

THE EMETINE ALKALOIDS¹

WOLFGANG WIEGREBE,² WENDY J. KRAMER, and MAURICE SHAMMA

Department of Chemistry, The Pennsylvania State University, University Park, PA 16802

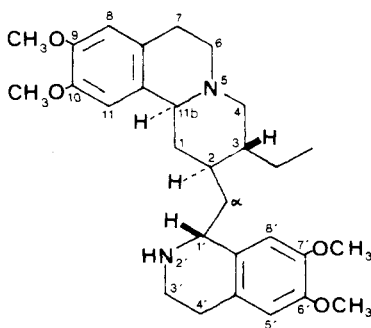
The present listing includes emetine and emetine analogs, all of which incorporate as part of their structures a top isoquinoline portion originating from tyrosine and a lower portion of monoterpene origin. Tubulosine and related bases are also included; these consist of a top isoquinoline portion, a middle portion of monoterpene origin, and a lower pendant indole system originating from tryptophan.

The last alkaloid to be mentioned is the recently characterized bharatamine (**30**), which occupies an anomalous position. Biogenetically, it is related to emetine (**1**) because its upper moiety emanates from tyrosine and its lower half is very probably of terpenoid derivation. From a purely structural aspect, however, this compound may be considered a protoberberine, even though it lacks the two oxygenated substituents always present in ring D of the protoberberines. Because of this ambiguity, bharatamine is included in this listing and will also be mentioned in a forthcoming review of the protoberberines.

Emetine and emetine analogs occur with certainty in only three plant families: Alangiaceae, Icacinaceae, and Rubiaceae. *Psychotria ipecacuanha* Stokes (Rubiaceae) is one of the main sources for emetine and its analogs. The name of this plant is synonymous with *Cephaelis ipecacuanha* Rich. and also with *Uragoga ipecacuanha* Baill. Similarly, *Psychotria granadensis* Benth. ex Oerst is synonymous with *Uragoga granadensis*.

Uv data are in nm, and log ϵ values are quoted between parentheses. Ir frequencies are in cm^{-1} . Nmr spectra are at low resolution in CDCl_3 , unless stated otherwise. Chemical shifts are in δ units. Whenever two or more references are cited, it is usually the first reference that is actually quoted in the tables.

The numbering system for emetine (**1**) is as given below. Several reviews or listings of the emetine alkaloids have appeared in the literature (1a-o).

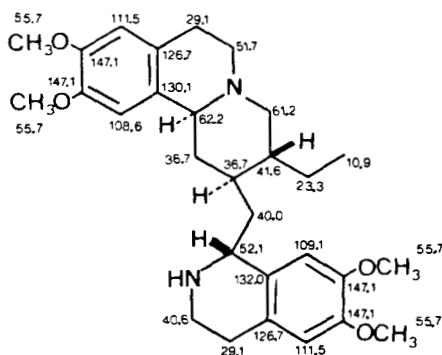


1

¹This paper is dedicated to Prof. Jack L. Beal in appreciation of his many years of unstinting service as editor of this journal.

²Permanent address: Faculty of Chemistry and Pharmacy, D-8400 Regensburg, West Germany.

1. EMETINE



$C_{29}H_{40}N_2O_4$: 480.2988

MP: 74° (1e), $104-105^\circ$ (1a)

$[\alpha]_D$: -46.55° ($CHCl_3$) (2)

-22° (EtOH) (1a)

-50° ($CHCl_3$) (1a)

-26° ($CHCl_3$) (1b)

ORD: (HBr) (3, no data)

CD: (EtOH; 0.1 N HCl) (4, figures)

UV: ($CHCl_3$) 285, 290 sh (5)

(HCl) 230 (4.23), 283 (3.87) (1g)

(1o, spectrum No. 330)

IR: (film) 3310, 1610 (6)

(Oxalate) (7, figure)

(1o, spectrum No. 330)

MS: 480 (M^+), 288, 272, 258, 246, 206, 192 (8, 9, 10, 1b)

CMR: (11, 1f)

SOURCES:

ALANGIACEAE: *Alangium lamarckii*

Thwaites (1b, 1g, 1i, 9)

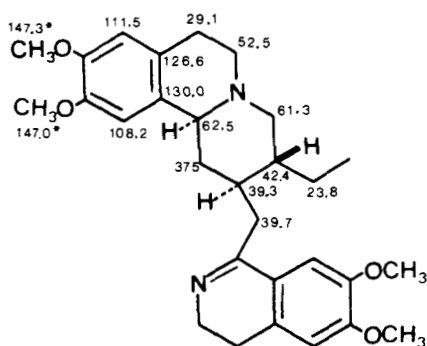
RUBIACEAE: *Cephaelis acuminata* Karsten

(biosynthesis) (15), *Psychotria granadensis* Benth.

ex Oerst and *P. ipecacuanha* Stokes (1a, 1b, 1e, 1i,

12, 13, 14, 6)

2. O-METHYLPSYCHOTRINE



$C_{29}H_{38}N_2O_4$: 478.2831

MP: $123-124^\circ$ (1e, 6, 12)

(Oxalate) 161° (dec.) (16, 17)

$[\alpha]_D$: 43.2° (EtOH) (1e)

ORD: (Oxalate) (c 2, H_2O)

$[\alpha]^{20}_D +37.3^\circ$, $[\alpha]^{20}_{578} +39.7^\circ$, $[\alpha]^{20}_{546} +47.6^\circ$,

$[\alpha]^{20}_{436} +130.1^\circ$, $[\alpha]^{20}_{365} +130.1^\circ$ (17)

UV: (0.1 N HCl) 241.5 (4.26), 288.5 (3.86), 305

(3.92), 354 (3.91) (18), (EtOH) (19)

(1o, spectrum No. 178)

IR: (Nujol) 1618, 1610, 1576 (6)

(1o, spectrum No. 178)

MS: 478 (M^+), 463, 449, 286, 274, 273, 272, 258,

244 (base), 239, 230, 206, 205, 192, 191, 190

(9, 10, 1g)

PMR: 0.98 (C-Me), 3.75, 3.82, 3.89, 3.92 (O-Me),

6.49, 6.54, 6.73, 7.03 (arom. H) (18)

