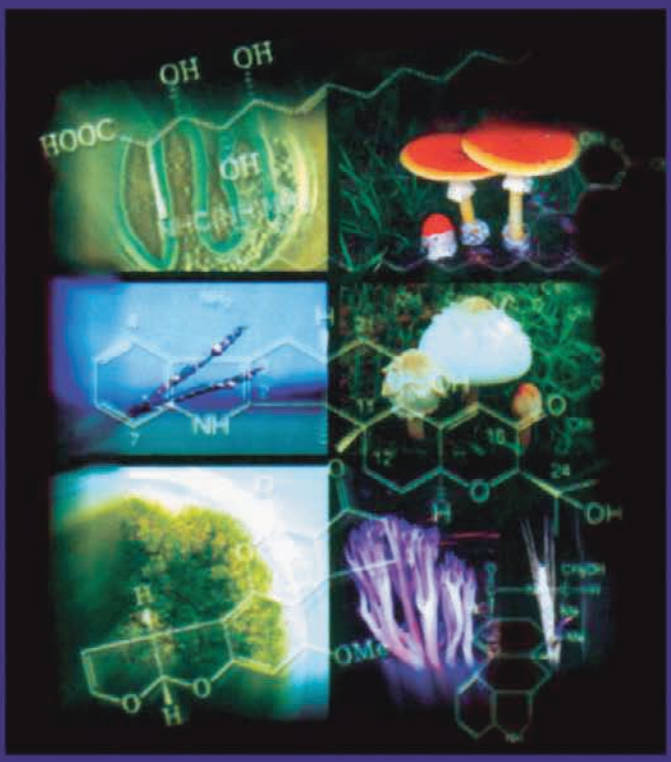
# HANDBOOK OF
# Secondary Fungal Metabolites
## VOLUME I




RICHARD J. COLE
MILBRA A. SCHWEIKERT

# Handbook of Secondary Fungal Metabolites

VOLUME I

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# Handbook of Secondary Fungal Metabolites

## VOLUME I

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*Cover images:* Photography by Dr. Bruce Horn and design by Brian E. Cole. The cover is a collage of various fungi, some presented in pure culture and others in their natural forms, i.e. mushrooms, which are the easily recognizable fruiting structures of some fungi, superimposed on these fungi are the chemical structures of some representative secondary fungal metabolites.

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# Contents

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# Preface

The "Handbook of Secondary Fungal Metabolites" is presented in three volumes and is comprehensive to the extent that all major groups of secondary fungal metabolites are included. The format is similar to that presented in the "Handbook of Toxic Fungal Metabolites" with the major exception that actual spectra are not included; however, spectral data are included where available. Also included in these volumes are the methods used by the authors to isolate and purify metabolites. Another major difference is that the appropriate references are presented with each metabolite, negating the need to turn to the end of each group to find the appropriate references. Each volume contains four indexes: secondary metabolite index, molecular formula index, molecular weight index, and fungal/plant source index. In a few instances, plant sources are included when the metabolites are closely related to fungal metabolites or the source of precursors may be fungal; i.e., the baccharins, which are found in extracts from *Baccharis megapotamica*. These metabolites are closely related to the macrocyclic trichothecenes found in extracts of fungi such as *Myrothecium* spp. and *Stachybotrys* spp. Also, metabolites from the fungal symbiont of lichens are sometimes presented. To aid in the interpretation of NMR data, the numbering system presented in the literature is included for the major representative fungal metabolite and, at times, for several related metabolites. Fungal sources are given as reported in the original references. It is recognized that the taxonomy in several cases has been revised, perhaps more than once. It is beyond the scope of these volumes to deal with what is "currently accepted taxonomy" because this is a dynamic science that, in many cases, is as yet undefined.

The "Handbook" has been divided into sections, and the placement of metabolites is based on chemical relationships. One section of each volume contains a miscellaneous section to accommodate metabolites difficult to place into one of the sections. The miscellaneous section of Volume III contains some metabolites related to those that appear in Volumes I and II. This occurred when related metabolites were discovered after Volumes I and II were completed.

It is hoped that this compilation of data on secondary fungal metabolites will aid investigators in the identification of known or related fungal metabolites. Because fungal metabolites represent a wide diversity of chemical species, these volumes will be useful to scientists interested in correlations of structural features with various spectral and biological characteristics. The known biological activity of metabolites is presented, which may aid in future studies related to the identification of new uses for fungal metabolites.

*Richard J. Cole*
*Milbra A. Schweikert*

# Acknowledgments

The authors thank the following investigators for their assistance in producing the "Handbook of Secondary Fungal Metabolites." Their contributions made this compilation of data on fungal metabolites possible.

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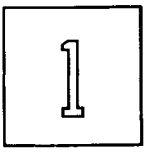


# Indole Alkaloids

3-(3-Indolyl)propane-1,2,3-triol
3-(3,3-Diindolyl)propane-1,2-diol
4-(3-Indolyl)butane-1,2,3-triol
*N*-Methyl-4-dimethylallyltryptophan
Lysergic Acid
Ergine; Lysergic acid amide
8-Hydroxyergine
Erginine; Isolysergic acid amide
8-Hydroxyerginine
Lysergol
Lysergene
Lysergine
Ergonovine; Ergometrine; Ergobasine
Ergonovinine; Ergometrinine; Ergobasinine
Agroclavine
6,7-*seco*-Agroclavine
Dihydroagroclavine
Festuclavine
Elymoclavine
Elymoclavine-*O*-ß-fructofuranoside
Elymoclavine-*O*-ß-fructofuranosyl-(2-1)-*O*-ß-D-fructofuranoside
Chanoclavine-I; Chanoclavine
Isochanoclavine-I
Chanoclavine-II
*N*-Demethylchanoclavine-II; Norchanoclavine II
Setoclavine
Isosetoclavine
Costaclavine
Pyroclavine
Molliclavine
Penniclavine
Cycloclavine
Ergotamine
Ergotaminine
8-Hydroxyergotamine
Ergosine
Ergosinine
Ergostine
Ergostinine
Ergonine
Ergovaline
Ergoptine
Ergocornine

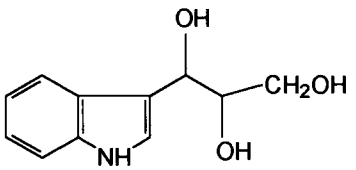
Ergocorninine
*O*-12'-Methylergocornine
Ergocristine
Ergocristinine
Ergosecaline
Ergosecalinine
Ergobalansine
Ergobalansinine
α-Ergocryptine
*O*-12'-Methyl-α-ergocryptine
β-Ergocryptine
5'-epimer of ß-Ergocryptine
β-Ergocryptam
β,β-Ergoannam
Ergobutine
Ergobutyrine
Rugulovasine A
8-Chlororugulovasine A
Rugulovasine B
8-Chlororugulovasine B
Fumigaclavine A; 9β-Acetoxy-6,8α-dimethylergoline
Roquefortine A; Isofumigaclavine A; 9-Acetoxy-6,8-dimethylergoline
Fumigaclavine B; 9-Hydroxy-6,8-dimethylergoline
Roquefortine B; Isofumigaclavine B; 9-Hydroxy-6,8-dimethylergoline
Fumigaclavine C; 2-Dimethylallyl-9-acetoxy-6,8-dimethylergoline

Common/Systematic Name

3-(3-Indolyl)propane-1,2,3-triol

Molecular Formula/Molecular Weight

$C_{11}H_{13}NO_3$; MW = 207.08954




General Characteristics

Red-violet color reaction with *p*-dimethylaminocinnamaldehyde.

Fungal Source

*Balansia epichloë.*

Isolation/Purification

Purification was achieved by column chromatography on Porapak Q and preparative TLC on silica gel $GF_{254}$ [TLC developing systems were chloroform-methanol (80:20, v/v) and benzene-dimethylformamide (86.5:13.5)].

Biological Activity

Toxic to fertile Leghorn chicken eggs: 23μg/egg = 80%; 68μg/egg = 100% mortality.

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 220(log ε=4.95), 273(4.00), 280(4.02), and 289nm (3.95).

IR:

(KBr) 1550, 1420, 1410, 1335, 1065, 1050, 740, and 780$cm^{-1}$.

Mass Spectrum:

207.08, 189.07, 188.06, 186.05, 172.07, 171.06, 170.05, 160.07, 159.06, 146.05, 145.05, 144.08, 144.04, 142.06, 130.06, 118.06, 117.05, 116.05, 103.05, 91.05, 90.04, and 89.03*m/e*.

Reference

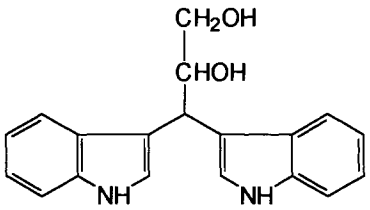
J. K. Porter, C. W. Bacon, J. D. Robbins, D. S. Himmelsbach, and H. C. Higman; Indole Alkaloids from *Balansia epichloë* (Weese); J. Agric. Chem., Vol. 25, pp. 88-93 (1977).

Common/Systematic Name

3-(3,3-Diindolyl)propane-1,2-diol

Molecular Formula/Molecular Weight

$C_{19}H_{18}N_2O_2$; MW = 306.13683




General Characteristics

Red-violet color reaction with *p*-dimethylaminocinnamaldehyde.

Fungal Source

*Balansia epichloë.*

Isolation/Purification

Purification was achieved by column chromatography on Porapak Q and preparative TLC on silica gel $GF_{254}$ [TLC developing systems were chloroform-methanol (80:20, v/v) and benzene-dimethylformamide (86.5:13.5, v/v)].

Biological Activity

Toxic to fertile Leghorn chicken eggs: 20μg/egg = 20%; 60μg/egg = 55% mortality; 99μg/egg = 100% mortality.

