Handbook of Secondary Fungal Metabolites

VOLUME I
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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.

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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-β-fructofuranoside
Elymoclavine-O-β-fructofuranosyl-(2-1)-O-β-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
Ergocomine
1. Indole Alkaloids

Ergocornine
O-12'-Methylergocornine
Ergocristine
Ergocristinine
Ergosecaline
Ergosecalinine
Ergobalansine
Ergobalansinine
α-Ergocryptine
O-12'-Methyl-α-ergocryptine
β-Ergocryptine
5'-epimer of β-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
1. Indole Alkaloids

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 $\rho$-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: 23\mu{g/egg} = 80\%; 68\mu{g/egg} = 100\% mortality.

Spectral Data
UV:  
$\lambda_{\text{max}}$^{MeOH} 220(log $\epsilon$=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
1. Indole Alkaloids

**Common/Systematic Name**
3-(3,3-Diindolyl)propane-1,2-diol

**Molecular Formula/Molecular Weight**
\[ C_{19}H_{18}N_2O_2; \text{MW} = 306.13683 \]

**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 GF254 [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: 20\( \mu \)g/egg = 20\%; 60\( \mu \)g/egg = 55\% mortality; 99\( \mu \)g/egg = 100\% mortality.

**Spectral Data**

**UV:**
\[ \lambda_{\text{max}}^{\text{MeOH}} = 221(\log \epsilon = 4.88), 275(3.97), 282(4.01), \text{and } 291\text{nm} (3.96). \]

**IR:**
\( \text{(KBr)} \) 1550, 1410, 1335, 1080, 1050, and 780cm\(^{-1}\).

**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 89.03m/e.

**Reference**
1. Indole Alkaloids

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:
λ_{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 780cm^{-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 89.08m/e.

Reference
1. Indole Alkaloids

Common/Systematic Name
N-Methyl-4-dimethylallyltryptophan

Molecular Formula/Molecular Weight
C_{17}H_{22}N_{2}O_{2}; MW = 286.16813

\[
\begin{align*}
\text{Me} & \\
\text{Me} & \\
\text{CO}_2\text{H} & \\
\text{N}-\text{Me} & \\
\text{NH} & \\
\end{align*}
\]

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:
\[ \lambda_{\text{max}}^{\text{MeOH}} \quad 274, 280, \text{and} \quad 295 \text{nm} \].
1. Indole Alkaloids

IR:
(KBr) 3580, 3250(broad) 1640, 1400, and 770cm⁻¹.

1H NMR:
(CD₂COOD) 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 154m/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 NH₃ atmosphere).
c) Chloroform-methanol-NH₃ (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

References

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

1. Indole Alkaloids

**Common/Systematic Name**
Lysergic acid

**Molecular Formula/Molecular Weight**
\( \text{C}_{18}\text{H}_{18}\text{N}_{2}\text{O}_{2}; \text{MW} = 268.12118 \)

![Chemical structure of lysergic acid](image)

**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\(_a\)=7.68. Moderately soluble in pyridine; sparingly soluble in water and neutral organic solvents; soluble in NaOH, NH\(_4\)OH, Na\(_2\)CO\(_3\), and HCl solutions; and slightly soluble in dilute H\(_2\)SO\(_4\). 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:**

- **\(^{13}\text{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.
1. Indole Alkaloids

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

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 Alkaloiide; Enke Verlag, Stuttgart, 218 pp., 1964.
Common/Systematic Name
Ergine; Lysergic acid amide

Molecular Formula/Molecular Weight
$\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}$; $\text{MW} = 267.13716$

![Chemical Structure](image)

General Characteristics
Crystallized from acetone as massive colorless prisms; m.p. $196^\circ\text{C}$; $[\alpha]_D^{20} + 414^\circ$, $[\alpha]_546^{20} + 520^\circ$ (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:

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 154m/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 NH₃ atmosphere).
c) Chloroform-methanol-NH₃ (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