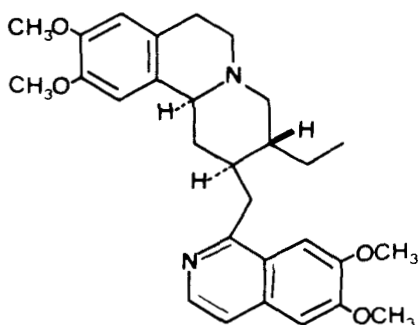
CMR: (18)

SOURCES:

RUBIACEAE: *Psychotria granadensis* Benth. ex

Oerst (1g, 6), *P. ipecacuanha* Stokes (1a)

3. EMETAMINE



$C_{29}H_{36}N_2O_4$: 476.2675

MP: $155-156^\circ$ (1a)

(Oxalate) $170-171^\circ$

(dec.) (6)

$[\alpha]_D$: 13.6° (EtOH) (1e)

(Oxalate) -5.5° (H_2O) (6)

UV: (EtOH) 236 (4.85), 283 (3.86) (1g)

MS: 476 (M^+), 461, 447, 286, 274, 273, 272 (base),

258, 244, 242, 238, 228, 204, 203, 192, 191,

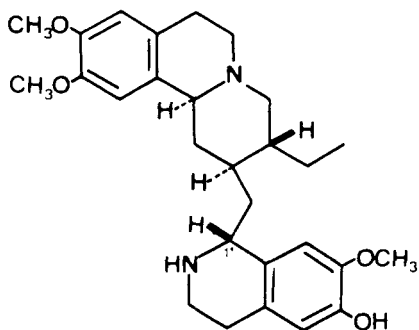
190 (9)

SOURCES:

RUBIACEAE: *Psychotria granadensis* Benth. ex

Oerst and *P. ipecacuanha* Stokes (1a, 1g, 6, 20)

4. CEPHAELINE

C₂₈H₃₈N₂O₄: 466.2831

MP: 115-116° (1e)

104-107° (1b, 2)

(HCl) 254-257° (22)

[α]²⁵_D: -43.4° (CHCl₃) (1e, 21)

UV: (19, figure)

MS: 466 (M⁺), 451, 437, 288, 274, 273, 272, 246,

244, 206, 205, 192, 178 (base) (9, 1b)

SOURCES:

ALANGIACEAE: *Alangium lamarckii* Thwaites (9, 21, 22, 1b), *A. salviifolium* (23, 24)RUBIACEAE: *Cephaelis acuminata* Karsten (biosynthesis) (15), *Psychotria granadensis* Benth. ex Oerst and *P. ipecacuanha* Stokes (1a, 1e, 13, 14)

5. ISOCEPHAELINE

Epimeric with cephaeline at C-1'

C₂₈H₃₈N₂O₄: 466.2831MP: 108-116° (Et₂O) (25)[α]²⁰_D: -69.8° (CHCl₃) (25)

UV: (EtOH) 228 sh, 286 (25)

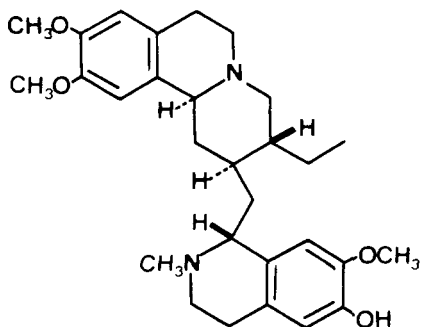
MS: (25)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (25)

6. ALAMARCKINE

(N-Methylcephaeline)

C₂₉H₄₀N₂O₄: 480.2988

MP: 191-192° (9)

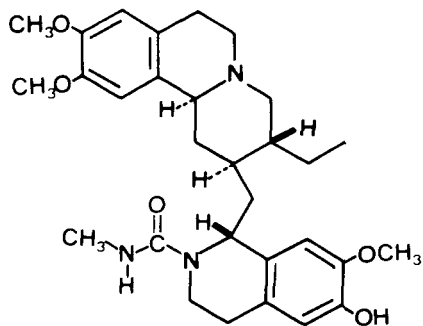
[α]_D: -50.5° (c 1.14, MeOH) (9)MS: 480 (M⁺), 455, 451, 288, 274, 273, 272, 246,

244, 206, 205, 192 (base), 191, 190, 177 (9)

SOURCES:

Semisynthetic; from N-methylation of the crude alkaloids of *Alangium lamarckii* Thwaites (Alangiaceae), or from N-methylation of cephaeline (9, 2)

7. ALANGAMIDE

C₃₀H₄₁N₃O₅: 523.3046MP: 213° (EtOH-H₂O) (26)[α]_D: -45 ± 2° (c 0.82, CHCl₃) (26)

UV: (EtOH or 0.1 N EtOH-HCl) 211 (4.66), 227 sh

(4.13), 286 (3.85) (26)

(0.1 N EtOH-NaOH) 222 (4.74), 230 sh (4.19),

289 (3.93), 302 sh (3.82) (26)

IR: (CHCl₃) 3500, 3200, 1631 (26)MS: 523 (M⁺), 522, 508, 494, 466, 274, 273, 246,

244, 192 (26)

PMR: 2.80, 2.88 (urea N-Me), 3.82, 3.86, 3.94

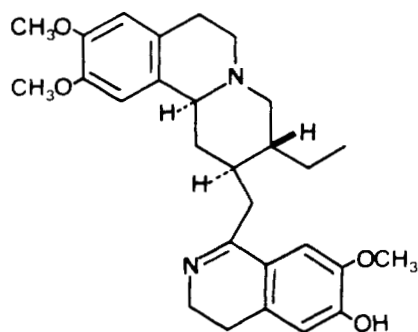
(three O-Me), 5.83 (N-H), 6.57 (two arom. H),

6.62, 6.92 (arom. H) (26)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (26)

8. PSYCHOTRINE

C₂₈H₃₆N₂O₄: 464.2674

MP: 138° (1a)

130-133° (Me₂CO-H₂O) (2)117-120° (Me₂CO-H₂O) (16, 17, 22)

108-112° (1b)

[α]_D: +69° (EtOH) (1a)

+75.5° (MeOH) (16)

+80.2° (MeOH) (22)