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 221(log ϵ=4.88), 275(3.97), 282(4.01), and 291nm (3.96).

IR:

(KBr) 1550, 1410, 1335, 1080, 1050, and 780$cm^{-1}$.

Mass Spectrum:

306.1368($M^+$), 272.1326, 270.1145, 258.1132, 257.1049, 256.0993, 245.1069, 218.0958, 217.0887, 188.0671, 171.0675, 170.06, 160.07, 159.06, 144.04, 142.06, 130.06, 118.06, 117.05, 116.05, 103.05, 91.05, 90.04, and 89.03*m/e*.

Reference

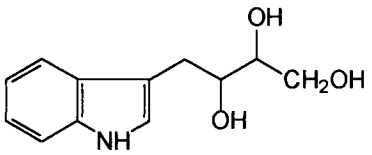
J. K. Porter, C. W. Bacon, J. D. Robbins, D. S. Himmelsbach, and H. C. Higman; Indole Alkaloids from *Balansia epichloë* (Weese); J. Agric. Chem., Vol. 25, pp. 88-93(1977).

Common/Systematic Name

4-(3-Indolyl)butane-1,2,3-triol

Molecular Formula/Molecular Weight

$C_{12}H_{15}NO_3$; MW = 221.10519




General Characteristics

Red-violet color reaction with *p*-dimethylaminocinnamaldehyde.

Fungal Source

*Balansia epichloë*

Isolation/Purification

Purification was achieved by column chromatography on Porapak Q and preparative TLC on silica gel $GF_{254}$ [TLC developing systems were chloroform-methanol (80:20, v/v) and benzene-dimethylformamide (86.5:13.5, v/v)].

Biological Activity

Toxic to fertile Leghorn chicken eggs: 57μg/egg = 53% mortality; 113μg/egg = 100% mortality.

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 221(log ϵ=4.65), 272(3.78), 279(3.8), and 288nm (3.73).

IR:

(KBr) 1550, 1410, 1340 1080, 1030, and 780$cm^{-1}$.

Mass Spectrum:

221.10($M^+$), 203.09, 201.08, 189.07, 188.07, 186.05, 172.07, 171.06, 170.06, 160.07, 159.06, 146.05, 145.05, 144.08, 144.04, 142.06, 130.06, 118.06, 117.05, 116.05, 103.05, 91.04, 91.05, 90.04, and 89.08*m/e*.

Reference

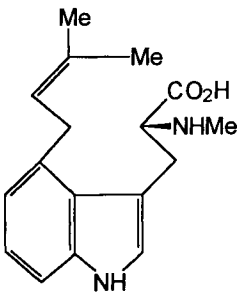
J. K. Porter, C. W. Bacon, J. D. Robbins, D. S. Himmelsbach, and H. C. Higman; Indole Alkaloids from *Balansia epichloë* (Weese); J. Agric. Chem., Vol. 25, pp. 88-93(1977).

Common/Systematic Name

*N*-Methyl-4-dimethylallyltryptophan

Molecular Formula/Molecular Weight

$C_{17}H_{22}N_2O_2$; MW = 286.16813




General Characteristics

*N*-Methyl-4-dimethylallyltryptophan crystallized from methanol as needles; mp., 232°C.

Fungal Source

*Claviceps fusiformis*.

Isolation/Purification

*Claviceps fusiformis* was grown aerobically in submerged cultures in both shaken flasks and stirred fermenters. When alkaloid production began, anaerobic conditions were imposed and the cultures stood for three days. Clavine alkaloids were extracted with chloroform at alkaline pH and then the amphoteric metabolites extracted with *n*-butanol at neutral pH. The butanol extract, which contained considerable quantities of chanoclavines and other oxygenated clavine alkaloids, was chromatographed on silica gel with chloroform/methanol/ammonia as the eluant.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 274, 280, and 295nm.

IR:

(KBr) 3580, 3250(broad) 1640, 1400, and 770cm$^{-1}$.

$^1$H NMR:

($CD_3COOD$) *inter alia* 8.64(s, 6H), 7.64(s, 3H), 5.06(t, 1H, *J*=7.0Hz), and 6.3-7.0ppm (complex, 4H).

Mass Spectrum:

286, 198, 156, 155, and 154*m/e*. The fragmentation under electron-impact was very similar to bis-seco-dehydrocyclopiazonic acid with allylic cleavage of the amino acid side chain giving the ion of *m/e* 198, followed by cyclization to a series of tricyclic ions *m/e* 156, 155, and 154 with elimination of a C-3 unit. Cyclization of this type is only possible if the two side chains are located in the *peri*-position of the indole nucleus, *i.e.* at positions 3 and 4.

TLC Purification

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated $NH_3$ atmosphere).
c) Chloroform-methanol-$NH_3$ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

References

K. D. Barrow and F. R. Quigley; Ergot Alkaloids III : The Isolation of *N*-Methyl-4-dimethylallyltryptophan from *Claviceps fusiformis;* Tetrahedron Letters, pp. 4269-4270 (1975).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

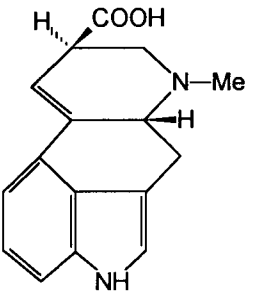
J. K. Porter; Analysis of Endophyte Toxins: Fescue and Other Grasses Toxic to Livestock; J. Animal Science, Vol. 73, pp. 871-880(1994).

Common/Systematic Name

Lysergic acid

Molecular Formula/Molecular Weight

$C_{16}H_{16}N_2O_2$; MW = 268.12118




General Characteristics

Hexagonal scales, plates from water (associated with one or two moles water); mp., 240°C (dec.); $[\alpha]_D^{20}$ +40° (*c*=0.5, in pyridine); $pK_a$=3.44/$pK_b$=7.68. Moderately soluble in pyridine; sparingly soluble in water and neutral organic solvents; soluble in NaOH, $NH_4OH$, $Na_2CO_3$, and HCl solutions; and slightly soluble in dilute $H_2SO_4$. Methyl ester derivative, thin leaflets from benzene; mp., 168°C.

Fungal Source

Sclerotia and saprophytic culture of *Claviceps purpurea*.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

IR:

See A. Hofmann, 1964.

$^{13}C$ NMR:

($CDCl_3$) (methyl lysergate) C-2, 118.2; C-3, 110.2; C-4, 26.9; C-5, 62.6; C-7, 54.6; C-8, 41.8; C-9, 117.6; C-10, 136.0; C-11, 127.6; C-12, 112.0; C-13, 122.9; C-14, 109.4; C-15, 133.7; C-16, 125.9; C-17, 172.4; Me, 51.9; and NMe, 43.4ppm.

Mass Spectrum:
LREIMS: 268($M^+$, 100%), 224, 221, 207, 192, 180, 167, and 154*m/e*.

References

N. J. Bach, H. E. Boaz, E. C. Kornfeld, C-J Chang, H. G. Floss, E. W. Hagaman, and E. Wenkert; Nuclear Magnetic Resonance Spectral Analysis of the Ergot Alkaloids; J. Org. Chem., Vol. 39, pp. 1272-1276(1974).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978) .

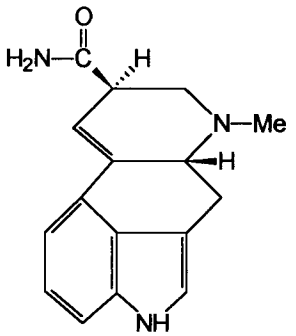
A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

Common/Systematic Name

Ergine; Lysergic acid amide

Molecular Formula/Molecular Weight

$C_{16}H_{17}N_3O$; MW = 267.13716




General Characteristics

Crystallized from acetone as massive colorless prisms; m.p. 196°C; $[\alpha]_D^{20}$ + 414°, $[\alpha]_{5461}^{20}$ + 520° (*c*=1.0, in $CHCl_3$); pK= 6.2 (in 80% methylcellosolve); blue color with Keller's reagent.

Fungal Source

Ergot of *Claviceps purpurea* and *Paspalum distichum L.* (also isolated from seeds of *Rivea corymbosa* (L.) and *Ipomoea tricolor*; Convolvulaceae).

Biological Activity

The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice. All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). Some ergopeptine alkaloids are used routinely in medical practice. Central American Indians used seeds of *Rivea corymbosa* and *Ipomoea tricolor* as a magic drug called "Ololiuqui".

Spectral Data

IR:

See A. Hofmann, 1964.

UV:

UV spectrum identical to that of lysergic acid or isolysergic acid.

Mass Spectrum:
LREIMS: 267($M^+$, 100%), 249, 224, 221, 207, 192, 180, 167, and 154*m/e*.

TLC Purification

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated $NH_3$ atmosphere).
c) Chloroform-methanol-$NH_3$ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

HPLC Data

Extract with alkaline methanol, filter, followed by direct HPLC analysis with fluorescence detection; mobile phase, either 60% or 70% alkaline methanol. This technique works well for ergopeptide alkaloids.

References

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

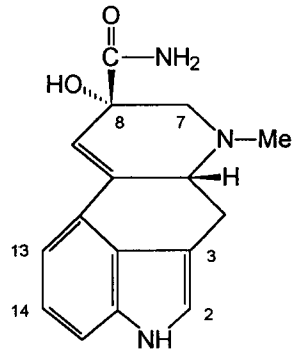
A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

Common/Systematic Name

8-Hydroxyergine

Molecular Formula/Molecular Weight

$C_{16}H_{17}N_3O_2$; MW = 283.13208




Fungal Source

*Claviceps paspali* (strain MG-6).