A. Hofmann; Die Mutterkorn Alkaloid, Enke Verlag, Stuttgart, 218 pp., 1964.
**Common/Systematic Name**
8-Hydroxyergine

**Molecular Formula/Molecular Weight**
C\textsubscript{16}H\textsubscript{17}N\textsubscript{3}O\textsubscript{2}; MW = 283.13208

\begin{center}
\includegraphics[width=0.3\textwidth]{alkaloid.png}
\end{center}

**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\textsubscript{254}, Merck preparative TLC plates and eluted with chloroform-isopropyl alcohol-ammonia (90:10:0.036, v/v/v); R\textsubscript{f} values of 8-hydroxyergine and 8-hydroxyerginine were 0.50 and 0.91, respectively. Prepurified alkaloids were chromatographed on a Separon SGX C\textsubscript{18} column (Tessek, Czechoslovakia) particle size 7\textmu m. The mobile phase consisted of (A) MeOH-H\textsubscript{2}O-NH\textsubscript{3} (90:10:0.036, v/v/v) and (B) MeOH-H\textsubscript{2}O-NH\textsubscript{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 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.
1. Indole Alkaloids

Spectral Data

\(^1\text{H NMR:}\)

\((\text{CD}_3\text{OD})\) H-2, 6.984\((J_{2,4a}=1.8\text{Hz})\); H-4a, 2.749; H-4b, 3.569\((J_{4a,4b}=>0, J_{4a,4b}=14.5\text{Hz})\); H-5, 3.265\((J_{4b,5}=11.8\text{Hz}, J_{4b,5}=5.9\text{Hz})\); H-7a, 2.936\((J_{3,7a}=11.7\text{Hz}, J_{3,7a}=0.7\text{Hz})\); H-7b, 2.965; H-9, 6.358\((J_{4b,9}=0, J_{5,9}=2.1\text{Hz})\); H-12, 7.193\((J_{12,13}=7.4\text{Hz}, J_{12,14}=0.7\text{Hz})\); H-13, 7.107\((J_{13,14}=7.9\text{Hz})\); H14, 7.231; and N-Me, 2.590ppm.

\(^{13}\text{C NMR:}\)

\((\text{CD}_3\text{OD})\) C-2, 120.66; C-3, 110.52; C-4, 27.15; C-5, 64.20; C-6, 62.71; 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\((M^+, \text{C}_{16}\text{H}_{17}\text{N}_3\text{O}_2, 61\%)\), 266\((\text{C}_{16}\text{H}_{16}\text{N}_3\text{O}, 27)\), 265\((\text{C}_{16}\text{H}_{14}\text{N}_3\text{O}, 37)\), 248\((\text{C}_{16}\text{H}_{13}\text{N}_2\text{O}, 59)\), 240\((\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_2, 86)\), 223\((\text{C}_{14}\text{H}_{12}\text{N}_2\text{O}_2, 86)\), 221\((\text{C}_{14}\text{H}_{13}\text{N}_2, 42)\), 206\((\text{C}_{14}\text{H}_{11}\text{N}_2, 19)\), 195\((\text{C}_{13}\text{H}_9\text{NO}, 36)\), 194\((\text{C}_{13}\text{H}_9\text{NO}, 32)\), 181\((\text{C}_{13}\text{H}_{11}\text{N}, 26)\), 180\((\text{C}_{13}\text{H}_{10}\text{N}, 26)\), 167\((\text{C}_{12}\text{H}_8\text{N}, 83)\), and 154\((\text{C}_{11}\text{H}_8\text{N}, 100)\).

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 \(\text{NH}_3\) atmosphere).
c) Chloroform-methanol-\(\text{NH}_3\) (94:5:1).
d) Chloroform-ethylamine (90:10).
e) Benzene-dimethylformamide (86.5:13.5).

References


Common/Systematic Name
Erginine; Isolysergic acid amide

Molecular Formula/Molecular Weight
C₁₆H₁₇N₃O₂, MW = 267.13716

General Characteristics
Crystallized from methanol as solvated prisms; mp., 132-134°C; [α]D ° + 480°, [α]360 ° + 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:
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 NH₃ atmosphere).
c) Chloroform-methanol-NH₃ (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.