+48° (CHCl₃) (1b)ORD: (c 1.0, EtOH) [α]_D²⁰ +68.4°, [α]_D²⁰₅₇₈ +73.8°, [α]_D²⁰₅₄₆ +90.3°, [α]_D²⁰₄₃₆ +91.4° (erratic measurement), [α]_D²⁰₃₆₅ 0° (17)CD: (EtOH) Φ²⁶ (nm) 0(460), +3520(402), +100(347), +1560(315), 0(285), -590(279), 0(275), +780(269), +200(264), +3320(244), 0(239), -11700(231), 0(224) (27)

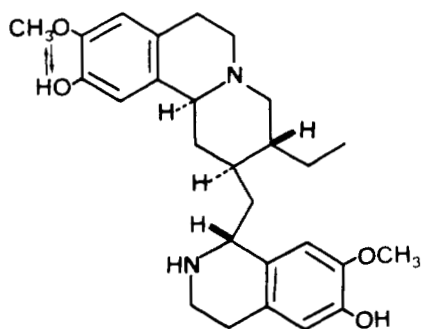
UV: (0.1 N HCl) 240 (4.14), 288 (3.76), 306 (3.80), 356 (3.83) (17, 1g)

IR: (CHCl₃) 3530, 1300, 1260 (17)MS: 464 (M⁺), 274, 273, 272, 258, 244 (base), 192, 191, 190 (9, 17)PMR: 3.62, 3.68, 3.77 (three O-CH₃), 6.45, 6.58, 7.02 (arom. H) (17)

SOURCES:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1b, 1g, 9, 16), *A. salviifolium* (23, 24)RHUBIACEAE: *Psychotria ipecacuanba* Stokes (1a, 1g, 12, 13)

9. DEMETHYLCEPHAELINE

C₂₇H₃₆N₂O₄: 452.2675

MP: 147-149° (22, 28)

[α]_D: -53.5° (CHCl₃) (22, 28)

UV: (EtOH) 211 (4.28), 225 sh (3.91), 286 (3.69) (22)

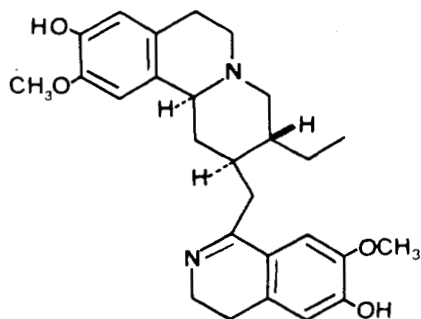
(0.1 N EtOH-NaOH) 213 (3.48), 227 (3.96), 247 (4.05), 301 (3.81) (22)

IR: (Nujol) 1010-1030 cm⁻¹ (22)MS: 452 (M⁺), 274, 272, 260, 259, 258, 232, 230, 192, 191, 178 (base) (22)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (22, 28)

The synthesis of (-)-9- and of (-)-10-demethylcephaeline has been reported, but a comparison with the natural product could not be carried out (28)

10. DEMETHYLPSYCHOTRINE
(9-Demethylpsychotrine) (29)C₂₇H₃₄N₂O₄: 450.2518

MP: 166-168° (EtOH) (16)

[α]_D: 67.9° (MeOH) (16)

72.3° (MeOH) (22)

UV: (EtOH) 223 (3.95), 277 (3.83), 310 (3.34), 410 (3.96) (16)

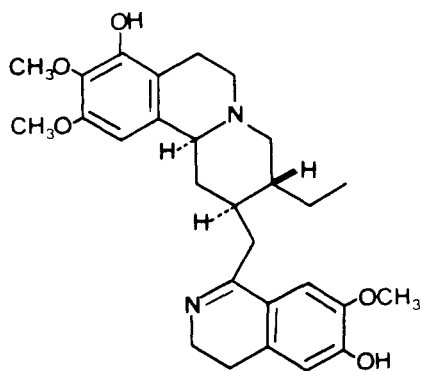
(0.1 N NaOH) 243 (4.41), 307 (4.28), 326 (4.32) (16)

IR: (CHCl₃) 3509 (16)MS: 435, 421, 272, 260, 259, 258, 256, 244, 230 (base), 228, 225 (M⁺⁺), 216, 192, 191, 190, 178, 177, 176 (16)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1g, 16, 22)

11. ALANGICINE

C₂₈H₃₆N₂O₅; 480.2624

MP: 147-148° (EtOH) (16, 27)

[α]_D: 64.1° (c 0.26, MeOH) (16, 27)CD: (EtOH) Φ²⁶ (nm) 0(448), +3010(402), +100(349), +1500(315), 0(285), -2000(275), +1000(269), -1670(265), 0(255), +1340(246), 0(241), -8850(233), 0(225) (27)

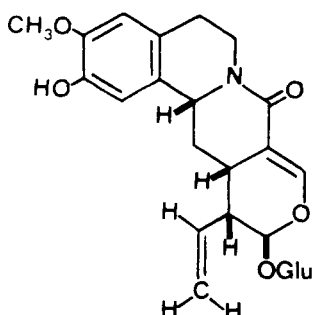
UV: (EtOH) 275 (3.84), 312 (3.42), 408 (4.09) (16) (0.1 N NaOH) 238 (4.17), 292 (3.82), 328 (4.07) (16)

MS: 465, 451, 302, 290, 289, 288, 274, 260 (base), 258, 240 (M⁺⁺), 216, 207, 206, 192, 191, 190, 178 (16)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1g, 16, 27)

12. ALANGISIDE

C₂₅H₃₁NO₁₀; 505.1948

MP: 187° (30)

[α]_{26D}: -105° (c 1.0, MeOH) (30, 31)

UV: (MeOH) 237 (4.27), 285 (3.68) (30)

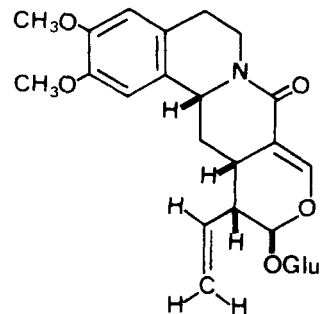
IR: (KBr) 3350, 1650, 1585, 1510, 1450, 1440, 1020, 910 (30, 31)