Isolation/Purification

The strain *C. paspali* MG-6 was isolated from the grass *Paspalum dilatatum* in the vicinity of Rome. Alkaloids were separated by adsorption on bentonite (Flieger *et al.*, 1989b). A crude alkaloid mixture was chromatographed on Kieselgel 60 $F_{254}$, Merck preparative TLC plates and eluted with chloroform-isopropyl alcohol-ammonia (90:10:0.036, v/v/v); $R_f$ values of 8-hydroxyergine and 8-hydroxyerginine were 0.50 and 0.91, respectively. Prepurified alkaloids were chromatographed on a Separon SGX $C_{18}$ column (Tessek, Czechoslovakia) particle size 7μm. The mobile phase consisted of (A) MeOH-$H_2O$-$NH_3$ (90:10:0.036, v/v/v) and (B) MeOH-$H_2O$-$NH_3$ (20:80:0.036, v/v/v). The column was equilibrated with 4% A in B and subsequently eluted with a linear gradient up to 54% A in B.

Biological Activity

The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice. All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medicine.

Spectral Data

$^1$H NMR:

(CD$_3$OD) H-2, 6.984($J_{2,4a}$=1.8Hz); H-4a, 2.749; H-4b, 3.569($J_{2,4b}$=>0, $J_{4a,4b}$=-14.5Hz); H-5, 3.265($J_{4a,5}$=11.8Hz, $J_{4b,5}$=5.9Hz); H-7a, 2.936($J_{7a,7b}$=-11.7Hz, $J_{7a,9}$=1.0Hz); H-7b, 2.965; H-9, 6.358($J_{4b,9}$=>0, $J_{5,9}$=2.1Hz); H-12, 7.193($J_{12,13}$=7.4Hz, $J_{12,14}$=0.7Hz); H-13, 7.107($J_{13,14}$=7.9Hz); H14, 7.231; and N-Me, 2.590ppm.

$^{13}$C NMR:

(CD$_3$OD) C-2, 120.66; C-3, 110.52; C-4, 27.15; C-5, 64.20; C-6, 62.7 1; C-7, 73.84; C-8, 121.00; C-9, 139.91; C-10, 128.13; C-11, 113.43; C-12, 123.93; C-13, 111.95; C-14, 136.02; C-15, 128.13; C-16, 177.92; and N-Me, 43.75ppm.

Mass Spectrum:

EIMS: 283($M^+$, $C_{16}H_{17}N_3O_2$, 61%), 266($C_{16}H_{16}N_3O$, 27), 265($C_{16}H_{15}N_3O$, 37), 248($C_{16}H_{12}N_2O$, 59), 240($C_{14}H_{12}N_2O_2$, 86), 223($C_{14}H_{12}N_2O_2$, 86), 221($C_{15}H_{13}N_2$, 42), 206($C_{14}H_{10}N_2$, 19), 195($C_{13}H_9NO$, 36), 194($C_{13}H_8NO$, 32), 181($C_{13}H_{11}N$, 26), 180($C_{13}H_{10}N$, 26), 167($C_{12}H_9N$, 83), and 154($C_{11}H_8N$, 100).

TLC Purification

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated $NH_3$ atmosphere).
c) Chloroform-methanol-$NH_3$ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

References

M. Flieger, R. Linhartova, P. Sedmera, J. Zima, P. Sajdl, J. Stuchlik, and L. Cvak; New Alkaloids of *Claviceps paspali*; J. Nat. Prod., Vol. 52, pp. 1003-1007 (1989a).

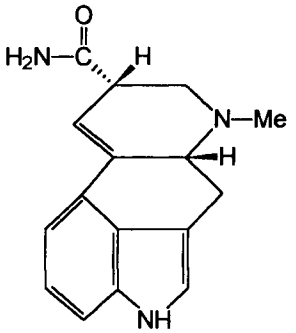
J. K. Porter; Analysis of Endophyte Toxins: Fescue and Other Grasses Toxic to Livestock; J. Animal Science, Vol. 73, pp. 871-880(1994).

Common/Systematic Name

Erginine; Isolysergic acid amide

Molecular Formula/Molecular Weight

$C_{16}H_{17}N_3O$; MW = 267.13716




General Characteristics

Crystallized from methanol as solvated prisms; mp., 132-134°C; $[\alpha]_D^{20}$ + 480°, $[\alpha]_{5461}^{20}$ + 608° (*c*=0.5, in pyridine); pK=6.1 (in 80% methylcellosolve).

Fungal Source

Ergot and saprophytic culture of *Claviceps purpurea*. Epimers are not considered as naturally occurring, but as products formed during extraction and purification; epimerization at C-8 occurs in either acid or base.

Biological Activity

The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice. All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). Some ergopeptine alkaloids are used routinely in medical practice. Central American Indians used seeds of *Rivea corymbosa* and *Ipomoea tricolor* as a magic drug called "Ololiuqui".

Spectral Data

IR:

See A. Hofmann, 1964.

TLC Purification

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated $NH_3$ atmosphere).
c) Chloroform-methanol-$NH_3$ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

HPLC Data

Extract with alkaline methanol, filter, followed by direct HPLC analysis with fluorescence detection; mobile phase, either 60% or 70% alkaline methanol. This technique works well for ergopeptide alkaloids.

References

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

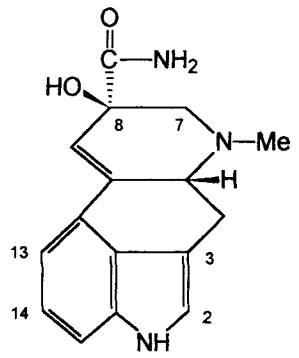
J. K. Porter; Analysis of Endophyte Toxins: Fescue and Other Grasses Toxic to Livestock; J. Animal Science, Vol. 73, pp. 871-880(1994).

Common/Systematic Name

8-Hydroxyerginine

Molecular Formula/Molecular Weight

$C_{16}H_{17}N_3O_2$; MW = 283.13208




Fungal Source

*Claviceps paspali* MG-6.

Epimers are not considered as naturally occurring but as products formed during extraction and purification; epimerization at C-8 occurs in either acid or base.

Isolation/Purification

The strain *C. paspali* MG-6 was isolated from the grass *Paspalum dilatatum* in the vicinity of Rome. Alkaloids were separated by adsorption on bentonite (Flieger *et al.*, 1989b). A crude alkaloid mixture was chromatographed on Kieselgel 60 $F_{254}$, Merck preparative TLC plates, and eluted with chloroform-isopropyl alcohol-ammonia (90:10:0.036, v/v/v); $R_f$ values of 8-hydroxyergine and 8-hydroxyerginine were 0.50 and 0.91, respectively. Prepurified alkaloids were chromatographed on a Separon SGX $C_{18}$ column (Tessek, Czechoslovakia) of particle size 7μ. The mobile phase consisted of (A) MeOH-$H_2O$-$NH_3$ (90:10:0.036, v/v/v) and (B) MeOH-$H_2O$-$NH_3$ (20:80:0.036, v/v/v). The column was equilibrated with 4% A in B and subsequently eluted with a linear gradient up to 54% A in B.

Spectral Data

$^1$H NMR:

($CD_3OD$) H-2, 6.974($J_{2,4a}$=1.6Hz); H-4a, 2.649; H-4b, 3.606($J_{2,4b}$=>0, $J_{4a,4b}$=-14.6Hz); H-5, 3.150($J_{4a,5}$=11.5Hz, $J_{4b,5}$=5.9Hz); H-7a, 3.080($J_{7a,7b}$=-11.3Hz, $J_{7a,9}$=1.5Hz); H-7b, 2.626; H-9, 6.268($J_{4b,9}$=0.8Hz, $J_{5,9}$=2.2Hz); H-12, 7.118($J_{12,13}$=7.0Hz, $J_{12,14}$=1.7Hz); H-13, 7.090($J_{13,14}$=7.2Hz); H-14, 7.219ppm; and N-Me, 2.614ppm.

$^{13}C$ NMR:

($CD_3OD$) C-2, 120.53; C-3, 110.55; C-4, 28.27; C-5, 64.11; C-6, 63.06; C-7, 71.87; C-8, 124.30; C-9, 139.13; C-10, 128.04; C-11, 113.15; C-12, 123.96; C-13, 111.72; C-14, 135.95; C-15, 127.99; C-16, 179.59; and N-Me, 43.39ppm.

Mass Spectrum:

EIMS: 283($M^+$, $C_{16}H_{17}N_3O_2$, 100), 266($C_{16}H_{16}N_3O$, 14), 265($C_{16}H_{15}N_3O$, 29), 248($C_{16}H_{12}N_2O$, 35), 240($C_{14}H_{12}N_2O_2$, 93), 223($C_{14}H_{12}N_2O_2$, 31), 221($C_{15}H_{13}N_2$, 42), 206($C_{14}H_{10}N_2$, 12), 195($C_{13}H_9N$, 60), 194($C_{13}H_8N$, 61), 181($C_{13}H_{11}N$, 50), 180($C_{13}H_{10}N$, 20), 167($C_{12}H_9N$, 94), and 154($C_{11}H_8N$, 96%).

Reference

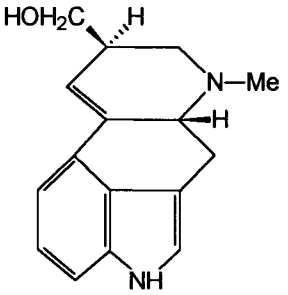
M. Flieger, R. Linhartova, P. Sedmera, J. Zima, P. Sajdl, J. Stuchlík, and L. Cvak; New Alkaloids of *Claviceps paspali*; J. Nat. Prod.; Vol. 52, pp. 1003-1007(1989a).

Common/Systematic Name

Lysergol

Molecular Formula/Molecular Weight

$C_{16}H_{18}N_2O$; MW = 254.14191




General Characteristics

Colorless prisms from ethanol; mp., 245°C (uncorr. decomp.); as plates and prisms; mp., 253-255°C (dec.); $[\alpha]_D^{18}$ +49° (*c*=0.2, in pyridine); $[\alpha]_D^{20}$ +54°, $[\alpha]_{5461}^{20}$ +87° (*c*=0.3, in pyridine). Gave a light purple and purplish blue colors with van Urk's and Allport-Cocking's reagents, respectively. Sublimes at high vacuum at 180°C; pK=6.6 (in 80% aqueous methylcellosolve). Soluble in 350 parts of boiling methanol or 100 parts boiling ethanol, sparingly soluble in chloroform or water.

