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Alkaloids in Certain Species of *Virola* and Other South American Plants of Ethnopharmacologic Interest

STIG AGURELL,* BO HOLMSTEDT, JAN-ERIK LINDGREN

Dept. of Toxicology, Swedish Medical Research Council, Karolinska Institutet, S-104 01 Stockholm 60, Sweden

and

RICHARD EVANS SCHULTES

Botanical Museum, Harvard University, Oxford Street, Cambridge 38, Mass., U.S.A.

Virola theiodora, a botanical source of intoxicating snuffs used by certain South American Indian tribes, has been shown to contain the hallucinogen 5-methoxy-*N*,*N*-dimethyltryptamine as well as a number of other indoles. One Indian snuff proved to be unusually high in alkaloid content (11 %). Considerable differences in the alkaloid composition of different parts of single plants were encountered, *N*,*N*-dimethyltryptamine being the major component in the leaves and 5-methoxy-*N*,*N*-dimethyltryptamine in the bark of *Virola theiodora*. Of other species of *Virola* investigated *V. rufula* contained substantial amounts of tryptamines, whereas *V. multinervia* and *V. venosa* were almost devoid of alkaloids. *V. calophylla* contained high amounts of alkaloids only in the leaves. Two new β-carbolines of a type carrying the substituents in the 6-position of the β-carboline nucleus were found in *V. theiodora*, *V. rufula*, and *Anadenanthera (Piptadenia) peregrina*. By spectrometric and other data their structures have been shown to be 2-methyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline and 1,2-dimethyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline.

The ethnology, botany, and pharmacology, as well as chemical constituents, of South American snuffs other than tobacco and coca have recently been discussed at length.[1] Previous investigations have indicated that the seed of *Anadenanthera (Piptadenia) peregrina* was the most widely recognized botanical source of snuffs made by South American Indian tribes and inhaled

* Present address: Faculty of Pharmacy, S-113 86 Stockholm, Sweden.

to produce visions and hallucinations. Schultes, however, as early as 1954 pointed out at least one other kind of hallucinogenic snuff derived from species of *Virola* (Myristicaceae). Snuff of this type brought back by the explorer George J. Seitz, analyzed [2] by two of us, proved to contain, as its main constituent, 5-methoxydimethyltryptamine; and this compound was likewise found to be the main constituent of bark from Brazil said to be derived from species of *Virola*.

Our investigation [2] showed the existence of simple indoles in both the botanical and ethnological material. In general there has been a lack of correlation between what can be observed in the field, botanical identification, and pharmacological and chemical examination. In the summer of 1967 two of us had the advantage of participating in the Alpha Helix Phase C Expedition to the Amazon and the Rio Negro.[3]

Several tribes of the Waiká Indians were visited in the Rio Negro Basin. The mode of preparations of their snuffs was recorded and the plants used for the preparation identified. Voucher specimens are deposited in the Economic Herbarium of Oakes Ames in the Botanical Museum of Harvard University.[3]

This paper describes the analysis of the alkaloids in several species of *Virola* as well as in the snuff prepared by the Waikás at the Rio Cauaburí (Maturacá) and the Rio Tototobí.

EXPERIMENTAL

List of abbreviations

DMT	= *N*,*N*-Dimethyltryptamine
MMT	= *N*-Methyltryptamine
T	= Tryptamine
5-MeO–DMT	= 5-Methoxy-*N*,*N*-dimethyltryptamine
5-MeO–MMT	= 5-Methoxy-*N*-methyltryptamine
5-MeO–T	= 5-Methoxytryptamine
5-OH–DMT	= 5-Hydroxy-*N*,*N*-dimethyltryptamine (bufotenine)
5-OH–MMT	= 5-Hydroxy-*N*-methyltryptamine
5-OH–T	= 5-Hydroxytryptamine (serotonin)
MTHC	= 2-Methyl-1,2,3,4-tetrahydro-β-carboline
6-MeO–THC	= 2-Methyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline
6-MeO–DMTHC	= 1,2-Dimethyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline

Material. The botanical material and snuff preparations were collected in connection with the Alpha Helix Amazon Expedition Phase C in the summer of 1967. All material was preserved in ethanol.

Some species of *Virola* were collected outside Manaus, at Flores and at the Reserva Ducke. Other plants were collected in the Rio Cauaburí region; others outside Boa Vista; *Virola theiodora* was collected also at Rio Tototobí. All plants were identified by R. E. Schultes. The numbers of the voucher specimens given in the tables refer to the collection number of R. E. Schultes.

Isolation of alkaloids. The powdered plant material (2–185 g) was extracted with methanol. The dried extract was treated according to a procedure used by Fish *et al.*[4] for the isolation of tryptamine derivatives. After the final chloroform extraction of the alkaloids from the alkaline aqueous phase we further extracted the aqueous solution with an equal volume of butanol to facilitate the recovery of compounds such as serotonin and *N*-oxides, if present.