MS: 505 (M⁺), 343, 274 (base), 272, 178, 177, 176 (30)PMR: (DMSO-*d*₆) 3.79 (O-Me), 5.4 (3H, olefinic), 6.75 (arom. H), 7.39 (vinylic enol ether) (30, 31)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1g, 30)

13. O-METHYLALANGISIDE

C₂₆H₃₃NO₁₀; 519.2104

MP: 236° (EtOAc) (30)

IR: (KBr) 3375, 1655 (30)

MS: 519 (m⁺), 505, 358, 357, 356, 340, 288 (base), 274, 272, 270, 258, 257, 256, 192, 191, 178, 177, 176, 149, 145 (30)

PMR: 3.86, 3.90 (O-Me), 5.4 (olefinic H), 6.65, 6.8 (arom. H), 7.58 (O-CH=) (30)

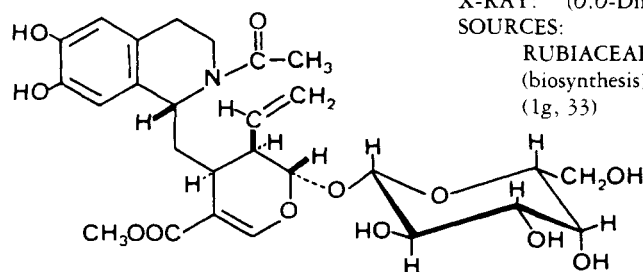
O-Methylalangiside tetraacetate at 270 MHz (32, 33)

CMR: O-Methylalangiside tetraacetate (33)

SOURCE:

Semi-synthetic from alangiside (30, 33)

14. IPECOSIDE

C₂₇H₃₅NO₁₂; 565.2159

MP: 176-178° (33)

CD: (Hexaacetate) (32)

UV: (EtOH) 227 (4.14), 287 (3.58) (33)

IR: 1690, 1630 (34)

MS: 220, 206, 178, 164, 43 (34)

PMR: (Trimethylsilyl ether) (34)

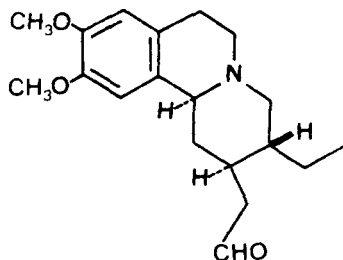
(Hexaacetate) (33)

X-RAY: (O,O-Dimethylipicoside) (35)

SOURCES:

RUBIACEAE: *Cephaelis acuminata* Karsten (biosynthesis) (15), *Psychotria ipecacuanha* Stokes (1g, 33)

15. PROTOEMETINE

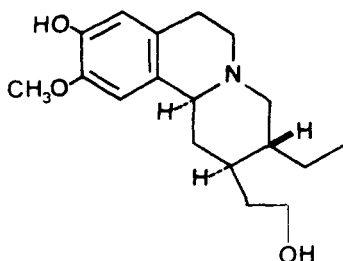


$C_{19}H_{27}NO_3$: 317.1990
 MP: (Perchlorate) 193-195° (MeOH) (1a, 1b)
 $[\alpha]_D$: (Perchlorate) -11° (EtOH) (1a, 1b)
 UV: (Perchlorate) (EtOH) 232 (3.92), 283 (3.61) (6, 1g)
 IR: ($CHCl_3$) 1725 (36, 6)
 MS: 317 (M^+) (36)
 PMR: 0.8-1.16 (CH_2CH_3), 3.91 (O-Me), 6.70 (arom. H), 6.77 (arom. H), 10.0 (CHO) (36)
 SOURCE:
 RUBIACEAE: *Psychotria ipecacuanha* Stokes (1a, 1g, 6)

16. PROTOEMETINOL
 (Dihydroprotoemetine)
 Aldehyde function of protoemetine (15)
 reduced to alcohol

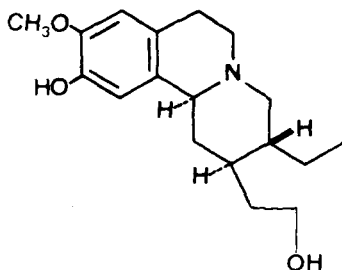
$C_{19}H_{29}NO_3$: 319.2147
 MP: (Perchlorate) 199-200° (EtOH-H₂O) (6)
 IR: (Nujol) 3550 (6)
 MS: 319 (M^+), 288, 272, 246, 205, 191, 190, 178 (21, 37)
 SOURCE:
 ALANGIACEAE: *Alangium lamarckii* Thwaites (1b, 21)
 Also from reduction of protoemetine (1g, 6)

17. 9-DEMETHYLPROTOEMETINOL



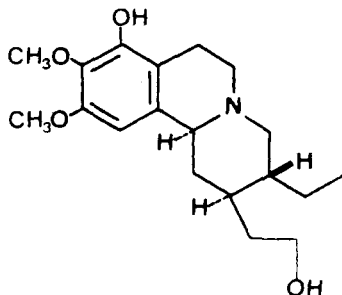
$C_{18}H_{27}NO_3$: 305.1991
 MP: 157-158.5° (38)
 $[\alpha]^{25}_D$: -61° (c 0.5, EtOH) (38)
 SOURCE:
 ALANGIACEAE: *Alangium lamarckii* Thwaites (39)

18. 10-DEMETHYLPROTOEMETINOL



$C_{18}H_{27}NO_3$: 305.1991
 MP: Glass (38, 39)
 $[\alpha]^{17}_D$: -35.2° (c 0.5, EtOH) (38)
 $[\alpha]_D$: -11.9 ($CHCl_3$) (39)
 UV: (EtOH) 227 (4.01), 286 (3.77) (39)
 IR: (Diacetate) (39)
 MS: 305 (M^+ , 51), 304 (80), 260 (28), 258 (17), 232 (base), 191 (93), 177 (98) (39)
 PMR: (Diacetate) (39)
 SOURCE:
 ALANGIACEAE: *Alangium lamarckii* Thwaites (39)