Fungal Source

Saprophytic cultures of *Elymus*-type ergot fungus.

Isolation/Purification

Purified either by countercurrent distribution or by column chromatography using Hyflo Super Cell treated with a buffer solution (McIlvaine).

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 225, 242, and 312nm.

IR:
See A. Hofmann, 1964.

Mass Spectrum:
LREIMS: 254($M^+$, 100%), 235, 223, 221, 207, 205, 193, 192, 180, 167, and 154*m/e*.

References

M. Abe, S. Yamatodani, T. Yamano, and M. Kusumoto; Isolation of Lysergol, Lysergene and Lysergine from the Saprophytic Cultures of Ergot Fungi; Agric. Biol. Chem. [Tokyo], Vol. 25, pp. 594-595(1961).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

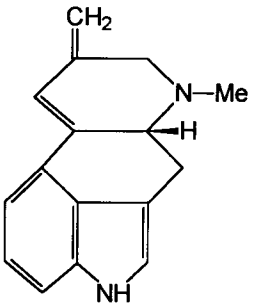
A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

Common/Systematic Name

Lysergene

Molecular Formula/Molecular Weight

$C_{16}H_{16}N_2$; MW = 236.13135




General Characteristics

Colorless needles or prisms from ethyl acetate; mp., 244°C (uncorr. decomp.); colorless needles or prisms from methanol, 247-249°C (dec.); $[\alpha]_D^{18}$ +461 ($c$=0.2, in pyridine); $[\alpha]_D^{20}$ +504° ($c$=0.4, in pyridine). Sparingly soluble in most organic solvents, moderately soluble in chloroform or pyridine. Gave a yellowish-green color with both van Urk's and Allport-Cocking's reagents, respectively.

Fungal Source

Saprophytic cultures of *Elymus*-type ergot fungus.

Isolation/Purification

Purified either by countercurrent distribution or by column chromatography using Hyflo Super Cell treated with a buffer solution (McIlvaine).

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 243, 263, and 335nm.

IR:

See A. Hofmann, 1964.

References

M. Abe, S. Yamatodani, T. Yamano, and M. Kusumoto; Isolation of Lysergol, Lysergene and Lysergine from the Saprophytic Cultures of Ergot Fungi; Agric. Biol. Chem. Vol., pp. 594-595(1961).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

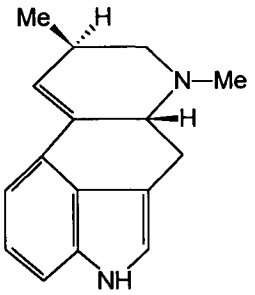
A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

Common/Systematic Name

Lysergine

Molecular Formula/Molecular Weight

$C_{16}H_{18}N_2$; MW = 238.14700




General Characteristics

Colorless prisms from ethyl acetate; mp., 275°C (uncorr. decomp.); prisms from methanol, ethanol, or ethyl acetate, 286-289°C (dec.); $[\alpha]_D^{18} = +70°$ ($c$=0.2, in pyridine), $[\alpha]_D^{20}$ +65° ($c$=0.5, in pyridine); sparingly soluble in methanol, ethanol, and ethyl acetate.

Fungal Source

Ergot or saprophytic cultures of *Agropyrum* sp.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

Very similar to lysergic acid.

IR:

See A. Hofmann, 1964.

References

Abe, S. Yamatodani, T. Yamano, and M. Kusumoto; Isolation of Lysergol, Lysergene and Lysergine from the Saprophytic Cultures of Ergot Fungi; Agric. Biol. Chem. [Tokyo], Vol. 25, pp. 594-595(1961).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978)

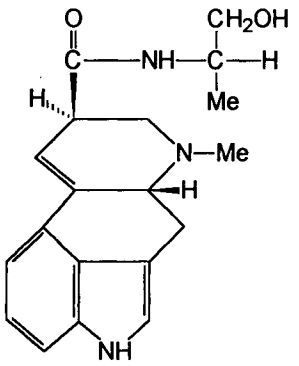
A. Hofmann; Die Mutterkorn Alkaloide, Enke Verlag, Stuttgart, 218 pp., 1964.

Common/Systematic Name

Ergonovine; Ergometrine; Ergobasine

Molecular Formula/Molecular Weight

$C_{19}H_{23}N_3O_2$; MW = 325.17903




General Characteristics

Tetrahedra from ethyl acetate; fine needles from benzene; tendency to form solvated crystals; mp., 162°C (nonsolvated, mp., 212°C, dec.); $[\alpha]_D^{20}$ + 90°(*c*=0.23, in water); -16° (*c*=1.0, in pyridine); $[\alpha]_D^{20}$ + 41°, $[\alpha]_{5461}^{20}$ + 60° (*c*=1.0, in alcohol); pK = 6.8. Freely soluble in lower alcohols, ethyl acetate, and acetone; more soluble in water than other principal alkaloids of ergot; slightly soluble in chloroform.

Fungal Source

*Claviceps purpurea*, *Balansia epichloë*, *B. henningsiana*, and *B. claviceps.*

Isolation/Purification/Analysis

Extract with either aqueous tartaric or lactic acid solution, partition chromatography with chloroform or methylene chloride at appropriate pH, column clean-up procedures using either silica, alumina or ion exchange resin, and identification and analysis using a combination of co-chromatography using TLC and/or HPLC with UV or fluorescence detection. Mass spectrometry is quite useful for identification, analysis and quantitation.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components). MLD (IV) in rabbits was 7.5mg/kg.

Spectral Data

IR:
See A. Hofmann, 1964.

UV:
Identical to that of lysergic acid or isolysergic acid.

$^{13}C$ NMR:
(DMSO-$d_6$) C-2, 119.1; C-3, 108.9; C-4, 26.8; C-5, 62.6; C-7, 55.5; C-8, 42.8; C-9, 120.1; C-10, 135.0; C-11, 127.4; C-12, 111.0; C-13, 122.4; C-14, 109.0; C-15, 133.7; C-16, 125.8; C-17, 171.2; Me, 17.4; NCH, 46.4; $OCH_2$, 64.4; and N-Me, 43.4ppm.

TLC Purification

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1) followed by rechromatography in chloroform-methanol (9:1 or 4:1) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography:

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated $NH_3$ atmosphere).
c) Chloroform-methanol-$NH_3$ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

HPLC Data

Extract with alkaline methanol, filter, followed by direct HPLC analysis with fluorescence detection; mobile phase, either 60% or 70% alkaline methanol. This technique works well for ergopeptide alkaloids.

References

N. J. Bach, H. E. Boaz, E. C. Kornfeld, C-J Chang, H. G. Floss, E. W. Hagaman, and E. Wenkert; Nuclear Magnetic Resonance Spectral Analysis of the Ergot Alkaloids; J. Org. chem., Vol. 39, pp. 1272-1276(1974).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Lysergic Acid Amide Derivatives from *Balansia epichloë* and *Balansia claviceps* (Clavicipitaceae); J. Nat. Prod., 42: 309-314 (1979).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Laboratory Production of Ergot Alkaloids by Species of *Balansia*; J. Gen. Microbiol., 113: 119-126(1979).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Ergot Alkaloids Biosynthesis by Isolates of *Balansia epichloë* and *Balansia henningsiana*; Can. J. Bot., 59: 2534-2538(1981).

C. W. Bacon, J. K. Porter, J. D. Robbins, and D. Betowski; Ergot Alkaloids Identification in Clavicipitaceae Systemic Fungi of Pasture Grass; J. Agric. Food Chem., 29: 653-657 (1981).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

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W. A. Jacobs and L. C. Craig; On an Alkaloid from Ergot; Science, Vol. 82, pp. 16-17 (1935).

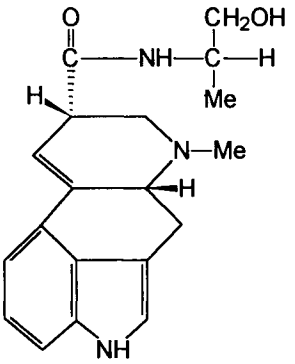
J. K. Porter; Analysis of Endophyte Toxins: Fescue and Other Grasses Toxic to Livestock; J. Animal Science, Vol. 73, pp. 871-880(1994).

Common/Systematic Name

Ergonovinine; Ergometrinine; Ergobasinine

Molecular Formula/Molecular Weight

$C_{19}H_{23}N_3O_2$; MW = 325.17903




General Characteristics

Forms large colorless prisms from acetone; mp., 196°C (dec.); $[\alpha]_D^{20}$ + 414°, $[\alpha]_{5461}^{20}$ + 520° (*c*=1.0, in $CHCl_3$); pK=6.2 (in 80% methylcellosolve); blue color with Keller's reagent.

Fungal Source

*Claviceps purpurea*.

Epimers are not considered as naturally occurring, but as products formed during extraction and purification; epimerization at C-8 occurs in either acid or base.

Isolation/Purification/Analysis

Extract with either aqueous tartaric or lactic acid solution, partition chromatography with chloroform or methylene chloride at appropriate pH, column clean-up procedures using either silica, alumina or ion exchange resin, and identification and analysis using a combination of co-chromatography using TLC and/or HPLC with UV or fluorescence detection. Mass spectrometry is quite useful for identification, analysis and quantitation.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism and adrenergic blockage) and central nervous system effects (bulbomedullary and mesodiencephalic components). MLD (IV) in rabbits was 7.5mg/kg.

Spectral Data

IR:
See A. Hofmann, 1964.