Gas chromatography (GLC). Gas chromatographic analysis was performed with two commercial apparatus (F and M Model 400 and Varian Aerograph Model 2100) equipped

with hydrogen flame ionization detection systems. The column support, 100—120 mesh Gas Chrom P, was size-graded, acid-washed, and silanized according to the method described by Horning *et al.*[5] The coating was applied by the filtration technique.[6] The stationary phases used were

1) 7 % F-60 and 2 % EGSS—Z (1.80 m × 3.2 mm glass tube)
2) 5 % SE-30 (2.25 m × 3.2 mm glass tube)
3) 5 % OV-17 (2.25 m × 3.2 mm glass tube)

The columns were operated at 193° and the injector block and the detector chamber were kept at 250°. The amount of alkaloids in mg/100 g plant material and the percentage of each alkaloid in the alkaloid mixture was determined with a Servogor 512 Disc Integrator using DMT as a standard. Pure alkaloids were isolated by preparative chromatography using the effluent splitter on the F and M apparatus.

Gas chromatography-mass spectrometry (GLC—MS). The principles of the technique have been described earlier.[2] The mass spectrometry work was carried out with an LKB 9000 gas chromatograph-mass spectrometer. The ion source was 270°, the electron energy was 70 eV and the electron ionization current 60 μA, respectively. The separations were made on columns consisting of 3 % PDEAS at 190° and 3 % OV-17 (2 m × 3.2 mm glass tube) at 200°.

Paper and thin-layer chromatography. Alkaloidal constituents were separated by chromatography on formamide impregnated paper with chloroform-pyridine (6:1) as solvent (FCP)[7] and by thin-layer chromatography on Silica Gel G with methanol-glacial acetic acid-water (75:10:15) as solvent. Tryptamines were located with Ehrlich's reagent.

Spectrophotometry. Fluorescence spectra were obtained with an Aminco-Bowman spectrophotofluorometer. Spectra were recorded in ethanol solution and in 3 M HCl. UV-spectra were obtained with a Beckman DB spectrophotometer.

Reference compounds. 2-Methyl-6-methoxytetrahydro-β-carboline[8] (IVb) was synthesized from *N*-methyl-5-methoxytryptamine and formaldehyde by heating for 1/2 h at 50° in a weakly acid solution as described for tetrahydroharman.[9] UV-spectrum (ethanol) max. 225, 275, 294, and 307 mμ. 2-Methyltetrahydro-β-carboline[10] (IVa) was prepared from *N*-methyltryptamine and formaldehyde in a similar manner. UV-spectrum Fig. 8A.

1,2-Dimethyl-6-methoxytetrahydro-β-carboline[11] (V) was synthesized from *N*-methyl-5-methoxytryptamine and acetaldehyde. UV-spectrum Fig. 8D.

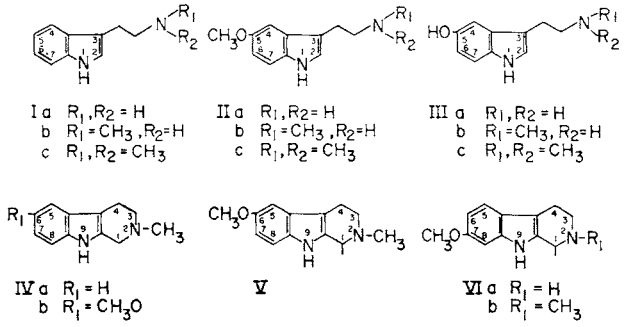

Fig. 1. Ia. tryptamine Ib. *N*-methyltryptamine Ic. *N,N*-dimethyltryptamine IIa. 5-methoxytryptamine IIb. 5-methoxy-*N*-methyltryptamine IIc. 5-methoxy-*N,N*-dimethyltryptamine IIIa. 5-hydroxytryptamine (serotonin) IIIb. 5-hydroxy-*N*-methyltryptamine IIIc. 5-hydroxy-*N,N*-dimethyltryptamine (bufotenine) IVa. 2-methyltetrahydro-β-carboline IVb. 2-methyl-6-methoxytetrahydro-β-carboline V. 1,2-dimethyl-6-methoxytetrahydro-β-carboline VIa. tetrahydroharmine VIb. 2-methyltetrahydroharmine.

2-Methyltetrahydroharmine (VIb) was prepared by methylation of harmalin with dimethylsulphate in benzene. The resulting quaternary amine was reduced with an excess of sodium borohydride in water to VIb. M.p. picrate 253–255°. UV-spectrum Fig. 8E. Other reference compounds have been described earlier.[2]

RESULTS

The results are presented in Table 1 and Figs. 2–5.

Table 1. Distribution of indole alkaloids.

Species	Part of plant	Alkaloids: mg/100 g dry plant	Alkaloids	%
"Epéna"	Snuff	715	5-MeO–DMT	72
No. 24574			DMT	20
Origin: Rio Cauaburí,			MTHC	4
Brazil			6-MeO–THC	2
			MMT	2
"Nyakwána"	Snuff	11 000	5-MeO–DMT	88
No. 24626			DMT	11
Origin: Tototobí,			MMT	
Brazil			5-MeO–MMT	
			6-MeO–THC	
V. theiodora Warb.	Bark	250	DMT	52
No. 24595			5-MeO–DMT	43
Origin: Manaus,			6-MeO–THC	4
Brazil			MMT	1
	Root	17	5-MeO–DMT	62
			DMT	22
			5-MeO–MMT	15
	Flow.shoots	470	DMT	93
			MMT	7
	Leaves	44	DMT	99
			5-MeO–DMT	
V. theiodora Warb.	Bark	65	5-MeO–DMT	95
No. 24626			DMT	5
Origin: Tototobí,	Leaves	21	DMT	98
Brazil			MTHC	2
V. calophylla Warb.	Bark	9	DMT	91
No. 24603			5-MeO–DMT	9
Origin: Manaus,	Root	1	DMT	87
Brazil			5-MeO–DMT	13
	Flow.shoots	193	DMT	96
			MMT	4
	Leaves	155	DMT	96
			MMT	4

Table 1. Continued.