### 1. Indole Alkaloids

**Common/Systematic Name**

8-Hydroxyerginine

**Molecular Formula/Molecular Weight**

$C_{16}H_{17}N_{3}O_{2}$; MW = 283.13208

![Chemical Structure of 8-Hydroxyerginine](image)

**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$_2$O-NH$_3$ (90:10:0.036, v/v/v) and (B) MeOH-H$_2$O-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:  

$$\text{(CD$_2$OD)}$$ H-2, 6.974($J_{2,4a}=1.6$Hz); H-4a, 2.649; H-4b, 3.606($J_{4a,4b}=0, J_{4a,4b}=-14.6$Hz); H-5, 3.150($J_{4b,5}=11.5$Hz, $J_{4b,5}=-5.9$Hz); H-7a, 3.080($J_{7a,7b}=-11.3$Hz, $J_{7a,7b}=1.5$Hz); H-7b, 2.626; H-9, 6.268($J_{9,9}=0.8$Hz, $J_{9,9}=-2.2$Hz); H-12, 7.118($J_{12,13}=7.0$Hz, $J_{12,14}=1.7$Hz); H-13, 7.090($J_{13,14}=7.2$Hz); H-14, 7.219ppm; and N-Me, 2.614ppm.
1. Indole Alkaloids

$^{13}$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, 43.39 ppm.

Mass Spectrum:

EIMS: 283($M^+$, C$_{16}$H$_{17}$N$_3$O$_2$, 100), 266(C$_{16}$H$_{16}$N$_3$O, 14), 265(C$_{16}$H$_{15}$N$_3$O, 29), 248(C$_{16}$H$_{12}$N$_2$O, 35), 240(C$_{16}$H$_{12}$N$_2$O$_2$, 93), 223(C$_{16}$H$_{12}$N$_2$O$_2$, 31), 221(C$_{15}$H$_{13}$N$_2$, 42), 206(C$_{14}$H$_{10}$N$_2$, 12), 195(C$_{13}$H$_9$N, 60), 194(C$_{13}$H$_8$N, 61), 181(C$_{13}$H$_7$N, 50), 180(C$_{13}$H$_{10}$N, 20), 167(C$_{12}$H$_9$N, 94), and 154(C$_{11}$H$_8$N, 96%).

Reference

Common/Systematic Name
Lysergol

Molecular Formula/Molecular Weight
C_{16}H_{11}N_{2}O; MW = 254.14191

General Characteristics
Colorless prisms from ethanol; mp., 245°C (uncorr. decomp.); as plates and prisms; mp., 253-255°C (dec.); \([\alpha]_D^{18} +49° (c=0.2, \text{in pyridine}), [\alpha]_D^{20} +54°, [\alpha]_{MeI}^{20} +87° (c=0.3, \text{in pyridine}).\) Gave a light purple and purplish blue colors with van Urk's and Aliport-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:
\(\lambda_{max}^{MeCH} 225, 242, \text{and } 312 \text{nm.}\)
1. Indole Alkaloids

IR:

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

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 Alkaloiden; Enke Verlag, Stuttgart, 218 pp., 1964.
**Common/Systematic Name**
Lysergene

**Molecular Formula/Molecular Weight**
\[ C_{16}H_{16}N_2; \text{MW} = 236.13135 \]

\[
\begin{array}{c}
\text{NH} \\
\text{N-Me} \\
\text{CH}_2
\end{array}
\]

**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, \text{in pyridine}); \]
\([\alpha]_D^{20} +504° \ (c=0.4, \text{in pyridine}). \text{ 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:**
\[ \lambda_{\text{max}}^{\text{MeOH}} \ 243, 263, \text{and } 335\text{nm.} \]

**IR:**
1. Indole 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.
1. Indole Alkaloids

Common/Systematic Name
Lysergine

Molecular Formula/Molecular Weight
C_{16}H_{16}N_{2}; MW = 238.14700

![Molecular Structure]

General Characteristics
Colorless prisms from ethyl acetate; mp., 275°C (uncorr. decomp.); prisms from methanol, ethanol, or ethyl acetate, 286-289°C (dec.); \([\alpha]_{D}^{20} = +70°\) (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:

References
1. Indole Alkaloids

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

Common/Systematic Name
Ergonovine; Ergometrine; Ergobasine

Molecular Formula/Molecular Weight
C_{19}H_{23}N_{3}O_{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.); [α]_D^{20} + 90° (c=0.23, in water); -16° (c=1.0, in pyridine); [α]_D^{20} + 41°, [α]_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, Balansa epichiloë, 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.
1. Indole Alkaloids

Spectral Data

IR:

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


1. Indole Alkaloids


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).