UV:
Identical to that of lysergic acid or isolysergic acid.

$^{13}C$ NMR:
(DMSO-$d_6$) C-2, 119.0; C-3, 108.9; C-4, 26.9; C-5, 62.0; C-7, 54.0; C-8, ca. 42.2; C-9, 119.0; C-10, 136.1; C-11, 127.6; C-12, 111.0; C-13, 122.1; C-14, 109.8; C-15, 133.7; C-16, 125.7; C-17, 172.1; Me, 17.2; NCH, 46.2; $OCH_2$, 64.3; and N-Me, 43.6ppm.

TLC Purification

Silica gel plates developed with methylene chloride-isopropyl alcohol (92:8, v/v) three times which results in the separation of alkaloids into the isolysergic acid group, the ergotoxine group, the ergoxine group and a mixture of the ergotamine and clavine groups. Extraction of the alkaloids from the silica using methanol-chloroform (1:4 or 1:1, v/v) followed by rechromatography in chloroform-methanol (9:1 or 4:1, v/v) separates ergovaline from the clavine alkaloids (agroclavine and chanoclavines).

TLC Solvent systems for silica gel chromatography (v/v):

a) Methylene chloride-isopropyl alcohol (92:8; 90:10; 75:25).
b) Chloroform-methanol (90:10; 80:20; 90:10 in saturated $NH_3$ atmosphere).
c) Chloroform-methanol-$NH_3$ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

HPLC Data

Extract with alkaline methanol, filter, followed by direct HPLC analysis with fluorescence detection; mobile phase, either 60% or 70% alkaline methanol. This technique works well for ergopeptide alkaloids.

References

N. J. Bach, H. E. Boaz, E. C. Kornfeld, C-J Chang, H. G. Floss, E. W. Hagaman, and E. Wenkert; Nuclear Magnetic Resonance Spectral Analysis of the Ergot Alkaloids; J. Org. chem., Vol. 39, pp. 1272-1276(1974).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Lysergic Acid Amide Derivatives from *Balansia epichloë* and *Balansia claviceps* (Clavicipitaceae); J. Nat. Prod., 42: 309-314 (1979).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Laboratory Production of Ergot Alkaloids

by Species of *Balansia*; J. Gen. Microbiol., 113: 119-126(1979).

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A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

W. A. Jacobs and L. C. Craig; On an Alkaloid from Ergot; Science, Vol. 82, pp. 16-17 (1935).

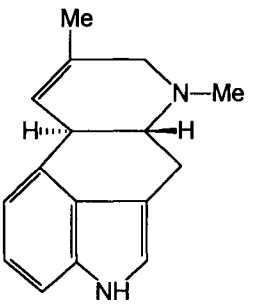
J. K. Porter; Analysis of Endophyte Toxins: Fescue and Other Grasses Toxic to Livestock; J. Animal Science, Vol. 73, pp. 871-880(1994).

Common/Systematic Name

Agroclavine

Molecular Formula/Molecular Weight

$C_{16}H_{18}N_2$; MW = 238.14700




General Characteristics

Colorless needles from acetone; mp., 205-206°C; sublimed under high vacuum between 110-130°C; $[\alpha]_D^{20}$ -155° (*c*=0.9 in $CHCl_3$); $[\alpha]_D^{20}$ -182° (*c*=0.5 in pyridine); pK=6.8 (in 80% aqueous methylcellosolve). Violet/blue color with Keller's reagent.

Fungal Source

First found from sclerotia and cultures of *Agropyrum semicostatum* Nees and *A. ciliare* Fr. Also found in *Pennisetum typhoideum*.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 225, 284 and 293nm (log $\epsilon$=4.47, 3.88 and 3.81, respectively).

IR:

See A. Hofmann, 1964.

$^1$H NMR:

(pyridine-$d_5$) H-6, 2.38(3H, s); H-7, 2.73(1H, d); H-4, 2.90(1H, ddd); H-7', 3.18(1H, d); H-4', 2.51(1H, ddd); H-5, 3.36(1H, dd); H-10, 3.89(1H, m); 7-$CH_3$ , 1.68(3H, s);

H-9, 6.30(1H, m); aromatic-H, 7.1-7.4(4H, m); and H-1, 11.43ppm (1H, s). (Note: Possible incorrect assignment of the 4α, 4β, and 5 hydrogens).

($CDCl_3$) H-4α, 2.78(dd, *J*=15, 12Hz); H-4β, 3.31(dd, *J*=15, 4Hz); H-5, 2.52(ddd, *J*=12, 9.5 and 4Hz); H-7α, 3.24(d, *J*=17Hz); H-7β, 2.93(dd, broad signal, *J*=17, 4Hz); H-9α and β, 6.18(s, broad signal); H-10, 3.74(dd, broad signal, *J*=9.5, 4Hz); H-17, 1.77(s); and N-Me, 2.49ppm (s).

$^{13}C$ NMR:
(pyridine-$d_5$) C-2, 118.3; C-3, 111.2; C-4, 26.4; C-5, 63.6; C-7, 60.2; C-8, 131.9; C-9, 119.4; C-10, 40.8; C-11, 131.9; C-12, 112.0; C-13, 122.0; C-14, 108.4; C-15, 134.0; C-16, 126.6; C-17, 19.9; and N-Me, 40.2ppm.

Mass Spectrum:
LREIMS: 238($M^+$, 52%), 237(100), 167(17), and 154*m/e* (16).

References

M. Abe, T. Yamano, Y. Kozu, and M. Kusumoto; Isolation of Further Two Water-soluble Ergot Alkaloids; J. Age. Chem. Soc., Vol. 28, pp. 501-510(1954).

N. J. Bach, H. E. Boaz, E. C. Cornfield, C-J Chang, H. G. Floss, E. W. Hegemon, and E. Wenkert; Nuclear Magnetic Resonance Spectral Analysis of the Ergot Alkaloids; J. Org. Chem., Vol. 39, pp. 1272-1276(1974).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology, Springer-Verlag, New York (1978).

A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

R. G. Mrtek, H. L. Crespi, G. Norman, M. I. Blake, and J. J. Katz; Biosynthesis of Clavine Alkaloids: Proton Magnetic Resonance Studies; Phytochemistry, Vol. 7, pp. 1535-1541(1968).

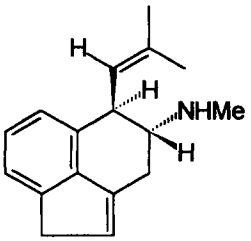
A. Stoll, A. Brack, H. Kobel, A. Hofmann, and R. Brunner; Die Alkaloide eines Mutterkornpilzes von *Pennisetum typhoideum* rich. und deren Bildung in Saprophytischer Kultur; Helvetica Chimica Acta, Vol. 37, pp. 1815-1825(1954).

Common/Systematic Name

6,7-*seco*-Agroclavine

Molecular Formula/Molecular Weight

$C_{16}H_{20}N_2$; MW = 240.16265




General Characteristics

Crystals; mp., 126-129°C subl.; gives a blue color with Allport and Cocking's reagent.

Fungal Source

*Claviceps purpurea*, strain AA-218, *Balansia epichloë*, *B. strangulans*, and *Epichloë typhina*.

Isolation/Purification

Purified by HPLC followed by PLC using 1% conc. ammonia, 5% MeOH, and 94% chloroform. TLC using silica gel with same solvent system.

Spectral Data

UV:

$\lambda_{max}^{EtOH}$ 225, 283, and 293nm.

IR:

($CHCl_3$): 3480(indole NH), 3320(aliphatic NH), 1605, and 1445$cm^{-1}$ (C=C).

$^1H$ NMR:

($CDCl_3$): 1.85(s, 6H); 2.53(s, with hyperfine splitting, 3H); 2.4(br s, 1H); 2.6-3.5(m, 4H); 3.75-4.15(m, 1H); 5.0-5.3(d, 1H (C-10-H)); 6.6-7.3(m, 4H); and 8.1-8.5ppm (br s, 1H(indole)).

Mass Spectrum:

EIMS: 240, 225, 208, 197, 184, 168, and 155*m/e*.

References

C. Horwell and J. P. Verge; Isolation and Identification of 6,7-*seco*-Agroclavine from *Claviceps purpurea*; Phytochemistry, Vol. 18, p. 519 (1979).

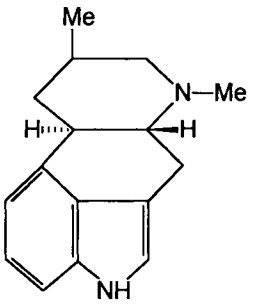
J. K. Porter, C. W. Bacon, J. D. Robbins, and D. Betowski; Ergot Alkaloid Identification in Clavicipitaceae Systemic Fungi of Pasture Grasses; J. Agric. Food Chem., 29: 653-657 (1981).

Common/Systematic Name

Dihydroagroclavine

Molecular Formula/Molecular Weight

$C_{16}H_{20}N_2$; MW = 240.16265




General Characteristics

Crystals as long needles from toluene, benzene, ether, chloroform, ethyl acetate, acetone, methanol, ethanol or pyridine; mp., 242°C (dec.); $[\alpha]_D^{20}$ - 69°, $[\alpha]_{5461}^{20}$ - 83° (*c*=0.5, in $CHCl_3$); $[\alpha]_D^{0}$ - 111°, $[\alpha]_{5461}^{20}$ - 129° (*c*=0.5, in pyridine). Insoluble in toluene, benzene and ether; readily soluble in chloroform, ethyl acetate, acetone, methanol, ethanol and pyridine. Succinate derivative, $C_{16}H_{20}N_2$. 0.5 $C_4H_6O_4$, crystals as prisms from water; mp., 213°C (dec.); $[\alpha]_D^{17}$ - 87° (*c*=0.13, in pyridine).

Fungal Source

Ergot and saprophytic culture of *Phalaris* and *Agropyrum* sp.