V. rufula (A.DC.) Warb.	Bark	200	5-MeO—DMT	95
No. 24612			DMT	4
Origin: Manaus,			5-MeO—MMT	
Brazil			6-MeO—THC	
	Root	144	5-MeO—DMT	94
			5-MeO—MMT	4
			DMT	1
			6-MeO—THC	
	Leaves	98	DMT	94
			MMT	6
V. multinervia Ducke	Bark	1	DMT	
No. 24614	Root	1	5-MeO—DMT	59
Origin: Manaus,			DMT	41
Brazil	Leaves	—	—	
V. multinervia Ducke	Bark	1	DMT	
No. 24616	Flow.shoots	—	—	
Origin: Manaus,	Leaves	—	—	
Brazil				
V. venosa (Benth.) Warb.	Bark	—	—	
No. 24613	Root	1	5-MeO—DMT	
Origin: Manaus,	Leaves	1	DMT	
Brazil			5-MeO—DMT	
Anadenanthera	Bark	42	5-MeO—DMT	59
(Piptadenia)			5-MeO—MMT	36
peregrina (L.) Speg.			6-MeO—DMTHC	2
No. 24625			6-MeO—THC	2
Origin: Boa Vista,			DMT	1
Brazil			MMT	
			5-OH—DMT	
	Leaves	13	DMT	49
			5-MeO—DMT	48
			MMT	

DISCUSSION

The first active components of South American snuffs were identified by Stromberg [12] and Horning and co-workers [4] who isolated simple indole alkaloids from the seeds of *Anadenanthera (Piptadenia) peregrina*, a leguminous plant. They found the seeds to contain DMT, DMT-*N*-oxide and bufotenine (5-OH—DMT) and its corresponding *N*-oxide. Later simple indoles have been identified in *Anadenanthera (Piptadenia)* species and in other species used for snuff preparations; *cf.* Ref. 2.

We earlier found 5-MeO—DMT to be the main and possibly the most important constituent of snuff prepared from a species of *Virola*.[2] We also proved the existence of several other indoles in both the crude drugs prepared by the Indians and in plant material.

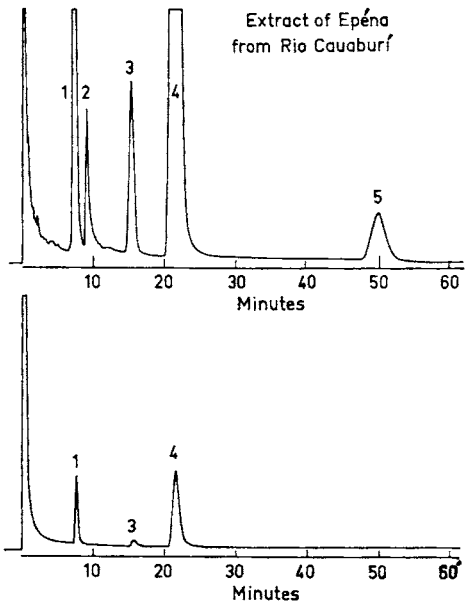

Fig. 2. Gas chromatogram of alkaloid fraction of Epéna snuff. 7 % F-60/2 % EGSS—Z. Upper panel: high magnification. Lower panel: low magnification. Peak 1=DMT, peak 2=MMT, peak 3=MTHC, peak 4=5-MeO—DMT, peak 5=6-MeO—THC.

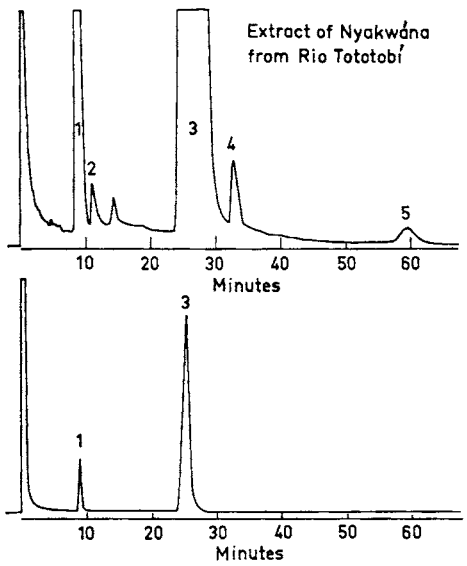

Fig. 3. Gas chromatogram of alkaloid fraction of Nyakwána snuff. 7 % F-60/2 % EGSS—Z. Upper panel: high magnification. Lower panel: low magnification. Peak 1=DMT, peak 2=MMT, peak 3=5-MeO—DMT, peak 4=5-MeO—MMT, peak 5=6-MeO—THC.