Common/Systematic Name
Ergonovinine; Ergometrinine; Ergobasinine

Molecular Formula/Molecular Weight
C₁₉H₂₃N₃O₂; MW = 325.17903

General Characteristics
Forms large colorless prisms from acetone; mp., 196°C (dec.); [α]D₂⁰ + 414°, [α]₅₄₆¹²⁰ + 520° (c=1.0, in CHCl₃); pKₐ=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.
1. Indole Alkaloids

Spectral Data

IR:

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, 43.6 ppm.

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):

- 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


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


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.

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

Common/Systematic Name
Agroclavine

Molecular Formula/Molecular Weight
C₁₆H₁₈N₂; MW = 238.14700

General Characteristics
Colorless needles from acetone, mp., 205-206°C, sublimed under high vacuum between
110-130°C; [α]D²⁰ = -155° (c=0.9 in CHCl₃); [α]D²⁰ = -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:
λ_max 225, 284 and 293nm (log ε=4.47, 3.88 and 3.81, respectively).

IR:

¹H NMR:
(pyridine- d₅) 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-CH₃, 1.68(3H, s);
1. Indole Alkaloids

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).

\[(\text{CDCl}_3) \text{ H-4α, 2.78(dd, } J=15, 12\text{Hz); H-4β, 3.31(dd, } J=15, 4\text{Hz); H-5, 2.52(ddd, J=12, 9.5 and 4Hz); H-7α, 3.24(d, } J=17\text{Hz); H-7β, 2.93(dd, broad signal, } J=17, 4\text{Hz); H-9α and β, 6.18(s, broad signal); H-10, 3.74(dd, broad signal, } J=9.5, 4\text{Hz); H-17, 1.77(s); and N-Me, 2.49ppm (s).\]

\[13\text{C NMR:} \]
\[\text{(pyridine-d}_5\text{) C-2, 118.3; C-3, 111.2; C-4, 26.4; C-5, 63.6; C-7, 60.2; C-8, 131.9; C-9, 119.4; C-10, 40.8; C-11, 131.9; C-12, 112.0; C-13, 122.0; C-14, 108.4; C-15, 134.0; C-16, 126.6; C-17, 19.9; and N-Me, 40.2ppm.}\]

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

References


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


1. Indole Alkaloids

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:
\[ \lambda_{\text{max}}^{\text{ethanol}} = 225, 283, \text{and} 293 \text{nm} \]

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

\(^1\)H 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 8.1-8.5 ppm (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).
1. Indole Alkaloids

1. Indole Alkaloids

Common/Systematic Name
Dihydroagroclavine

Molecular Formula/Molecular Weight
\( \text{C}_{16}\text{H}_{20}\text{N}_{2}; \text{MW} = 240.16265 \)

![Chemical structure of Dihydroagroclavine]

General Characteristics
Crystals as long needles from toluene, benzene, ether, chloroform, ethyl acetate, acetone, methanol, ethanol or pyridine; mp., 242°C (dec.); \([\alpha]_D^{20} - 69°, [\alpha]_\text{CHCl}_3^{20} - 83° (c=0.5, \text{in CHCl}_3); [\alpha]_D^0 - 111°, [\alpha]_\text{pyridine}^{5461} - 129° (c=0.5, \text{in pyridine})\). Insoluble in toluene, benzene and ether; readily soluble in chloroform, ethyl acetate, acetone, methanol, ethanol and pyridine. Succinate derivative, \( \text{C}_{16}\text{H}_{20}\text{N}_{2}.0.5\text{C}_4\text{H}_6\text{O}_4 \), crystals as prisms from water; mp., 213°C (dec.); \([\alpha]_D^{17} - 87° (c=0.13, \text{in pyridine})\).

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 \( \text{C}_{16}\text{H}_{20}\text{N}_{2} \): C 79.95, H 8.39, N 11.66).