Spectral Data

Mass Data:

Found: C 79.94, H 8.34, N 11.64 (calcd. for $C_{16}H_{20}N_2$: C 79.95, H 8.39, N 11.66).

Reference

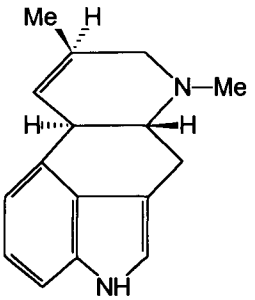
M. Abe and S. Yamatodani; Isolation of Further Two Water Soluble Ergot Alkaloids; J. Agr. Chem. Soc., Vol. 28, p. 501 (1954).

Common/Systematic Name

Festuclavine

Molecular Formula/Molecular Weight

$C_{16}H_{20}N_2$; MW = 240.16265




General Characteristics

Crystals (long needles) from methanol; mp., 238-239°C (dec.); 242-244°C (dec.); $[\alpha]_D^{15}$ -98° (*c*=0.3, pyridine); $[\alpha]_D^{20}$ -70°, $[\alpha]_{5461}^{20}$ -83° (*c*=0.5, in $CHCl_3$); $[\alpha]_D^{20}$ -110°, $[\alpha]_{5461}^{20}$ -128°; pK=7.4 (in 80% aqueous methylcellosolve); positive for van Urk's reaction; insoluble in petroleum ether, sparingly soluble in ethyl acetate, moderately soluble in benzene and chloroform and readily soluble in acetone, methanol, ethanol, and pyridine.

Fungal Source

*Penicillium chermesinum* (PC 106-I), *Agropyrum* type ergot fungus parasitic on *Agropyrum semicostatum*, *Trisetum bifidum* Ohwi, *Festuca rubra* L., etc. growing in Japan.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 224(log ε=4.54), 275(3.81), and 281nm (3.84).

IR:

See A. Hofmann, 1964.

$^1$H NMR:

($CDCl_3$) H-4α, 2.68(dd, *J*=15.0, 11.5Hz); H-4β, 3.39(dd, *J*=15.0, 4.5Hz); H-5, 2.10(ddd, *J*=11.5, 9.5, 4.5Hz); H-7α, 2.95(d[broad], *J*=11.0Hz); H-7β, 1.87(t, *J*=11.0Hz); H-8, 2.01(ddd, *J*=12, 11, 6.5Hz); H-9α, 2.63(dd, *J*=12.0, 3.5Hz); H-9β, 1.08(q, *J*=12.0Hz); H-10, 2.97(ddd, *J*=12.0, 9.5, 3.5Hz); H-17, 0.99(d, *J*=6.5Hz); and N-Me, 2.45ppm (s).

$^{13}$C NMR:

($CDCl_3$) C-2, 117.7; C-3, 110.5; C-4, 26.6; C-5, 66.7; C-7, 65.0; C-8, 30.2; C-9, 36.2; C-10, 40.4; C-11, 132.7*; C-12, 112.0; C-13, 122.0; C-14, 108.3; C-15, 133.1; C-16, 125.9; C-17, 19.3; and N-Me, 42.7ppm.

* Assignment may be reversed.

Mass Spectrum:

LREIMS: 240($M^+$, 100%), 197, 182, 167, 154, and 144*m/e*.

References

N. J. Bach, H. E. Boaz, E. C. Kornfeld, C-J Chang, H. G. Floss, E. W. Hagaman, and E. Wenkert; Nuclear Magnetic Resonance Spectral Analysis of the Ergot Alkaloids; J. Org. Chem., Vol. 39, pp. 1272-1276(1974).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

A. Hofmann; Die Mutterkorn Alkaloide, Enke Verlag, Stuttgart, 218 pp., 1964.

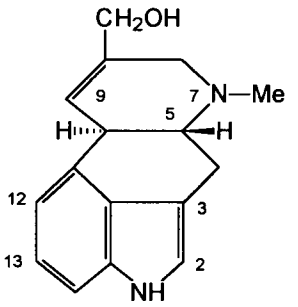
S. Ohmomo, T. Sato, T. Utagawa, and M. Abe; Isolation of Festuclavine and Three New Indole Alkaloids, Roquefortine A, B and C from the Cultures of *Penicillium roqueforti*; Agr. Biol. Chem., Vol. 39, pp. 1333-1334(1975).

Common/Systematic Name

Elymoclavine

Molecular Formula/Molecular Weight

$C_{16}H_{18}N_2O$; MW = 254.14191




General Characteristics

Crystallized as prisms from methanol; mp., 245-249°C; $[\alpha]_D^{20}$ -152° (*c*=0.9, in pyridine), $[\alpha]_D^{20}$ -111° (*c*=0.1, in EtOH); pK=6.7 (in 80% aqueous methylcellosolve); violet-blue color with Keller's reagent.

Fungal Source

Saprophytic culture of ergot fungus *Claviceps* sp. SD 58 (ATCC 26019), *Pennisetum typhoideum* sclerotia and saprophytic cultures, and *Elymus mollis*.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 227, 283, and 293nm (log $\epsilon$=4.31, 3.84, and 3.76, respectively).

IR:

See A. Hofmann, 1964.

$^1$H NMR:

(pyridine-$d_5$) H-6, 2.41(3H, s); H-7, 3.05(1H, d); H-4, 2.92(1H, ddd); H-7', 3.61(1H, d); H-4', 2.59(1H, ddd); H-5, 3.35(1H, dd); H-10, 3.94(1H, m); H-17, 4.36(2H); 17-

OH, 4.75(1H, s); H-9, 6.71(1H, m); aromatic-H, 7.1-7.4(4H, m); and H-1, 11.40ppm(1H, s). ($CD_3OD$) H-2, 6.922; H-4α, 2.798; H-4β, 3.357; H-5, 2.622; H-7α, 3.026; H-7β, 3.444; H-9, 6.464; H-10, 3.798; H-12, 6.967; H-13, 7.121; H-14, 7.191; H-17upfield, 4.106; H-17downfield, 4.141; and N-Me, 2.523ppm.

$^{13}C$ NMR:
($CD_3OD$) C-2, 119.09; C-3, 111.45; C-4, 27.17; C-5, 64.76; N(6)-Me, 41.15; C-7, 57.20; C-8, 134.37; C-9, 121.55; C-10, 40.98; C-11, 131.74; C-12, 112.83; C-13, 123.12; C-14, 109.60; C-15, 136.12; C-16, 126.88; and C-17, 65.06ppm.

Mass Spectrum:
LREIMS: 254($M^+$, 52%), 253(100), 237(23), 167(36), and 154*m/e* (30).

References

N. J. Bach, H. E. Boaz, E. C. Kornfeld, C-J Chang, H. G. Floss, E. W. Hagaman, and E. Wenkert; Nuclear Magnetic Resonance Spectral Analysis of the Ergot Alkaloids; J. Org. Chem., Vol. 39, pp. 1272-1276(1974).

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

M. Flieger, N. F. Zelenkova, P. Sedmera, V. Kren, J. Novak, V. Rylko, P. Sajdl, and Z. Řeháček, Ergot Alkaloid Glycosides from Saprophytic Cultures of *Claviceps*, I. Elymoclavine Fructosides; J. Natural Products, Vol. 52, pp. 506-510(1989).

A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

R. G. Mrtek, H. L. Crespi, G. Norman, M. I. Blake, and J. J. Katz; Biosynthesis of Clavine Alkaloids: Proton Magnetic Resonance Studies; Phytochemistry, Vol. 7, pp. 1535-1541(1968).

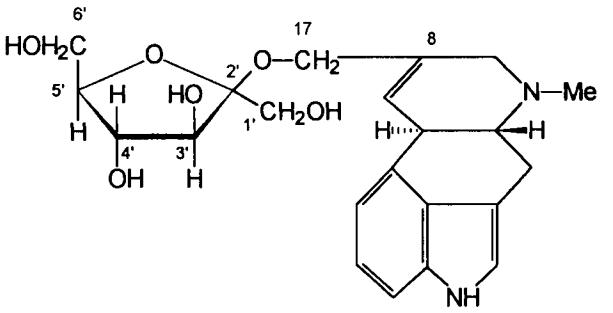
A. Stoll, A. Brack, H. Kobel, A. Hofmann, and R. Brunner; Die Alkaloide eines Mutterkornpilzes von *Pennisetum typhoideum* rich. und deren Bildung in Saprophytischer Kultur; Helvetica Chimica Acta, Vol. 37, pp. 1815-1825(1954).

Common/Systematic Name

Elymoclavine-*O*-β-fructofuranoside

Molecular Formula/Molecular Weight

$C_{22}H_{28}N_2O_6$; MW = 416.19474




Fungal Source

Saprophytic culture of ergot fungus *Claviceps* sp. SD 58 (ATCC 26019) and 88 EP; evidence suggested that this alkaloid formed from elymoclavine and the sucrose in the medium by the action of invertase present in the fungal mycelium.

Isolation/Purification

Alkaloids were separated from the culture broth (pH adjusted to 7.5 with concentrated $NH_3$) by adsorption on bentonite (Lachema, Brno, Czechoslovakia) and desorbed with MeOH and the crude alkaloid solution was concentrated to a final volume of 10ml under low pressure conditions. The MeOH solution was loaded on a Separon SGX $C_{18}$ column and eluted with MeOH-$H_2O$-concentrated $NH_3$ (30:70:0.34, v/v/v). The column effluent was monitored by UV (288nm). The first alkaloid fraction contained a mixture of all elymoclavine fructosides. The mixture of elymoclavine fructosides was repeatedly loaded on Separon SGX $C_{18}$ column and eluted with the above-mentioned mixture. A base line separation of all fructosides was reached. The Separon SGX $C_{18}$ column with the same mobile phase was also used for checking purity. Column effluent was monitored by UV at 224nm.