Snuff. The Waikás, an Indian tribe living in the northeast Amazon, prepare their snuffs in different ways. Two such snuffs have been analyzed. One is called "Epéna" (Fig. 2) from Rio Cauaburí and the other "Nyakwána" (Fig. 3) from Rio Tototobí. The "Epéna" is prepared from the bark of *Virola theiodora*, to which is added the crushed and powdered leaf material from leaves of *Justicia pectoralis* var. *stenophylla*. These two ingredients are finally mixed with the ashes of *Elizabetha princeps*. The full details have been given by Schultes-Holmstedt.[3] The "Nyakwána" of the Tototobí Waikás on the other hand contains as its only ingredient the resin from the bark of *Virola theiodora*. Examination shows that "Epéna" contains less than 1/10 of the alkaloid content of "Nyakwána", which proved to contain no less than 11 % of alkaloids. This very high alkaloid content of "Nyakwána" may explain, why the resin of *V. theiodora* besides being used for snuff preparation also is used as an arrow poison.[3] When examining the relative proportions of the constituents in the preparations, it is apparent that the main constituent is 5-MeO—DMT, with lesser amount of DMT.

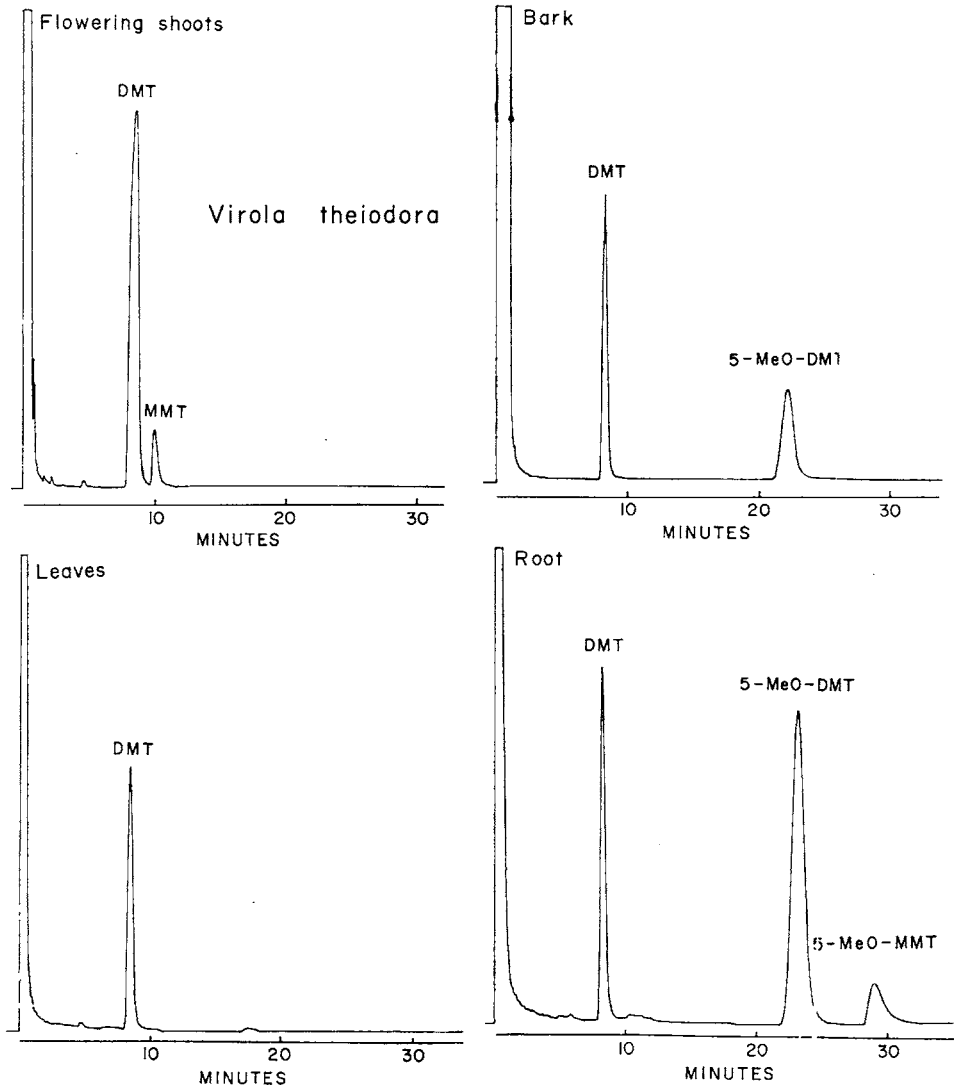

Fig. 4. Gas chromatogram of alkaloid fractions from *Virola theiodora*. Comparison of alkaloids in flowering shoots, leaves, bark, and root. 7 % F-60/2 % EGSS–Z.