19. ANKORINE

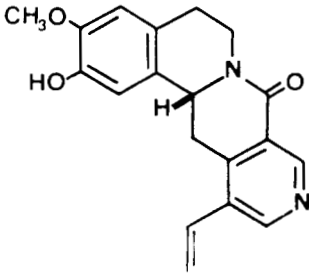


$C_{19}H_{29}NO_4$: 335.2096
 MP: 174-176° (40, 37)
 $[\alpha]^{20}_D$: -53.11° ($CHCl_3$) (40, 42)
 $[\alpha]_D$: -62° ($CHCl_3$) (37)
 UV: (EtOH) 272 (2.96) (37, 41, 42), (10, spectrum No. 805)
 IR: 3518, 3250 (37, 40, 42) ($CHCl_3$) 3630, 3530, 2800, 2750 (41), (10, spectrum No. 805)
 MS: 335 (M^+), 334 (base), 320, 318, 262, 221, 207, 192 (37, 41, 42)
 PMR: 0.88 (CH_2CH_3), 3.67 (CH_2OH), 3.76 (O-Me), 3.78 (O-Me), 6.24 (arom. H) (37, 41, 42)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites
(1b, 1f, 40, 37)
A. salviifolium (Linn.) Wangerin (24)

20. ALANGIMARIDINE



$C_{19}H_{18}N_2O_3$: 322.1317

MP: 278° (43)

[α]_D: 429° (c 0.35, CHCl₃) (?) (43)

UV: (EtOH) 220 (4.53), 255 (4.00), 284 (3.84) (43)

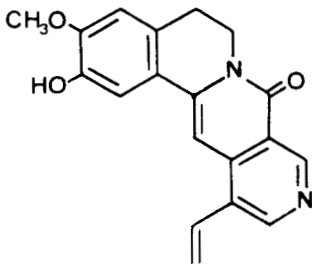
MS: 322 (M^+), 177, 175, 145, 117 (43)

PMR: (Acetate) (43)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites
(43)

21. ALANGIMARINE



$C_{19}H_{16}N_2O_3$: 320.1161

MP: 247° (43)

UV: (EtOH) 220 (4.37), 261 (4.11), 290 sh (3.83),
365 (4.42) (43)

IR: (Nujol) 1650 (43)

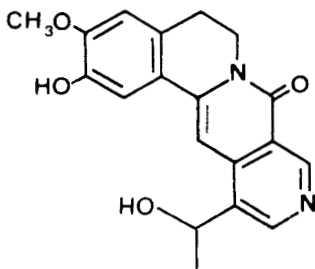
MS: 305 ($M^+ - 15$) (43)

PMR: (Acetate) (43)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites
(43)

22. ALAMARINE



$C_{19}H_{18}N_2O_4$: 338.1266

MP: 288° (EtOH) (43)

[α]_D: 0° (43)

UV: (EtOH) 220 (4.37), 253 (4.20), 363 (4.44) (43)

MS: 338 (M^+) (43)

PMR: (Diacetate) (43)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites
(43)

23. ISOALAMARINE

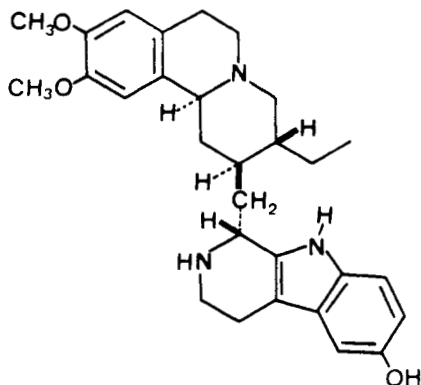
As in alamarine (22), but with positions of phenolic and methoxy functions probably reversed.

$C_{19}H_{18}N_2O_4$: 338.1266

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites
(43)

24. TUBULOSINE
(Marckine) (44)



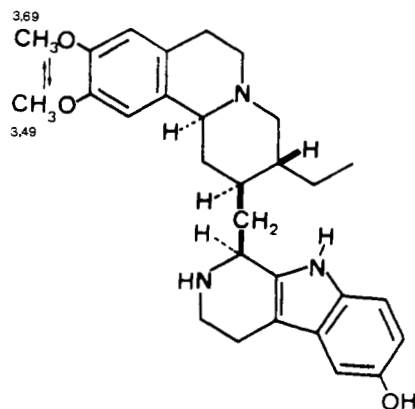
$C_{29}H_{37}N_3O_3$: 475.2835
 MP: 257-260° (MeOH) (21, 45, 46)
 $[\alpha]_D$: -72.0 (pyridine) (21, 45)
 UV: (MeOH) 223 (4.60), 279 (4.16), 310 sh (3.67) (21, 45)
 IR: (KBr) 3401, 1631, 1600 (21)
 MS: 475 (M^+), 288, 275-272, 246, 244, 206, 205, 201, 192, 191, 187 (base) (45, 48, 21)
 PMR: 0.95 (CH_2CH_3), 3.75 (O-Me), 4.15 (N-H), 6.5-7.3 (five arom. H), 8.4 (OH), 10.4 (indole N-H) (45, 21)

SOURCES:

ALANGIACEAE: *Alangium lamarckii* Thwaites (21, 46)
 RUBIACEAE: *Pogonopus tubulosus* Schumann (45)

The position of the phenolic function has been settled conclusively (47).

25. ISOTUBULOSINE

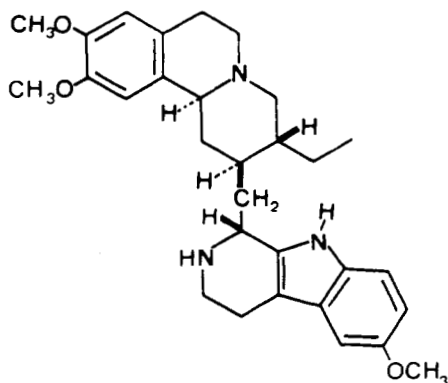


$C_{29}H_{37}N_3O_3$: 475.2835
 MP: 177-178° (EtOH) (1b, 49)
 $[\alpha]^{25}_D$: -84.0° (pyridine) (1b, 49)
 UV: (MeOH) 279 (4.08) (49)
 IR: (49)
 MS: 288, 274, 273, 272, 244, 205, 201, 192, 191, 190, 187 (base), 160, 146 (49)
 PMR: (DMSO- d_6) (49)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1b, 49)