Spectral Data

$^1$H NMR:

($CD_3OD$) 6.937, H-2; 2.797, H-4α; 3.379, H-4β; 2.691, H-5; 3.174, H-7α; 3.631, H-7β; 6.553, H-9; 3.854, H-10; 6.950, H-12; 7.163, H-13; 7.143, H-14; 4.112, H-17u; 4.327, H-17d; 2.588, N-Me; 3.590, H-1'u; 3.717, H-1'd; 4.154, H-3'; 4.008, H-4'; 3.779, H-5'; 3.628, H-6'u; and 3.734ppm, H-6'd.

$^{13}C$ NMR:

($CD_3OD$) C-2, 119.98; C-3, 111.58; C-4, 27.56; C-5, 65.87; N(6)-Me, 41.02; C-7, 58.13; C-8, 134.63; C-9, 123.34; C-10, 41.65; C-11, 131.91; C-12, 113.51; C-13, 123.74; C-14, 110.35; C-15, 135.61; C-16, 127.74; C-17, 65.01; C-1', 62.41; C-2', 105.79; C-3', 78.85; C-4', 77.26; C-5', 83.82; and C-6', 64.88ppm.

Mass Spectrum:

CIMS: ($NH_3$) 417(33%), 416(22), 254(23), 253(30), 237(100), 236(85), 223(9), 207(6), 167(9), 154(6), and 127*m/e* (1).

References

M. Flieger, N. F. Zelenkova, P. Sedmera, V. Kren, J. Novak, V. Rylko, P. Sajdl, and Z. Řeháček; Ergot Alkaloid Glycosides from Saprophytic Cultures of *Claviceps*, I. Elymoclavine Fructosides; J. Natural Products, Vol. 52, pp. 506-510(1989).

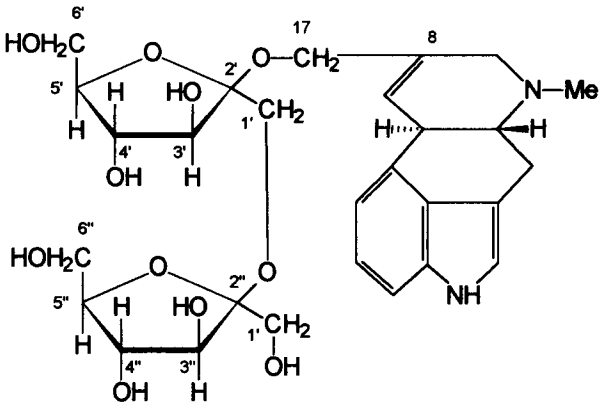
H. G. Floss, H. Gunter, U. Mothes, and I. Becker. Z.; Isolierung von Elymocalvin-*O*-β-fruktosid aus Kulturen des Mutterkornpilzes; Naturforsch,. Vol. 22b, pp. 399-402(1967).

Common/Systematic Name

Elymoclavine-*O*-β-fructofuranosyl-(2→1)-*O*-β-D-fructofuranoside

Molecular Formula/Molecular Weight

$C_{28}H_{38}N_2O_{11}$; MW = 578.24756




Fungal Source

Saprophytic culture of ergot fungus *Claviceps* sp. SD 58 (ATCC 26019) and 88 EP.

Isolation/Purification

Alkaloids were separated from the culture broth (pH adjusted to 7.5 with concentrated $NH_3$) by adsorption on bentonite (Lachema, Brno, Czechoslovakia) and desorbed with MeOH and the crude alkaloid solution concentrated to a final volume of 10ml under low pressure conditions. The MeOH solution was loaded on a Separon SGX $C_{18}$ column and eluted with MeOH-$H_2O$-concentrated $NH_3$ (30:70:0.34, v/v/v). The column effluent was monitored by UV (288nm). The first alkaloid fraction contained a mixture of all elymoclavine fructosides. The mixture of elymoclavine fructosides was repeatedly loaded on Separon SGX $C_{18}$ column and eluted with the above-mentioned mixture. A base line separation of all fructosides was reached. The Separon SGX $C_{18}$ column with the same mobile phase was also used for checking purity. Column effluent was monitored by UV at 224nm.

Spectral Data

$^1$H NMR:

($CD_3OD$) 6.949, H-2; 2.841, H-4α; 3.404, H-4β; 2.797, H-5; 3.230, H-7α; 3.676, H-7β; 6.557, H-9; 3.851, H-10; 6.966, H-12; 7.073, H-13; 7.151, H-14; 4.131, H-17u; 4.328, H-17d; 2.648, N-Me; 3.577, H-1'u; 3.649, H-1'd; 4.165, H-3'; 4.012, H-4'; N. D., H-5'; 3.627, H-6'u; and N. D., H-6'd.

$^{13}C$ NMR:

($CD_3OD$) C-2, 120.07; C-3, 111.30; C-4, 27.38; C-5, 65.82; N(6)-Me, 40.81; C-7, 58.02; C-8, 134.13; C-9, 123.62; C-10, 41.43; C-11, 131.58; C-12, 113.58; C-13, 123.76; C-14, 110.44; C-15, 135.60; C-16, 127.67; C-17, 64.81; C-1', 62.54; C-2', 105.52; C-3', 79.21; C-4', 77.06; C-5', 83.80; C-6', 64.77; C-1", 62.85; C-2", 105.00; C-3", 80.01; C-4", 76.50; C-5", 83.67; and C-6", 63.91ppm.

Mass Spectrum:

CIMS: ($NH_3$) 579(25%), 578(8), 416(25), 254(60), 253(45), 237(100), 236(93), 223(7), 207(3), 167(9), 154(10), and 127*m/e* (24).

Reference

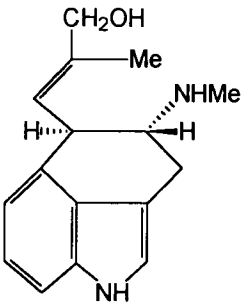
M. Flieger, N. F. Zelenkova, P. Sedmera, V. Křen, J. Novák, V. Rylko, P. Sajdl, and Z. Řeháček; Ergot Alkaloid Glycosides From Saprophytic Cultures of *Claviceps*, I. Elymoclavine Fructosides; J. Natural Products, Vol. 52, pp. 506-510(1989).

Common/Systematic Name

Chanoclavine-I; Chanoclavine

Molecular Formula/Molecular Weight

$C_{16}H_{20}N_2O$; MW = 256.15756




General Characteristics

Prisms and polyhedral crystals from acetone/methanol; mp., 220-222°C (dec.), $[\alpha]_D^{20}$ - 240°; $[\alpha]_{5461}^{20}$ - 294° (*c*=1.0, in pyridine); $[\alpha]_D^{20}$ - 205° (*c*=0.75, in alcohol); $pK_b$=5.80; pK=8.2 (in aqueous methylcellosolve); violet-blue color with Keller's or van Urk's reagents. *N*-acetyl derivative crystallized as massive prisms; mp., 226-227° C (dec.); $[\alpha]_D^{20}$ - 180° (*c*=0.5, in pyridine).

Fungal Source

Saprophytic culture of ergot fungus isolated from a tropical millet (*Pennisetum typhoideum*). Ergots of *Elymus* sp., *Phragmites* sp., *Phalaris* sp., *Agropyrum* sp., *Balansia epichloë, B. strangulans, B. claviceps, B. henningsiana,* and *Acremonium coenophialum*.

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 225, 284, and 293nm (log $\epsilon$=4,44, 3.82, and 3.76, respectively).

IR:

1600-1650$cm^{-1}$ (characteristic of indole); see A. Hofmann, 1964.

Mass Spectrum:
256($M^+$), 237, 183(100%), 182, 167, 168, 154, and 155*m/e*.

References

W. Achlin, T. Fehr, and D. Arigoni; The Stereochemistry of Chanoclavine-I and Isochanoiclavine-I; Chemical Communications, pp. 799-800(1966).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Lysergic Acid Amide Derivatives from *Balansia epichloë* and *Balansia claviceps* (Clavicipitaceae); J. Nat. Prod., 42: 309-314 (1979).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Laboratory Production of Ergot Alkaloids by Species of *Balansia*; J. Gen. Microbiol., 113: 119-126(1979).

C. W. Bacon, J. K. Porter, and J. D. Robbins; Ergot Alkaloids Biosynthesis by Isolates of *Balansia epichloë* and *Balansia henningsiana*; Can. J. Bot., 59: 2534-2538(1981).

C. W. Bacon, J. K. Porter, J. D. Robbins, and D. Betowski; Ergot Alkaloids Identification in Clavicipitaceae Systemic Fungi of Pasture Grass; J. Agric. Food Chem., 29: 653-657 (1981).

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A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart 218 pp., 1964.

A. Hofmann, R. Brunner, H. Kobel, and A. Brack; Neue Alkaloide aus der saprophytischen Kultur des Mutterkornpilzes von *Pennisetum typhoideum* Rich.; Helvetica Chimica Acta, Vol. XI, pp. 1358-1373(1957)

P. C. Lyons, R. D. Plattner, and C. W. Bacon; Occurance of Peptide and Clavine Ergot Alkaloids in Tall Fescue Grass; Science, 232: 487-489(1986).

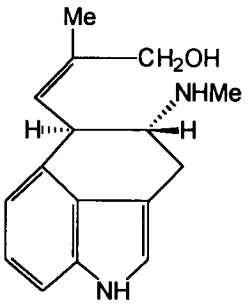
D. Stauffacher and H. Tscherter; Isomere des Chanoclavins aus *Claviceps purpurea* (Fr.) Tul.; Helvetica Chimica Acta, Vol. 47, pp. 2186-2194(1964).

Common/Systematic Name

Isochanoclavine-I

Molecular Formula/Molecular Weight

$C_{16}H_{20}N_2O$; MW = 272.15248




General Characteristics

Crystals; mp., 190°C, $[\alpha]_D$ -208° (in pyridine); rods from isopropanol; mp., 181°C,; $[\alpha]_D^{20}$ -216° (*c*=0.5, in pyridine); blue color with van Urk's reagent; violet-blue with Keller's reagent.