Reference
1. Indole Alkaloids

**Common/Systematic Name**

Festuclavine

**Molecular Formula/Molecular Weight**

\[ C_{16}H_{20}N_2; \text{MW} = 240.16265 \]

**General Characteristics**

Crystals (long needles) from methanol; mp., 238-239°C (dec.); 242-244°C (dec.); \([\alpha]_D^{15} -98^\circ\) (c=0.3, pyridine); \([\alpha]_D^{10} -70^\circ\), \([\alpha]_{5461}^{20} -83^\circ\) (c=0.5, in CHCl₃); \([\alpha]_D^{20} -110^\circ\), \([\alpha]_{5461}^{20} -128^\circ\); \(pK=7.4\) (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 106-1), *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:**

\[ \lambda_{\text{MeOH}}^{\text{max}} 224(\log \epsilon=4.54), 275(3.81), \text{and } 281\text{nm (3.84)}. \]

**IR:**

1H NMR:
(CDCl₃) 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).

13C NMR:
(CDCl₃) 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 144m/e.

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 Alkaloid, Enke Verlag, Stuttgart, 218 pp., 1964.

1. Indole Alkaloids

Common/Systematic Name
Elymoclavine

Molecular Formula/Molecular Weight
C16H18N2O; MW = 254.14191

\[
\begin{align*}
\text{CH}_2\text{OH} & \\
\text{N-Me} & \\
\text{H} & \\
\text{H} & \\
\text{H} & \\
\text{NH} & \\
\text{2} & \\
\text{3} & \\
\text{4} & \\
\text{5} & \\
\text{6} & \\
\text{7} & \\
\text{8} & \\
\text{9} & \\
\text{10} & \\
\text{11} & \\
\text{12} & \\
\text{13} & \\
\end{align*}
\]

General Characteristics
Crystallized as prisms from methanol; mp., 245-249°C; \([\alpha]_D^{20} = -152° \ (c=0.9, \text{in pyridine}), \]
\([\alpha]_D^{20} = -111° \ (c=0.1, \text{in EtOH}); pK=6.7 \ (\text{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:
\[\lambda_{\text{max}}^{\text{MeOH}} = 227, 283, \text{and 293nm} \ (\log e=4.31, 3.84, \text{and 3.76, respectively}).\]

IR:

\(^1\)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). (CD3OD) 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:
(CD3OD) 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

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.


1. Indole Alkaloids

Common/Systematic Name
Elymoclavine-O-β-fructofuranoside

Molecular Formula/Molecular Weight
C_{22}H_{28}N_{2}O_{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_{2}O-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

\[^{1}\text{H} \text{NMR:}
\]
\[(\text{CD}_{3}\text{OD}) \, 6.937, \, H-2; \, 2.797, \, H-4\alpha; \, 3.379, \, H-4\beta; \, 2.691, \, H-5; \, 3.174, \, H-7\alpha; \, 3.631, \, H-7\beta; \, 6.553, \, H-9; \, 3.854, \, H-10; \, 6.950, \, H-12; \, 7.163, \, H-13; \, 7.143, \, H-14; \, 4.112, \, H-17\alpha; \, 4.327, \, H-17\beta; \, 2.588, \, N-Me; \, 3.590, \, H-1\alpha'; \, 3.717, \, H-1\beta'; \, 4.154, \, H-3'; \, 4.008, \, H-4'; \, 3.779, \, H-5'; \, 3.628, \, H-6\alpha'; \, \text{and} \, 3.734\text{ppm,} \, H-6\beta'.\]
\[ ^{13}C \text{NMR:} \]
\[(\text{CD}_3\text{OD}) \]
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\textsubscript{3}) 417(33%), 416(22), 254(23), 253(30), 237(100), 236(85), 223(9), 207(6), 167(9), 154(6), and 127m/e (1).

References

Common/Systematic Name
Elymoclavine-O-β-fructofuranosyl-(2→1)-O-β-D-fructofuranoside

Molecular Formula/Molecular Weight
C_{28}H_{35}N_{2}O_{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_{2}O-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:
13C NMR:
(CD3OD) 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: (NH3) 579(25%), 578(8), 416(25), 254(60), 253(45), 237(100), 236(93), 223(7), 207(3), 167(9), 154(10), and 127m/e (24).

