

ALKALOIDS FROM PLANTS OF THE SUBFAMILY WURMBAEOIDEAE

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Abstract - This review gives a survey of the most important papers on the isolation and chemistry of alkaloids (i.e. the tropolone alkaloids, their precursors, and the minor alkaloids) from plants of the subfamily Wurmbaeoideae, and of those of the biosynthesis of these compounds.

INTRODUCTION

The tropolone alkaloids from plants of the subfamily Wurmbaeoideae¹⁻¹⁰ form an independent group of compounds. They arise from the phenethyltetrahydroisoquinoline precursor - autumnaline (XVa). For a long time, the only known representative of this group was colchicine (Ia) which was isolated from the plant Colchicum autumnale L. This group of alkaloids also includes intermediary products (XV-XIX), leading to the formation of colchicine alkaloids with tropolone ring, and the side-products (XX-XXIX) (minor alkaloids) of this biosynthesis. The Colchicum alkaloids occur only in the plants of the sub-family Wurmbaeoideae (Family Liliaceae)^{11,12} (Table A) and in Kreysigia multiflora Reichb.^{13,14} whose definite classification to this sub-family has not been carried out as yet.

The colchicine alkaloids are highly toxic, in animal cell they inhibit cellular division in the metaphase (stathmokinetic or mitotic effect), and in plants they bring about polyploidy.^{2,10}

The alkaloids of the Wurmbaeoideae plants are usually classified as follows:

I. Alkaloids with tropolone ring and their important derivatives

- | | |
|--|-----------|
| (1) Neutral and phenolic compounds (I, III, IV, V) | } Table B |
| (2) Basic compounds (II) | |

- (3) Compounds without amino group or with keto group at C₇-position
- (4) Compounds obtained by conversion of alkaloids with tropolone ring
 - (a) Lumiderivatives (VI and VII) of the compounds given sub (1) and (2) and lumicolchicone (VIII)
 - (b) 10,11-Oxy-10,12a-cyclo-10,11-secocolchicine (IX)
 - (c) 10,12a-Oxycolchicine (X)
 - (d) Colchicide (XI)
 - (e) Colchinole and its methylether (XII)
 - (f) Colchicinic acid (Allocolchiceine) (XIIIa) and its methyl ester (Allocolchicine) (XIIIb)
 - (g) Colchinale (XIV)

II. Alkaloids without tropolone ring (Tables C - H)

- (1) Phenethyltetrahydroisoquinoline bases (XV)
- (2) Androcymbine alkaloids (XVI)
- (3) Dihydro- and tetrahydroandrocymbine alkaloids (XVII - XIX)

}	Homopromorphinane group
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- (4) Homoproaporphine alkaloids (XX - XXVIII)
- (5) Homoaporphine alkaloids (XXIX)
- (6) Alkaloids without tropolone ring whose constitution is still unknown
- (7) Benzyltetrahydroisoquinoline - Isocorydine (XXX)

THE ISOLATION AND THE STRUCTURES OF ALKALOIDS WITH TROPOLONE RING AND OF SOME OF THEIR DERIVATIVES

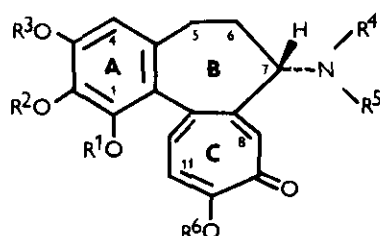
Pelletier and Caventou (1820) were the first research workers in this field. They investigated the corms of Colchicum plants contrary to Geiger (1833), Oberlin (1857), Zeisel (1883), Houdé (1884), and Merck (1916) who studied the Colchicum seeds (Summarizingly^{1-7,16}). In the latter, the major alkaloid was colchicine. Therefore, for more than 60 years, it was assumed^{15,16} that it was the only toxic compound contained therein. During the following years, by application of new separation methods, ca. 100 alkaloids (Tables B - H) were detected in the seeds, corms, flowers, and leaves of the Wurmbaeoideae. Recently, two new alkaloids were isolated from Colchicum latifolium, namely colchiciline (Ij) with a hydroxyl group at C₆-position in trans-configuration to the amidic group at C₇, and 10,11-oxy-10,12a-cyclo-10,11-secocolchicine (IX).^{17,18}

Table A. Genera of the sub-family Wurmbaeoideae¹² and their groups of alkaloids

Family: <u>Liliaceae</u>	Alkaloids		
	with tropolone ring (Table B)		without tropolone ring (Tables C - H)
	phenolic and neutral	basic	
Tribe: <u>Glorioseae</u>			
Genus: <u>Gloriosa</u>	++	-	++
Littonia	++	-	++
Sandersonia	++	-	++
<u>Iphigenieae</u>			
Iphigenia	++	-	++
Camptorrhiza	+	-	+++
Ornithoglossum	++	-	++
<u>Baeometreae</u>			
Baeometra	+	-	+++
<u>Colchiceae</u>			
Colchicum	+++	++ or -	+ or -
Merendera	++	++ or -	+ or -
Androcymbium	+	+	+++
<u>Kreysigia multiflora</u>	++	+	+++
<u>Neodregeae</u>			
Dipidax	+++	+	+
Neodregea	?	?	?
<u>Wurmbaeae</u>			
Wurmbaea	+	+ ?	+
Anguillaria	+	+ ?	+