26. O-METHYLTUBULOSINE

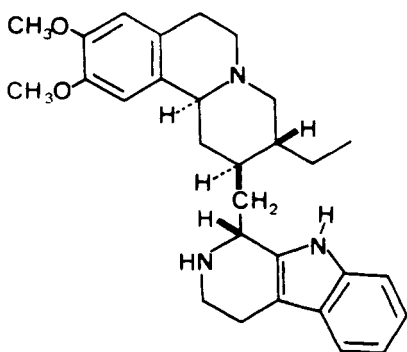


$C_{30}H_{39}N_3O_3$: 489.2991
 MP: 183° ((+)-enantiomer) (48)
 146-148° (MeOH) (racemate) (36)
 $[\alpha]^{20}_D$: 15.4° (c 1.0, MeOH) (48)
 IR: ($CHCl_3$) 3510 (36)
 MS: 489 (M^+) (36)
 PMR: 0.77-1.16 (CH_2CH_3), 3.86 (O-Me), 6.69-7.16 (arom. H), 7.81 (N-H) (36)

SOURCE:

Semisynthetic. (+)-Enantiomer from tubulosine (48). Racemate from racemic 4-oxoprotoemetine (36)

27. DEOXYTUBULOSINE

C₂₉H₃₇N₃O₂: 459.2886

MP: 230-232° (1b)

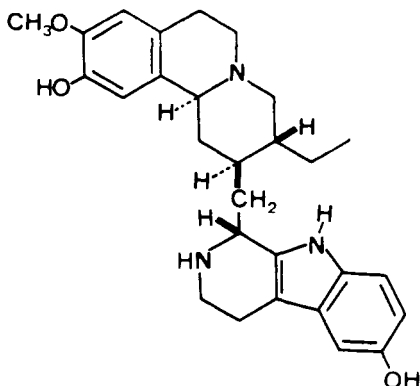
[α]_D: -24° (CHCl₃) (50, 1b)-17° (CHCl₃) (1b)IR: (CHCl₃) 3530 (36, 50)MS: 459 (M⁺), 288, 286, 275-272, 246, 244, 185, 171 (50)

PMR: 6.58 (1H, arom. H), 6.70 (1H, arom. H), 7.0-7.4 (4H, arom. H) (50)

SOURCES:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1b, 50, 51)ICACINACEAE: *Cassinopsis ilicifolia* Kuntze (1b, 52)

28. 10-DEMETHYLTUBULOSINE

C₂₈H₃₅N₃O₃: 461.2679MP: 198-200° (MeOH-CH₂Cl₂) (1b, 48)[α]_D²³: -51.9 (c 1, pyridine) (1b, 48)

UV: (MeOH) 278 (4.10 (48)

IR: 3500 (48)

MS: 259, 258, 246, 230, 201, 191, 187, 178, 177, 176 (48)

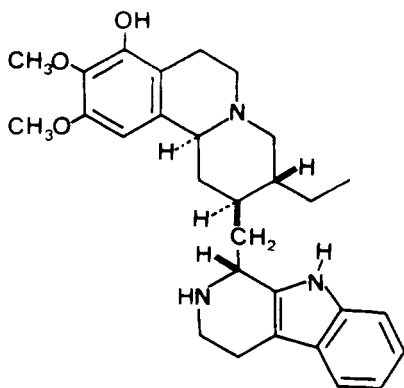
PMR: (Pyridine-d₅) 3.76 (48)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1b, 48)

For the location of the phenolic function, see (53).

29. ALANGIMARCKINE

C₂₉H₃₇N₃O₃: 475.2835

MP: (Hydrate) 184-186° (37, 4)

[α]_D²⁵: -67.7° (pyridine) (37, 4)

UV: (EtOH) 226 (4.28), 283 (4.18) (54)

IR: 3508, 3460 (37)

MS: 171 (base) (37)

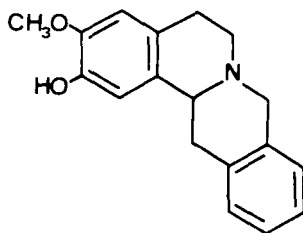
PMR: 0.84, 1.94, 3.70, 3.76 (two O-Me), 4.16 (CH₂CH-Ar-NH), 6.27, 6.9-7.5 (arom. H) (37)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites (1b, 54)

The alkaloid AL 64 (54) may be alangimarckine.

30. BHARATAMINE

C₁₈H₁₉NO₂: 281.1416MP: 182-183° (petroleum ether-CHCl₃) (55)[α]_D: 0° (55)UV: (EtOH) 206 (5.08), 290 (2.77) (55)
(0.01 N NaOH) 208 (4.85), 295 (3.91), 310
(2.71) (55)

IR: (Nujol) 3160 (55)

MS: 281 (M⁺), 280 (base), 176, 104 (55)PMR: 2.48-4.12 (aliphatic H), 3.84 (O-Me), 6.60,
6.84, 7.74 (arom. H) (55)

SOURCE:

ALANGIACEAE: *Alangium lamarckii* Thwaites
(55)

Occurrence of the Alkaloids by Plant Sources

Alangiaceae

Alangium lamarckii Thwaites

- Emetine (1)
- Emetamine (3)
- Cephaeline (4)
- Isocephaeline (5)
- Alangamide (7)
- Psychotrine (8)
- Demethylcephaeline (9)
- Demethylpsychotrine (10)
- Alangicine (11)
- Alangiside (12)
- Protoemetinol (16)
- 9-Demethylprotoemetinol (17)
- 10-Demethylprotoemetinol (18)
- Ankorine (19)
- Alangimaridine (20)
- Alangimarine (21)
- Alamarine (22)
- Isoalamarine (23)
- Tubulosine (24)
- Isotubulosine (25)
- Deoxytubulosine (27)
- 10-Demethyltubulosine (28)
- Alangimarckine (29)
- Bharatamine (30)

Alangium salviifolium

- Cephaeline (4)
- Psychotrine (8)
- Ankorine (19)

Icacinaeae

Cassinopsis ilicifolia Kuntze

- Deoxytubulosine (27)

Rubiaceae

Cephaelis acuminata Karsten

- Emetine (1)
- Cephaeline (4)
- Ipecoside (14)

Pogonopus tubulosus Schumann

- Tubulosine (24)

Psychotria granadensis Benth. ex Oerst

- Emetine (1)
- O-Methylpsychotrine (2)
- Emetamine (3)
- Cephaeline (4)

Psychotria ipecacuanha Stokes

- O-Methylpsychotrine (2)
- Emetamine (3)
- Cephaeline (4)
- Psychotrine (8)
- Ipecoside (14)
- Protoemetine (15)

Unconfirmed Occurrence of Emetine-Type Alkaloids

Emetine has been reported to be present in *Borreria verticillata* (Rubiaceae) (56). Other Central or South American Rubiaceae containing emetine, cephaeline, and psychotrine are *Bothriospora corymbosa*, *Capirona decorticans*, *Ferdinandusa elliptica*, *Tocoyena longiflora*, *Remija amazonica*, and *Hillia ilustria* (57). A rather doubtful source of emetine is the common ivy, *Hedera helix* (Araliaceae) (58).