Reference
1. Indole Alkaloids

Common/Systematic Name
Chanoclavine-I; Chanoclavine

Molecular Formula/Molecular Weight
C_{15}H_{20}N_{2}O; MW = 256.15756

\[
\begin{align*}
\text{CH}_2\text{OH} & \\
\text{Me} & \\
\text{H} & \\
\text{NMe} & \\
\text{NH} & \\
\text{H} & \\
\end{align*}
\]

General Characteristics
Prisms and polyhedral crystals from acetone/methanol; mp. 220-222° C (dec.), \([\alpha]_D^{20} = -240°\); \([\alpha]_D^{20} = -294°\) (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

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:
\[ \lambda_{\text{max}}^{\text{MeOH}} = 225, 284, \text{and} 293 \text{nm (log } \epsilon = 4.44, 3.82, \text{and} 3.76, \text{respectively).} \]

IR:
1600-1650 cm\(^{-1}\) (characteristic of indole); see A. Hofmann, 1964.
Mass Spectrum:
256(M\(^+\)), 237, 183(100%), 182, 167, 168, 154, and 155m/e.

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


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 Alkaloiide; Enke Verlag, Stuttgart 218 pp., 1964.


Common/Systematic Name
Isochanoclavine-I

Molecular Formula/Molecular Weight
C_{16}H_{20}N_{20}; MW = 272.15248

Me

\[ \text{CH}_2\text{OH} \]

Me

\[ \text{NHMe} \]

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:

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

IR:


\[ ^1H \text{ NMR:} \]


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

Common/Systematic Name
Chanoclavine-II

Molecular Formula/Molecular Weight
C$_{16}$H$_{20}$N$_{2}$O; MW = 256.15756

![Chemical Structure of Chanoclavine-II]

General Characteristics
Prisms from acetone; mp., 174°C; [α]$_D$\(^{20}\) -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, [α]$_D$\(^{20}\) -271° (c=0.5, in 50% alcohol). N-Acetyl derivative, large crystalline prisms from methanol; mp., 203°C; [α]$_D$\(^{20}\) -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
Common/Systematic Name

\( \text{N-Demethylchanoclavine-II; Norchanoclavine II} \)

Molecular Formula/Molecular Weight

\( \text{C}_{15}\text{H}_{18}\text{N}_{2}\text{O}; \text{MW} = 242.14191 \)

\[
\begin{array}{c}
\text{CH}_2\text{OH} \\
\text{Me} \\
\text{NH}_2 \\
\text{H} \\
\text{NH}
\end{array}
\]

General Characteristics

Gray color, turning blue with Ehrlich's reagent.

Fungal Source

\( \text{Claviceps sp. (strain SD 58).} \)

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 a column of alumina (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:**

\[ \lambda_{\text{max}}^{\text{MeOH}} = 223, 274, 283, \text{ and } 294 \text{nm}. \]

**Mass Spectrum:**

HREIMS: 242.1430 (calcd for C_{15}H_{18}N_{2}O, 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**

Common/Systematic Name
Setoclavine

Molecular Formula/Molecular Weight
C_{16}H_{12}N_2O; MW = 254.14191

General Characteristics
Prisms from methanol-acetone; m.p. 229-234°C (dec.); [\alpha]_D^{20} + 174°C; [\alpha]_S_{461}^{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_{\text{max}}^{\text{MeOH}} 243 and 313 nm (log \epsilon=4.38 and 4.04).

IR:

Mass Spectrum:
254(M^+), 236, 235, 234, 219, 211, 196, 181, 168, and 154m/e (100%).
References


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

Indole Alkaloids

**Common/Systematic Name**
Isosetoclavine

**Molecular Formula/Molecular Weight**
\[ C_{16}H_{18}N_2O_2, \text{MW} = 254.14191 \]

**HO**
\[
\begin{array}{c}
\text{Me} \\
\text{N-Me} \\
\text{NH}
\end{array}
\]

**General Characteristics**
Large polyhedral crystals from methanol; m.p. 234-237°C; \([\alpha]_D^{20} + 107^\circ; [\alpha]_{345}^{20} + 147^\circ\) (c=0.5, in pyridine); \([\alpha]_D^{20} + 129^\circ\) (c=0.4, in alcohol); pK=5.9 (in 80% aqueous methylecellosolve). 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 typhoides*).

**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:**
\[
\lambda_{\text{max}}^{\text{MeOH}} 242 \text{ and } 317 \text{nm (log } \varepsilon=4.42 \text{ and } 4.10).\]

**IR:**