Plants. Previously only one *Virola* species, *Virola calophylla*, had been investigated for alkaloids.[2] The species of *Virola* collected in 1967 allowed us to compare different species as well as different parts of the same plant (especially with regard to the parts that are used by the Indians for their snuff preparations). Our survey revealed that the two collections of *Virola*

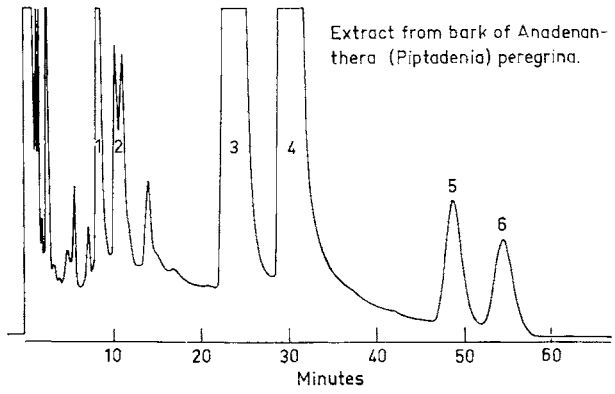

Fig. 5. Gas chromatogram of alkaloid fraction from *Anadenanthera peregrina*. 7 % F-60/2 % EGSS—Z. Peak 1=DMT, peak 2=MMT, peak 3=5-MeO—DMT, peak 4=5-MeO—MMT, peak 5=6-MeO—DMTHC, peak 6=6-MeO—THC.

theiodora contained large amounts of 5-MeO—DMT and DMT, as did *Virola rufula*.

Virola theiodora was examined (Fig. 4) for alkaloid content in the flowering shoots, in the leaves, in the bark and in the root. The examination demonstrated the highest content of alkaloids (DMT and MMT) in the flowering shoots. The bark contained less, but still a substantial amount of DMT and 5-MeO—DMT was recovered. Minor amounts were present in the roots and in the leaves. It is obvious that the most rapidly growing parts contain mainly DMT, whereas the bark (used by the Indians) and the root contain mainly 5-MeO—DMT. The "Nyakwána" snuff was actually prepared from the same tree that was analyzed under *V. theiodora No. 24626*, and as expected there is striking similarity between the alkaloids of the snuff and of the bark.

Virola multinervia and *Virola venosa* proved to be devoid of alkaloids. In *Virola calophylla*, previously identified [2] as a source of snuff, the species collected in Manaus contained in the bark little 5-MeO—DMT but instead a certain amount of DMT. The flowering shoots and the leaves of this plant contained high amounts of DMT.

Our material for analysis also consisted of alcohol-preserved *Anadenanthera (Piptadenia) peregrina* (bark and leaves). As previously demonstrated,[13] the bark of this plant contains a high amount of 5-MeO—DMT, whereas leaves contain almost equal parts of DMT and 5-MeO—DMT. In addition to that, we could prove the existence of five other compounds. Two new β-carboline alkaloids were discovered in *Anadenanthera (Piptadenia) peregrina*, namely 6-MeO—DMTHC (V) and 6-MeO—THC (IVb). No significant amounts of *N*-oxides were detected by TLC in any of the plants.

Confirmation of chemical structures. Compounds present in the alkaloid extracts were identified by the previously described technique [2] using GLC—MS: *viz.* each compound was found to have identical retention time and mass spectrum to that of the reference compound. Further proof was

obtained by gas, paper, and thin-layer chromatographic comparison with authentic samples. Chromatographic and mass spectrometric data for the reference compounds are presented in Table 2.

Table 2. Chromatographic and mass spectrometric data for reference compounds.

Compound [a]	Formula	Gas chromatography Ret. time (min.) [b] F60/Z 193°	Gas chromatography Ret. time (min.) [b] OV1 193°	Paper chromatography R_F in FCP [7]	Mass spectrum Lit. Ref. Major peaks at *m/e*:
5-MeO—DMT	II c	14.9	6.9	0.59	Ref. 2. 58 (base peak), 103, 117, 160, 173, 218 (M^+)
5-MeO—MMT	II b	18.6	6.7	0.36	Ref. 2. 44 (base peak), 103, 117, 160, 161, 173, 204 (M^+)
5-MeO—T	II a	20.9	6.1	0.09	This paper. 30 (11.6 %), 117 (3.0 %), 145 (11.6 %), 146 (9.5 %), 160 (100 %), 161 (81,4 %), 190 (M^+, 37.2 %)
DMT	I c	5.5	3.1	0.56	Ref. 2. 58 (base peak), 103, 115, 130, 143, 188 (M^+)
MMT	I b	6.5	3.0	0.32	Ref. 2. 44 (base peak), 103, 115, 130, 131, 143, 174 (M^+)
T	I a	7.0	2.7	0.07	This paper. 30 (16.4 %), 103 (3.3 %), 130 (96.7 %), 131 (100 %), 132 (11.5 %), 160 (M^+, 27.0 %)
5-OH—DMT	III c	—	8.5	0.14	Ref. 2. 58 (base peak), 103, 117, 146, 159, 204 (M^+)
5-OH—MMT	III b	—	8.7	0.04	This paper. 44 (80.3 %), 146 (33.9 %), 147 (100 %), 148 (11.8 %), 190 (M^+, 3.9 %)
5-OH—T	III a	—	8.6	0.00	This paper. 30 (15.0 %), 146 (100 %), 147 (84.4 %), 148 (9.4 %), 160 (3.1 %), 161 (2.2 %), 176 (M^+, 31.3 %)
MTHC	IV a	10.5	4.9	[c]	This paper, Fig. 6. 78, 102, 115, 143 (base peak), 186 (M^+)
6-MeO—THC	IV b	32.6	12.0	[c]	This paper, Fig. 6. 77, 103, 115, 130, 158, 173 (base peak) 216 (M^+)
6-MeO—DMTHC	V	29.6	11.5	[c]	This paper, Fig. 7. 77, 86, 107, 115, 144, 172, 187, 215 (base peak), 230 (M^+)

[a] For abbreviations, see Experimental.
[b] Varian Aerograph Modell 2100.
[c] No colour with Ehrlich's reagent.