Fungal Source

Saprophytic culture of ergot fungus, *Claviceps purpurea* (Fr.).

Isolation/Purification

The alkaloid was purified by aluminum oxide column chromatography (Act. III) eluted with chloroform/0.75% MeOH. The crude alkaloid fraction was crystallized from acetone followed by isopropanol to give rods, mp., 181°C; sublimed under high vacuum at 170°C.

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 222, 281, 275(sh), and 291nm (log $\epsilon$=4.5, 3.89, 3.86, and 3.82, respectively).

IR:

See Stauffacher and Tscherter, 1964.

$^1$H NMR:

See Stauffacher and Tscherter, 1964.

References

W. Achlin, T. Fehr, and D. Arigoni; The Stereochemistry of Chanoclavine-I and Isochanoclavine-I; Chemical Communications, pp. 799-800(1966).

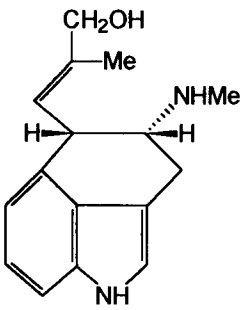
D. Stauffacher and H. Tscherter; Isomere des chanoclavins aus *Claviceps purpurea* (Fr.) Tul.; Helvetica Chimica Acta, Vol. 47, pp. 2186-2194(1964).

Common/Systematic Name

Chanoclavine-II

Molecular Formula/Molecular Weight

$C_{16}H_{20}N_2O$; MW = 256.15756




General Characteristics

Prisms from acetone; mp., 174°C; $[\alpha]_D^{20}$ -332° (*c*=0.5, in pyridine); violet-blue color with Keller's and blue with van Urk's reagents. HCl•salt crystals from alcohol; mp., 247°C, $[\alpha]_D^{20}$ -271° (*c*=0.5, in 50% alcohol). *N*-Acetyl derivative, large crystalline prisms from methanol; mp., 203°C; $[\alpha]_D^{20}$ -455° (*c*=0.54, in pyridine).

Fungal Source

Saprophytic culture of ergot fungus, *Claviceps purpurea* (FR.).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 222, 281, and 291nm (log ϵ=4,50, 3.89, and 3.82, respectively); shoulders at $\lambda_{max}$ 275(log ϵ=3.86), 245, and 289nm.

IR:

(Nujol) *N*-acetyl derivative: 1610cm$^{-1}$, (N-C)$CH_3$.

$^1$H NMR:

*N*-acetyl derivative: 4.82(1H, dd, *J*=10 and 4Hz, H-10); 5.53(1H, octet, *J*=4, 5, and 11Hz, H-5); and 2.67-3.61ppm (2H, AB part of an ABX system, $J_{AB}$=14Hz, $J_{AX}$=11Hz, $J_{BX}$=5Hz, H-4). *N*-acetyl derivative, 4.28ppm (2H, s, allyl-$CH_2$-O group).

Reference

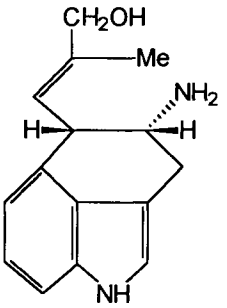
D. Stauffacher and H. Tscherter; Isomere des Chanoclavins aus *Claviceps purpurea* (Fr.) Tul.; Helvetica Chimica Acta, Vol. 47, pp. 2186-2194(1964).

Common/Systematic Name

*N*-Demethylchanoclavine-II; Norchanoclavine II

Molecular Formula/Molecular Weight

$C_{15}H_{18}N_2O$; MW = 242.14191




General Characteristics

Gray color, turning blue with Ehrlich's reagent.

Fungal Source

*Claviceps* sp. (strain SD 58).

Isolation/Purification

Culture filtrates were made alkaline to pH 11 with ammonia and extracted several times with chloroform or chloroform-isopropanol (3:1, v/v). The extracts were combined and evaporated to dryness in a vacuum. The residue was dissolved in 2% aqueous succinic acid, the solution washed 3 times with methylene chloride, made alkaline with ammonia to pH 11 and extracted with methylene chloride. This alkaloid extract was dried over anhydrous sodium sulfate, concentrated in a vacuum and left in the refrigerator overnight. The solution was filtered through a fine sintered glass funnel to remove the crystallized elymoclavine, which was washed with 3ml cold methylene chloride. The filtrate and washings were then passed through an alumina column(Brockmann activity II-III) suspended in methylene chloride. The column was eluted with methylene chloride containing 2% methanol until no more isochanoclavine-I could be detected in the eluate. These fractions contained agroclavine, elymoclavine and isochanoclavine-I, chanoclavine-II and chanoclavine-I. The elution was continued with methylene chloride containing 10% methanol to give two more fractions. The first contained the chanoclavine-I, some chanoclavine-II and *N*-demethylchanoclavine -II and the following fraction contained mainly *N*-demethylchanoclavine-II. These two fractions were evaporated and streaked, respectively, on silica gel G plates. The plates were developed twice in acetone-ethyl acetate-*N,N*-dimethylformamide (5:5:1, v/v/v) system. The band containing *N*-demethylchanoclavine-II was scraped off and the alkaloid was eluted from the gel. This material was rechromatographed in chloroform-methanol (9:1, v/v) in an ammonia atmosphere to yield a chromatographically homogeneous material.

Biological Activity

The ergopeptine alkaloids produce a wide range of biological activities and some are used routinely in medical practice.

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 223, 274, 283, and 294nm.

Mass Spectrum:

HREIMS: 242.1430 (calcd for $C_{15}H_{18}N_2O$, 242.1419). The mass spectrum also showed strong peaks at 154, 156, 167, 169, 182, 194, 209, and 223*m/e*. The $M^+$ ion peak (242*m/e*) was the base peak (100%).

Reference

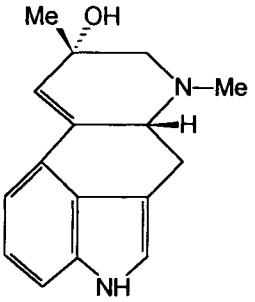
J. M. Cassady, C. I. Abou-chaar, and H. G. Floss; Ergot Alkaloids. Isolation of *N*-Demethylchanoclavine-II from *Claviceps* Strain SD 58 and the Role of Demethylchanoclavines in Ergoline Biosynthesis; Lloydia, Vol. 36, pp. 390-396(1973).

Common/Systematic Name

Setoclavine

Molecular Formula/Molecular Weight

$C_{16}H_{18}N_2O$; MW = 254.14191




General Characteristics

Prisms from methanol-acetone; m.p. 229-234°C (dec.); $[\alpha]_D^{20}$ + 174°; $[\alpha]_{5461}^{20}$ + 232° (*c*=1.1, in pyridine); $[\alpha]_D^{20}$ + 165° (*c*=0.3, in alcohol); pK=6.4 (in 80% aqueous methylcellosolve).

Fungal Source

Saprophytic culture of ergot fungus isolated from a tropical millet (*Pennisetum typhoideum*); *Elymus mollis, Agropyrum semicostatum, Trisetum bifidum,* and *Festuca rubra.*

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 243 and 313nm (log $\epsilon$=4.38 and 4.04).

IR:

See A. Hofmann, 1964.

Mass Spectrum:

254($M^+$), 236, 235, 234, 219, 211, 196, 181, 168, and 154*m/e* (100%).

References

B. Berde and H. O. Scheld (eds.); Ergot Alkaloids and Related Compounds; In Handbook of Experimental Pharmacology; Springer-Verlag, New York (1978).

A. Hofmann; Die Mutterkorn Alkaloide; Enke Verlag, Stuttgart, 218 pp., 1964.

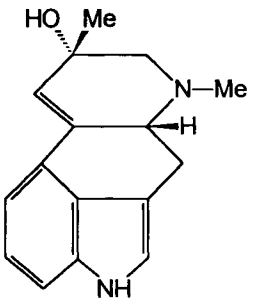
A. Hofmann, R. Brunner, H. Kobel, and A. Brack; Neue Alkaloide aus der saprophytischen Kultur des Mutterkornpilzes von *Pennisetum typhoideum* Rich.; Helvetica Chimica Acta, Vol. XI, pp. 1358-1373(1957).

Common/Systematic Name

Isosetoclavine

Molecular Formula/Molecular Weight

$C_{16}H_{18}N_2O$; MW = 254.14191




General Characteristics

Large polyhedral crystals from methanol; m.p. 234-237°C; $[\alpha]_D^{20}$ + 107°; $[\alpha]_{5461}^{20}$ + 147° (*c*=0.5, in pyridine); $[\alpha]_D^{20}$ + 129° (*c*=0.4, in alcohol); pK=5.9 (in 80% aqueous methylcellosolve). Soluble in 70 parts boiling methanol, 60 parts boiling acetone or 160 parts boiling chloroform. Responses to various color reactions were similar to setoclavine. Hydrochloride crystallized as rosettes from methanol diluted with acetone, did not melt at temperatures up to 300°C.

Fungal Source

Saprophytic culture of ergot fungus isolated from a tropical millet (*Pennisetum typhoideum*).

Biological Activity

All natural ergot alkaloids possess to a greater or lesser degree, biological effects that can be classified as direct peripheral effects on smooth muscle (uterine contraction and vasoconstriction), indirect peripheral effects (humoral, serotonin antagonism, and adrenergic blockage), and central nervous system effects (bulbomedullary and mesodiencephalic components).

Spectral Data

UV:

$\lambda_{max}^{MeOH}$ 242 and 317nm (log $\epsilon$=4.42 and 4.10).

IR:

See A. Hofmann, 1964.