Alphabetical Listing of the Alkaloids

Alamarckine (6)	Demethyltubulosine (28)
Alamarine (22)	Deoxytubulosine (27)
Alangamide (7)	Emetamine (3)
Alangicine (11)	Emetine (1)
Alangimarckine (29)	Ipecoside (14)
Alangimaridine (20)	Isoalamarine (23)
Alangimarine (21)	Isocephaline (5)
Alangiside (12)	Isorubulosine (25)
Ankorine (19)	Marckine (24)
Bharatamine (30)	O-Methylalangsine (13)
Cephaeline (4)	O-Methylpsychotrine (2)
Demethylcephaeline (9)	O-Methyltubulosine (26)
9-Demethylprotoemetinol (17)	Protoemetine (15)
10-Demethylprotoemetinol (18)	Protoemetinol (16)
Demethylpsychotrine (10)	Psychotrine (8)
	Tubulosine (24)

LITERATURE CITED

- For previous reviews on, or listings of, the emetine alkaloids, see:
 - H.-G. Boit, "Ergebnisse der Alkaloid-Chemie bis 1960," Berlin: Akademie-Verlag, 1961, p. 370.
 - A. Brossi, S. Teitel, and G.V. Parry, in: "The Alkaloids," vol. 13. Ed. by R.H.F. Manske, New York: Academic Press, 1971, p. 189.
 - R.H.F. Manske, in: "The Alkaloids," vol. 7. Ed. by R.H.F. Manske, New York: Academic Press, 1960, p. 419.
 - J.S. Glasby, "Encyclopedia of the Alkaloids," vol. 2. New York: Plenum Press, 1975.
 - M.M. Janot, in: "The Alkaloids," vol. 3. Ed. by R.H.F. Manske, New York: Academic Press, 1953, p. 363.
 - M. Shamma and J.L. Moniot, "Isoquinoline Alkaloid Research 1972-1977," New York: Plenum Press, 1978, p. 355.
 - M. Shamma, "The Isoquinoline Alkaloids," New York: Academic Press, 1972, p. 427.
 - T. Kametani, "The Chemistry of the Isoquinoline Alkaloids," vol. 2. Sendai, Japan: Kinkodo Publishing Co., 1974, p. 265.
 - T. Kametani, "The Chemistry of the Isoquinoline Alkaloids," vol. 1. New York: Tokyo Hirokawa Publishing Co., 1969, p. 160.
 - J.S. Glasby, "Encyclopedia of the Alkaloids," vol. 1, New York: Plenum Press, 1975.
 - N.J. McCorkindale, "The Alkaloids, A Specialist Periodical Report," vol. 7. M.F. Grondon sen. reporter, The Chemical Society, London, 1975, p. 147.
 - K.W. Bentley, "The Alkaloids, A Specialist Periodical Report," vol. 9. M.F. Grondon sen. reporter, The Chemical Society, London, 1977, p. 112.
 - K.W. Bentley, "The Alkaloids, A Specialist Periodical Report," vol. 10. M.F. Grondon sen. reporter, The Chemical Society, London, 1978, p. 107.
 - K.W. Bentley, "The Alkaloids, A Specialist Periodical Report," vol. 11, M.F. Grondon sen. reporter, The Chemical Society, London, 1979, p. 98.
 - J. Holubek and O. Štrouf, "Spectral Data and Physical Constants of Alkaloids," Prague: Publishing House of the Czechoslovak Academy of Science, London: (Heyden & Son Ltd.) A collection of spectra for 1000 alkaloids, published between 1965 and 1973.
- S.C. Pakrashi and P.P. Ghosh Dastidar, *Indian J. Chem.*, **2**, 379 (1964).
- E.E. van Tamelen and J.B. Hester, Jr., *J. Am. Chem. Soc.*, **81**, 507 (1959)
- T. Fujii, H. Kogen, and M. Ohba, *Tetrahedron Lett.*, 3111 (1978).
- M.A.H. Elsayed, M.A.A. Salam, N.A.A. Salam, and Y.A. Mohammed, *Planta Med.*, **34**, 430 (1978).
- A.R. Battersby, G.C. Davidson, and B.J.T. Harper, *J. Chem. Soc.*, 1744 (1959). A.R. Battersby and B.J.T. Harper, *ibid.*, 1748 (1959).
- R.N. Hazlett and W.E. McEwen, *J. Am. Chem. Soc.*, **73**, 2578 (1951).
- G. Spiteller and M. Spiteller-Friedmann, *Tetrahedron Lett.*, 153 (1963).
- H. Budzikiewicz, S.C. Pakrashi, and H. Vorbrüggen, *Tetrahedron*, **20**, 399 (1964).
- C. Schuij, G.M.J. Beijersbergen van Henegouwen, and K.W. Gerritsma, *J. Chem. Soc., Perkin 1*, 970 (1979).

