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Conopharyngine pseudoindoxyl, a new alkaloid from *Tabernamontana pachysiphon* Stapf. var *cumminsii* (Stapf.) H. Huber

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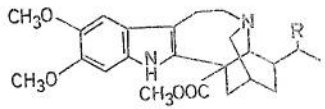
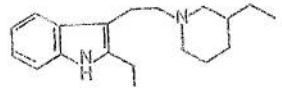
A chloroform extract of the residue, remaining after extraction of the bases obtained from the leaves of *T. pachysiphon* var *cumminsii** with ether, has been shown to contain the alkaloids conopharyngine, 20-hydroxyconopharyngine and conopharyngine pseudo-indoxyl, and two alkaloids of as yet unknown structure.

An ether-soluble extract obtained from the total basic component of the leaves of *T. pachysiphon* var *cumminsii** has previously been shown to contain mainly conopharyngine (I; R = H) (Thomas & Starmer, 1963; Crooks & Robinson, 1970a) with the minor bases 2-ethyl-3-[2-(3-ethylpiperidino)ethyl] indole (II) (Crooks, Robinson & Smith, 1968), jollyanine (III) (Crooks & Robinson, 1970a) and apparicine (IV) (Crooks & Robinson, 1970b).

The residue after removal of these bases has now been extracted with chloroform and the extract chromatographed on a column of alumina. The initial eluate afforded conopharyngine; later eluates consisted of four minor components (A-1 to A-4) which were separated by preparative thin layer chromatography. Insufficient of the first two components are currently available for structural investigation.



I



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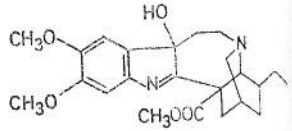
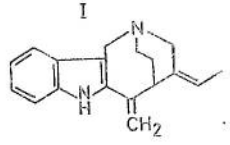
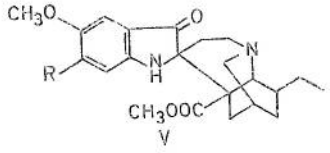


III



IV



V

Mass measurement of the molecular ion of the third base, A-3, showed a molecular formula of $C_{23}H_{30}N_2O_5$ (theoretical *m/e* 414·215458; found *m/e* 414·215683). The ultra violet, infrared and nmr spectra were identical with those reported for 20-hydroxyconopharyngine (I; R = OH) (Cava, Watanabe & others, 1968) which has

* This plant has previously (Crooks & Robinson, 1970a,b; Crooks, Robinson & Smith, 1968) been referred to as *Tabernamontana cumminsii*.

previously been isolated from *Conopharyngia jollyana* and *C. durissima* (Hootele Pecher & others, 1967) and *Tabernamontana crassa* (Cava & others, 1968).

The fourth and slowest-running base, A-4, was shown by mass measurement of t molecular ion to have a molecular formula $C_{23}H_{30}N_2O_5$ (theoretical *m/e* = 414·21545 found *m/e* = 414·215731). The ultraviolet spectrum showed λ_{max}217–219 nm (log = 4·20), λ_{max}243–246 nm (log ϵ = 4·26), λ_{max}389–391 nm (log ϵ = 3·62), λ_{sh}25 265 nm (log ϵ = 4·26), λ_{min} 226–227 nm (log ϵ = 4·10) and λ_{min} 320 nm (log ϵ = 3·0 which upon acidification with hydrochloric acid changed to λ_{max}217–219 nm (log ϵ 4·15), λ_{max}248–249 nm (log ϵ = 4·25), λ_{max}275–279 nm (log ϵ = 3·97), λ_{max}38 391 nm (log ϵ = 3·65), λ_{min} 229–231 nm (log ϵ = 4·04), λ_{min} 264–266 nm (log ϵ 3·90) and λ_{min} 320 nm (log ϵ = 3·01) which suggests the presence of a basic nitrog in or near the chromophore. The infrared spectrum had bands at 3290 (broad), 17 and 1670 cm^{-1} (N–H, ester C = O and conjugated or amide C = O stretching respectively). A 1,2,4,5-tetrasubstituted benzene nucleus (as present in conoohary gine) was indicated by 1-proton singlets at 3·02 and 3·70 τ in the proton magnet resonance spectrum, which also showed 3-proton singlets at 6·11 and 6·19 τ (2 arom tic CH_3O groups, *cf.* 20-hydroxyconopharyngine above) and 6·69 τ [$COOCH_3$ protons and a broad 1-proton singlet at 5·95 τ (N–H). The mass spectrum of A-4 showed similar fragmentation pattern to that of voacangine pseudoindoxyl (V; R = H (Thomas & Biemann, 1968), the significant differences being that the ions associate with the pseudoindoxyl moiety were 30 mass units higher in the spectrum of A- The above data suggest that A-4 is conopharyngine pseudoindoxyl (V; R = OCH_3 An authentic specimen of this was obtained by oxidation of conopharyngine (I; R = H) to jollyanine (III) (Crooks & Robinson, 1970a) followed by base catalysed r arrangement to conopharyngine pseudoindoxyl (V; R = OCH_3) under conditio described by Thomas & Biemann (1968). The two samples were identical.