New alkaloids. In addition to the previously known tryptamine derivatives, three β-carbolines were also encountered and found to have structures IVa, IVb, and V, respectively, as discussed hereafter. It is known [8] that 5-methoxy-*N*,*N*-dimethyltryptamine *N*-oxide may chemically rearrange under certain conditions to 6-MeO—THC (IVb) and other compounds. However, in spite

of several attempts, we have not succeeded in producing IVa or IVb as artefacts under the conditions used in this investigation.

"Alkaloid 216"=2-Methyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline (IVb). "Alkaloid 216" was first isolated from "Epéna" snuff and later recognized in two species of *Virola* and in *Anadenanthera peregrina* (Table 1). The mol.wt. of the unknown compound was 216 (M^+), *viz.* 2 mass units less than 5-MeO—DMT. Further, "alkaloid 216" possessed a UV spectrum not in contrast to that of an indole, but it gave a negative reaction with Ehrlich's reagent, indicating that the unknown compound, if an indole, was substituted in the 2-position.

The mass spectrum of "alkaloid 216" (Fig. 6) suggested that it was not an indole with an open side chain. The prominent peaks in the mass spectrum

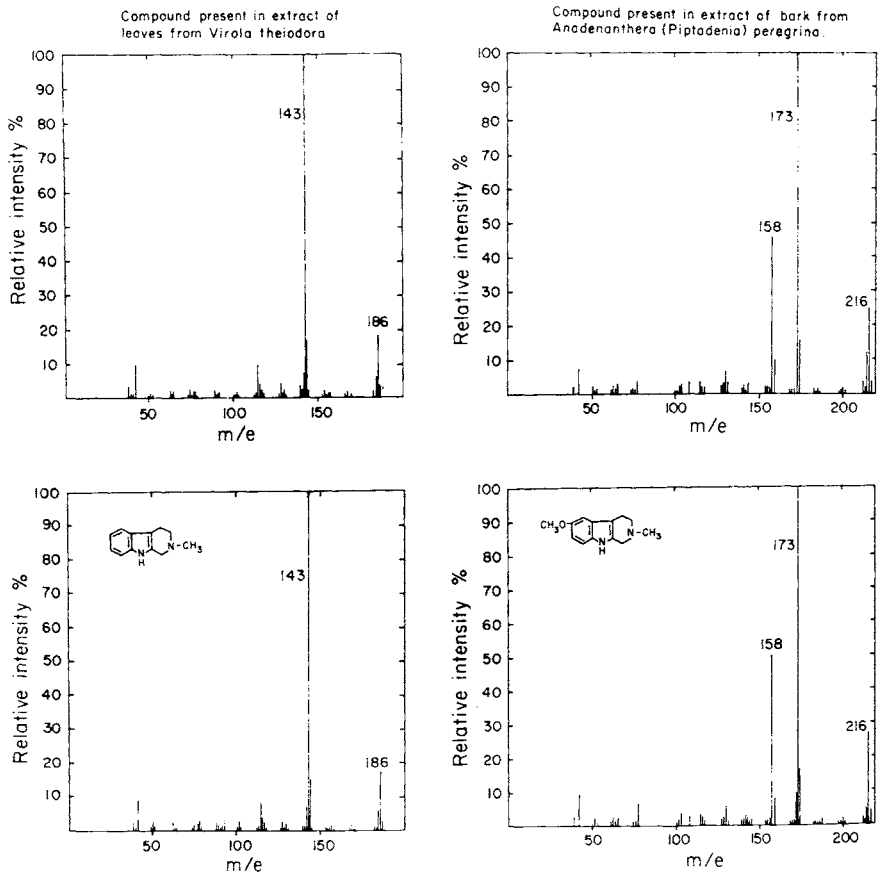

Fig. 6. Upper panel: mass spectra of "alkaloid 186" present in *Virola theiodora* and "alkaloid 216" present in *Anadenanthera peregrina*. Lower panel: mass spectra of reference compounds (IVa and IVb).

at *m/e* 173 and *m/e* 158 show a loss from the parent-ion of 43 and 58 mass units, respectively. If a structure such as IVb is assumed for "alkaloid 216", it can be readily accommodated to the mass spectrometric data. The proposed mechanism involves a retro-Diels-Alder fragmentation (*cf.* Ref. 14) of IVb with expulsion of 43 mass units to a fragment *m/e* 173, which can rearrange (*cf.* Refs. 15, 16) and lose a methyl group to yield a fragment *m/e* 158. Subsequently, compound IVb was synthesized by a Pictet-Spengler reaction from 5-methoxy-N-methyltryptamine and found to be identical in all respects (MS, GLC, UV and fluorescence spectra) to the natural compound.