11. M.C. Koch, M.M. Plat, and N. Préaux, *J. Org. Chem.*, **40**, 2836 (1975).
12. W.H. Brindley and F.L. Pyman, *J. Chem. Soc.*, 1067 (1927).
13. O. Keller, *Arch. Pharm.*, **249**, 512 (1911).
14. O. Keller, *Arch. Pharm.*, **251**, 701 (1913).
15. A.G. Garg and J.R. Gear, *Phytochemistry*, **11**, 689 (1972).
16. S.C. Pakrashi and E. Ali, *Tetrahedron Lett.*, 2143 (1967).
17. S. Teitel and A. Brossi, *J. Am. Chem. Soc.*, **88**, 4068 (1966).
18. T. Fujii, M. Ohba, O. Yonemitsu, and Y. Ban, *Chem. Pharm. Bull.*, **30**, 598 (1982).
19. H. Auterhoff and K. Merz, *Arch. Pharm.*, **291**, 326 (1958).
20. A.R. Battersby, R. Binks, and G.C. Davidson, *J. Chem. Soc.*, 2704 (1959).
21. J.D. Albright, J.C. Van Meter, and L. Goldman, *Lloydia*, **28**, 212 (1965).
22. S.C. Pakrashi and B. Achari, *Experientia*, **26**, 933 (1970).
23. P.D. Desai, A.K. Ganulgy, T.R. Govindachari, B.S. Joshi, V.N. Kamat, A.H. Manmade, P.A. Mohamed, S.K. Nagle, R.H. Nayak, A.K. Saksena, S.S. Sathe, and N. Viswanathan, *Indian J. Chem.*, **4**, 457 (1966).
24. M.J. Chen, L.L. Hou, H. Zhu, *Chih Wu Hsueh Pao*, **22**, 257 (1980); *Chem. Abstr.*, **94**, 12818 (1981).
25. B. Achari, E. Ali, P.P. Ghosh Dastidar, R.R. Sinha, and S.C. Pakrashi, *Planta Med.*, suppl., 5 (1980).
26. S.C. Pakrashi and E. Ali, *Indian J. Chem.*, **7**, 635 (1969).
27. T. Fujii, S. Yoshifuji, and S. Minami, *Heterocycles*, **8**, 175 (1977).
28. T. Fujii and M. Ohba, *Heterocycles*, **19**, 857 (1982).
29. T. Fujii, M. Ohba, S.C. Pakrashi, and E. Ali, *Tetrahedron Lett.*, 4955 (1979).
30. A. Shoeb, K. Raj, R.S. Kapil, and S.P. Popli, *J. Chem. Soc., Perkin I*, 1245 (1975).
31. R.S. Kapil, A. Shoeb, S.P. Popli, A.R. Burnett, G.D. Knowles, and A.R. Battersby, *Chem. Commun.*, 904 (1971).
32. N. Nagakura, G. Höfle, and M.H. Zenk, *Chem. Commun.*, 896 (1978).
33. G. Höfle, N. Nagakura, and M.H. Zenk, *Chem. Ber.*, **113**, 566 (1980).
34. A.R. Battersby, B. Gregory, H. Spencer, and J.C. Turner, *Chem. Commun.*, 219 (1967).
35. O. Kennard, P.J. Roberts, N.W. Isaacs, F.H. Allen, W.D.S. Motherwell, K.H. Gibson, and A.R. Battersby, *Chem. Commun.*, 899 (1971); and P.J. Roberts, N.W. Isaacs, F.H. Allen, W.D.S. Motherwell, and O. Kennard, *Acta Crystallog.*, **B30**, 133 (1974).
36. T. Kametani, Y. Suzuki, and M. Ihara, *Heterocycles*, **13**, 209 (1979).
37. A.R. Battersby, R.S. Kapil, D.S. Bhakuni, S.P. Poli, J.R. Merchant, and S.S. Salgar, *Tetrahedron Lett.*, 4965 (1966).
38. T. Fujii, M. Ohba, H. Suzuki, S.C. Pakrashi, and E. Ali, *Heterocycles*, **19**, 2305 (1982).
39. E. Ali, R.R. Sinha, B. Achari, and S.C. Pakrashi, *Heterocycles*, **19**, 2301 (1982).
40. B. Dasgupta, *J. Pharm. Sci.*, **54**, 481 (1965).
41. T. Fujii, S. Yoshifuji, and K. Yamada, *Tetrahedron*, **36**, 965 (1980).
42. T. Fujii and S. Yoshifuji, *J. Org. Chem.*, **45**, 1889 (1980).
43. S.C. Pakrashi, B. Achari, E. Ali, P.P. Ghosh Dastidar, and R.R. Sinha, *Tetrahedron Lett.*, **21**, 2667 (1980).
44. V.U. Ahmad, M.A. Ali, S. Siddiqui, *Pakistan J. Sci. Ind. Res.*, **8**, 161 and 166 (1965); *Chem. Abstr.*, **68**, 899d and 29931u (1968).
45. P. Brauchli, V. Deulofeu, H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 1895 (1964).
46. S.S. Salgar and J.R. Merchant, *Curr. Sci. (India)*, **35**, 281 (1966); *Chem. Abstr.*, **65**, 7624e (1966).
47. Cs. Szántay and Gy. Kalas, *Acta Chim. Acad. Sci. Hung.*, **49**, 427 (1966).
48. A. Popelak, E. Haack, and H. Spingler, *Tetrahedron Lett.*, 1081 (1966).
49. A. Popelak, E. Haack, and H. Spingler, *Tetrahedron Lett.*, 5077 (1966).
50. A.R. Battersby, J.R. Merchant, E.A. Ruveda, and S.S. Salgar, *Chem. Commun.*, 315 (1965).
51. J.R. Merchant and S.S. Salgar, *Indian J. Chem.*, **13**, 100 (1975).
52. H. Monteiro, H. Budzikiewicz, and C. Djerassi, *Chem. Commun.*, 317 (1965).
53. T. Fujii, M. Ohba, A. Popelak, S.C. Pakrashi, and E. Ali, *Heterocycles*, **14**, 971 (1980).
54. S.C. Pakrashi, *Indian J. Chem.*, **2**, 468 (1964).
55. S.C. Pakrashi, R. Mukhopadhyay, P.P. Ghosh Dastidar, A. Bhattacharjya, and E. Ali, *Tetrahedron Lett.*, **24**, 291 (1983).
56. O.O. Orazi, *Rev. Facultad Cienc. Quim.* (Univ. Nacl. La Plata), **19**, 17 (1946); *Chem. Abstr.*, **41** 2210c (1947).
57. W. Freise, *Pharm. Zentralhalle*, **76**, 233 (1935).
58. G.H. Mahran, S.H. Hilal, and T.S. El-Alfy, *Planta Med.*, **27**, 127 (1975).