1) R = Vr
(2) R = PhCO



(3) R^1 = Ac, R^2 = Vr
(4) R^1 = Ac, R^2 = PhCO
(5) R^1 = H, R^2 = Vr



(6)

Vr = veratroyl = 3,4-$(MeO)_2C_6H_3CO$

3·30, 3·34 and 3·45) and 2 aromatic OMe groups as a part of a veratroyl group (6H s at δ 3·92). The spectrum also exhibits a signal at δ 4·92, attributable to a proton attached to a carbon (C-14) carrying an aromatic ester group, a doublet at δ 5·57 (*J* 6 Hz) corresponding to one olefinic proton, and signals for a veratroyl group.

Mithaconitine, $C_{32}H_{43}NO_8$, $[\alpha]_D^{28}$ + 94° (*c* 1·0, abs. EtOH) was isolated in an amorphous form as a minor constituent. The i.r. spectrum exhibits absorption at 3470 (OH), 1720 (ester), 1630 (double bond), 1610 (aromatic), and 720 (mono-substituted aromatic ring) cm^{-1}. The ^1H n.m.r. spectrum indicates the presence of an NCH_2Me group (3H, t) at δ 1·10, and 4 aliphatic OMe groups (3H, s at δ 3·27, 3·32, 3·35, and 3·43). The spectrum shows a signal at δ 4·96 attributable to a proton attached to a carbon (C-14) carrying an aromatic ester group and another doublet at δ 5·57 (*J* 6 Hz) corresponding to one olefinic proton as found in falaconitine. The ^1H n.m.r. spectrum also indicates the presence of the aromatic protons of a benzoyl group between δ 7·38 and 8·12. The ^1H n.m.r. spectrum of mithaconitine is identical with falaconitine except for the presence of the benzoyl group instead of a veratroyl group.

Correlation of falaconitine and mithaconitine with the known compounds (**3**)—(**6**) was made through a study of their ^{13}C n.m.r. spectra. The pattern of ^{13}C shifts in these new alkaloids is similar to that of the known alkaloids (**3**)—(**6**) except for a few changes. Comparison of the ^{13}C chemical shifts of C-8 (singlets at δ 146·6 and 146·5 p.p.m.) and C-15 (doublets at δ 116·1 and 116·4 p.p.m.) in falaconitine (**1**) and mithaconitine (**2**), respectively, with those of pyrodelphinine (**6**) (C-8 singlet at δ 146·6 p.p.m. and C-15 doublet at δ 116·3 p.p.m.)[3] afforded evidence for the presence of a double bond between C-8 and C-15 in these new alkaloids. These data indicate that alkaloids (**1**) and (**2**) are similar to pseudaconitine[4] (**3**) and indaconitine[5] (**4**), respectively, except for the presence of the double bond between the C-8 and C-15 positions. Therefore, we assign structures (**1**) and (**2**) to falaconitine and mithaconitine, respectively. Finally, these structures were confirmed by comparison with the pyrolysis product[4] of pseudaconitine (**3**) and indaconitine (**4**), which were found to be identical with falaconitine (**1**) and mithaconitine (**2**), respectively.

It is interesting to note that falaconitine and mithaconitine are the first naturally occurring examples of an alkaloid with a pyrodelphinine-type structure. From this, it is, appealing to consider that these alkaloids may be biogenetic precursors for pseudaconitine, veratroylpseudaconine, and indaconitine, as well as other C_{19}-diterpenoid alkaloids containing a C-8 acetate and a C-15 hydroxy group, *e.g.* aconitine and hypaconitine.

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[1] N. Singh, G. S. Bajwa, and M. G. Singh, *Indian J. Chem.*, 1966, **4**, 39.
[2] S. W. Pelletier, N. V. Mody, and H. S. Puri, *Phytochemistry*, in the press.
[3] S. W. Pelletier and Z. Djarmati, *J. Amer. Chem. Soc.*, 1976, **98**, 2626.
[4] R. E. Gilman and L. Marion, *Tetrahedron Letters*, 1962, 923.
[5] Y. Tsuda and L. Marion, *Canad J. Chem.*, 1963, **41**, 1485.