The methoxy substituent of "alkaloid 216" could be present only in the 5-position of the indole nucleus as established by a closer inspection of the UV spectra (Fig. 8) of indoles substituted in different positions of the indole nucleus. This conclusion was supported by a study of the fluorescence spectra of a number of indoles (Table 3). It is known [17] that, of indoles, carrying an alkoxy, aryloxy, or hydroxy substituent in the 4-, 5-, 6-, or 7-position of the indole

Table 3. Comparison of fluorescence spectra. Activation at 280 mμ.

Compound	Position of indole nucleus substituted	Formula	Fluorescence maxima in ethanol mμ	Fluorescence maxima in 3 M HCl mμ
MTHC [a]	—	IV a	350	—
4-Benzyloxy-*N*,*N*-dimethyltryptamine	4	—	345	—
5-MeO—DMT [a]	5	II c	335	520
6-MeO—THC [a]	5	IV b	335	515
6-MeO—DMTHC [a]	5	V	335	520
Tetrahydroharmine	6	VI a	355	—
N-Methyltetrahydroharmine	6	VI b	355	—
7-Methoxy-*N*,*N*-dimethyltryptamine	7	—	355	—

[a] For abbreviations, see Experimental.

nucleus, only those substituted in the 5-position give a fluorescence peak at 520 mμ in 3 N HCl. As Table 3 shows both "alkaloid 216" and other 5-methoxy substituted indoles possess this fluorescence peak at 520 mμ in 3 N HCl.

The structure of "alkaloid 216" then is IVb.

"Alkaloid 186"=2-Methyltetrahydro-β-carboline (IVa). An unknown alkaloid present in *Virola theiodora* having a mol.wt. of 186 (Fig. 6) was, on arguments similar to those discussed above, assumed to have structure IVa. This structure was found to be correct by comparison with a synthetic reference compound.

2-Methyltetrahydro-β-carboline has previously been isolated by Platonova *et al.*[18] from *Arthrophytum leptocladum* M. Pop. together with leptocladine and dipterine.

"Alkaloid 230" = 1,2-Dimethyl-6-methoxy-1,2,3,4-tetrahydro-β-carboline (V). The mass spectrum (Fig. 7) of this alkaloid shows similarities to that of tetrahydroharmine.[2] The mass spectrum of tetrahydroharmine (VIa), lacking an *N*-methylgroup, shows a base peak at $M^+ - 15$ from the loss of the *C*-methyl group. Prominent peaks at *m/e* 187 and *m/e* 172 are in agreement with the fragmentation mechanism suggested for "alkaloid 216". The fragmentation pattern of "alkaloid 230" (V) is analogous to that of tetrahydroharmine except for the loss of 43 instead of 29 mass units due to the presence of an *N*-methyl group in "alkaloid 230". Compound V was synthesized and found to be identical (MS, GLC, UV and fluorescence spectra) with the natural product.

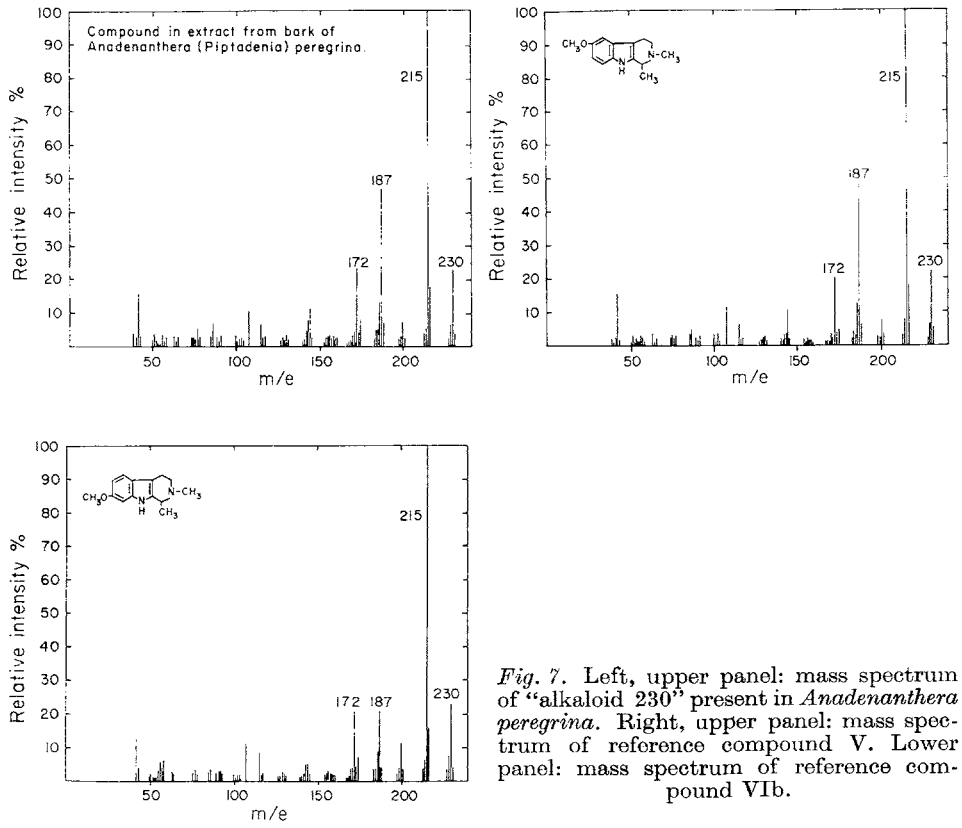

Fig. 7. Left, upper panel: mass spectrum of "alkaloid 230" present in *Anadenanthera peregrina*. Right, upper panel: mass spectrum of reference compound V. Lower panel: mass spectrum of reference compound VIb.