This is the fifth example of an Iboga pseudoindoxyl alkaloid isolated from plar sources (Dickel, Holden & others, 1958; Goutarel & Janot, 1953; Guise, Rasmusse & others, 1965; Niemann & Kessel, 1966; Thomas & Biemann, 1968). It has bee suggested that these are artifacts formed during the isolation procedure (Thomas Biemann, 1968). In the present case the pseudoindoxyl may also have been forme as an artifact during the storage of the solid total base extract for six years at roo temperature before examination.

EXPERIMENTAL CHEMISTRY

Ultraviolet spectra were measured in ethanolic solution, unless otherwise state on a Perkin-Elmer model 137 spectrophotometer, infrared spectra were recorded o a Perkin-Elmer model 237 spectrophotometer and proton magnetic resonanc spectra were recorded in $CDCl_3$ solution on a Varian H-220 spectrometer usin tetramethylsilane as internal standard. Low and high resolution mass spectra wer recorded on AEI MS-12 and MS-9 spectrometers, respectively. Solutions were drie with anhydrous magnesium sulphate and solvents were removed on a Buchi rotar evaporator under reduced pressure (water-pump).

Isolation of alkaloids. A total-base extract (24 g) was prepared from the leaves o *T. pachysiphon* var *cumminsii* as already described (Thomas & Starmer, 1963). Thi was extracted with ether (3 × 100 ml), the combined ethereal extracts dried an evaporated to afford a light-brown oil (14·2 g) which has already been fully investi

gated (Crooks & Robinson, 1970a, b; Crooks & others, 1968). The residue remaining after the ether extraction was extracted with chloroform (3 × 50 ml), the combined chloroform extracts dried and evaporated to leave a viscous dark-brown gum (5·9 g). This gum was subjected to column chromatography on alumina (Grade H) using ether as solvent. This led to the elution of a yellow band which upon evaporation of the solvent afforded a crystalline solid (4·3 g), m.p. 145°, which was shown to be identical with the alkaloid conopharyngine (I; R = H) (m.p., mixed m.p., ultraviolet, infrared and mass spectra) isolated previously (Crooks & Robinson, 1970a) from the ether extract. On gradually increasing the polarity of the eluting solvent by using ether-ethyl acetate mixtures, a diffuse yellow band was eluted which upon evaporation of the solvent afforded a brown oil (35 mg). This was subjected to preparative thin-layer chromatography on alumina (Type E, Merck) using ether–ethyl acetate (3:1 v/v) as solvent and ultraviolet irradiation for band detection. Four fluorescent bands were detected, extracted with methanol and the extracts evaporated to yield homogeneous basic products (see Table 1).

Table 1. *Thin layer chromatographic data for alkaloids A-1 to A-4.*

Alkaloid	Colour of fluorescence	R_F value	Yield (mg)
A-1	Pale-blue	0·81	9·0[a]
A-2	Blue	0·75	3·0[b]
A-3	Bright-green	0·63	4·5[b]
A-4	Pale-green	0·49	5·2[c]

(a) Brown oil; (b) White amorphous solids; (c) Yellow oil.

Jollyanine (III). Conopharyngine (0·4 g) in benzene (7 ml) was irradiated (8 h) with ultraviolet light ($\lambda = 230$ nm) with a slow stream of oxygen passed continuously through the solution. The resulting solution was diluted with ether (2 ml) and placed on a column of alumina (Grade H) which was then eluted using benzene–ether (3 : 1 v/v). The initial eluates gave conopharyngine (0·31 g) and subsequent eluates afforded jollyanine (50 mg), identified by comparison (m.p., mixed m.p., ultraviolet and infrared spectra) with that obtained from natural sources (Crooks & Robinson, 1970a).

Conopharyngine pseudoindoxyl (V; R = OCH_3). Jollyanine (12·9 mg) in freshly prepared methanolic sodium methoxide (3 ml) [an aliquot of a solution prepared by dissolving sodium (46 g) in dry methanol (550 ml)] was boiled under reflux for 15 min. Water (5 ml) was then added and the solution extracted with chloroform (2 × 10 ml). The combined chloroform extracts were washed with water (2 × 7 ml), dried and evaporated to afford a yellow oil (11·8 mg). This was placed on an alumina column (Grade H) using chloroform–benzene (1:1 v/v) as solvent which initially eluted unchanged jollyanine (5·3 mg). Further elution afforded a yellow oil (6·1 mg) identical (ultraviolet, infra-red and mass spectra) with the naturally-occurring conopharyngine pseudoindoxyl.

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