UV (Fig. 8 D) and fluorescence (Table 3) spectra proved the position of the methoxy group to be as shown in V. Compound V was readily distinguished from 2-methyl-tetrahydroharmine (VIb) by these spectra, although the compounds were difficult to separate by GLC. The mass spectra of V

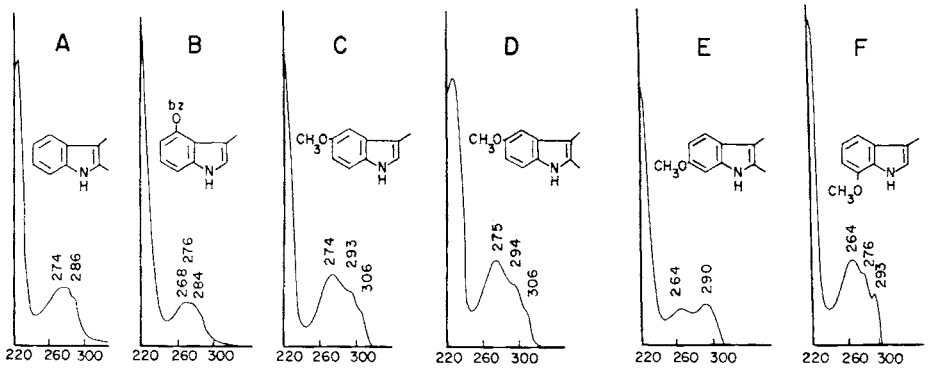

Fig. 8. UV-spectra (in ethanol) of tryptamines and β-carbolines. UV-maxima in mμ shown. A. MTHC B. 4-benzyloxy-*N*,*N*-dimethyltryptamine, C. 5-MeO—DMT, D. 6-MeO—DMTHC, E. 2-methyltetrahydroharmine, F. 7-methoxy-*N*,*N*-dimethyltryptamine.

and VIb (Fig. 7) were virtually identical except for the peak at *m/e* 187 which in compound V was 45 % and in VIb 22 % of the base peak.

The two new β-carbolines, IVb and V, belong to a group of compounds related both to serotonin and the harman alkaloids. They should prove to be pharmacologically interesting. The basic structure is previously represented only by plectocomine [14] (6-hydroxy-1,2,3,4-tetrahydro-β-carboline), present in *Plectocomiopsis geminiflorus* Becc. (fam. Palmae), a plant reported to be toxic.

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REFERENCES

1. Efron, D. H. (Ed.). *Ethnopharmacologic Search for Psychoactive Drugs*, U.S. Public Health Service Publ. No. 1645, 1967.
2. Holmstedt, B. and Lindgren, J.-E. *Ethnopharmacologic Search for Psychoactive Drugs*, U.S. Public Health Service Publ. No. 1645, 1967, p. 339.
3. Schultes, R. E. and Holmstedt, B. *Rhodora* **70** (1968) 113.
4. Fish, M. S., Johnson, N. M. and Horning, E. C. *J. Am. Chem. Soc.* **77** (1955) 5892.
5. Horning, E. C., Van den Heuvel, W. J. A. and Creech, B. G. *Methods Biochem. Anal.* **11** (1963) 69.
6. Horning, E. C., Moscatelli, E. and Sweely, C. C. *Chem. Ind. London* **1959** 751.
7. Agurell, S. and Ramstad, E. *Lloydia* **25** (1962) 67.
8. Ghosal, S. and Mukherjee, B. *J. Org. Chem.* **31** (1966) 2284.
9. Akabon, S. and Saito, K. *Ber.* **63** (1930) 2245.

10. Boit, H. G. *Ergebnisse der Alkaloidchemie bis 1960*, Akademie Verlag, Berlin 1961.
11. Taborsky, R. G. and McIsaac, W. M. *J. Med. Chem.* **7** (1964) 135.
12. Stromberg, V. L. *J. Am. Chem. Soc.* **76** (1954) 1707.
13. Legler, G. and Tschesche, R. *Naturwiss.* **50** (1963) 94.
14. Kiang, A. K., Chan, K. C. and Taylor, W. I. *Lloydia* **30** (1967) 189.
15. Biemann, K. *Fortschr. Chem. Org. Naturstoffe* **24** (1966) 56.
16. Budzikiewicz, H., Djerassi, C. and Williams, D. H. *Structure Elucidation of Natural Products by Mass Spectrometry*, Holden-Day Inc., 1964, Vol. I, p. 79.
17. Udenfriend, S., Bogdanski, D. F. and Weissbach, H. *Science* **122** (1955) 972.
18. Platonova, T. F., Kuzovkov, A. D. and Massagetov, P. S. *J. Gen. Chem. (UDSSR)* **28** (1958) 3159.

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