C. autumnale gave the new alkaloids colchifoline (IVa) and 2-demethylcolchifoline (IVb) which have a radical of glycolic acid instead of an acetyl group on the nitrogen.¹⁹⁻²¹ The leaves of this plant yielded cornigerine (Ib) which up till now has been isolated only from C. cornigerum growing on the Sinai peninsula.^{22,23} It is of interest that, in fresh leaves and flowers of Colchicum autumnale and C. speciosum, 2- and 3-demethylderivatives of colchicine cannot be detected.¹⁹

The alkaloids with tropolone ring (Table B) differ only by their substituents on

Table B. Constitution of tropolone alkaloids of the subfamily Wurmbaeoideae

Alkaloids	Substituents					
	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶
I						
Colchicine (Ia)	CH ₃	CH ₃	CH ₃	H	COCH ₃	CH ₃
Cornigerine (Ib)		-CH ₂ -	CH ₃	H	COCH ₃	CH ₃
3-Demethylcolchicine (Ic) (Alkaloid C)	CH ₃	CH ₃	H	H	COCH ₃	CH ₃
2-Demethylcolchicine (Id) (Alkaloid E ₁)	CH ₃	H	CH ₃	H	COCH ₃	CH ₃
Colchicoside (Ie)	CH ₃	CH ₃	Glucose	H	COCH ₃	CH ₃
Colchiceine (If)	CH ₃	CH ₃	CH ₃	H	COCH ₃	H
Cornigereine (Ig)		-CH ₂ -	CH ₃	H	COCH ₃	H
3-Demethylcolchiceine (Ih)	CH ₃	CH ₃	H	H	COCH ₃	H
2-Demethylcolchiceine (Ii)	CH ₃	H	CH ₃	H	COCH ₃	H
Colchiciline (Alkaloid CC-12 ?) (Ij) ^a	CH ₃	CH ₃	CH ₃	H	COCH ₃	CH ₃
N-Deacetyl-N-formylcolchicine (Ik)	CH ₃	CH ₃	CH ₃	H	CHO	CH ₃
3-Demethyl-N-deacetyl-N-formylcolchicine (I l)	CH ₃	CH ₃	H	H	CHO	CH ₃
2-Demethyl-N-deacetyl-N-formylcolchicine (Im)	CH ₃	H	CH ₃	H	CHO	CH ₃
N-Deacetyl-N-formylcolchiceine (In)	CH ₃	CH ₃	CH ₃	H	CHO	H
II						
N-Deacetylcolchicine (IIa)	CH ₃	CH ₃	CH ₃	H	H	CH ₃
N-Deacetylcolchiceine (IIb)	CH ₃	CH ₃	CH ₃	H	H	H
N-Deacetyl-3-demethylcolchicine (IIc)	CH ₃	CH ₃	H	H	H	CH ₃
N-Deacetyl-2-demethylcolchicine (IIId)	CH ₃	H	CH ₃	H	H	CH ₃
N-Deacetyl-2,3-demethylcolchicine (IIe)	CH ₃	H	H	H	H	CH ₃
N-Deacetyl-N-methylcolchicine (Deme-colcine, Colcemide, Colchamine). (IIIf)	CH ₃	CH ₃	CH ₃	H	CH ₃	CH ₃
N-Deacetyl-3-demethyl-N-methylcolchicine (Alkaloid CC-7) (IIg)	CH ₃	CH ₃	H	H	CH ₃	CH ₃
N-Deacetyl-2-demethyl-N-methylcolchicine (Alkaloid S) (IIh)	CH ₃	H	CH ₃	H	CH ₃	CH ₃
Demecolceine (IIi)	CH ₃	CH ₃	CH ₃	H	CH ₃	H
N-Deacetyl-N-dimethylcolchicine (IIj)	CH ₃	CH ₃	CH ₃	CH ₃	CH ₃	CH ₃
Speciosine (IIk) ⁴⁵	CH ₃	CH ₃	CH ₃	b	CH ₃	CH ₃

III

N-Methylcolchicine (N-acetyldemecolcine) (IIIa)	CH ₃	CH ₃	CH ₃	CH ₃	COCH ₃	CH ₃
N-Methyl-N-deacetyl-N-formylcolchicine (N-formyldemecolcine) (IIIb)	CH ₃	CH ₃	CH ₃	CH ₃	CHO	CH ₃

IV

Colchifoline (IVa)	CH ₃	CH ₃	CH ₃	H	COCH ₂ OH	CH ₃
2-Demethylcolchifoline (IVb)	CH ₃	H	CH ₃	H	COCH ₂ OH	CH ₃

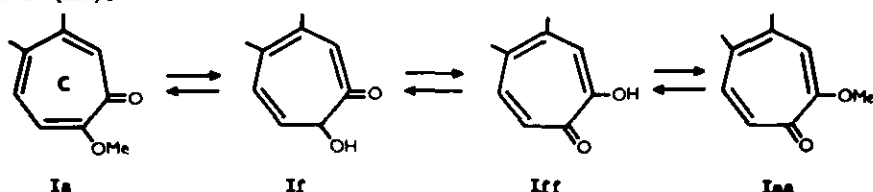
V

Thiocolchicine (V)	CH ₃	CH ₃	CH ₃	H	COCH ₃	c
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- a) 6-Hydroxycolchicine b) 2-Hydroxybenzyl
c) Methylthiogroup instead of methoxyl group

the aromatic ring A, on the ring B, and on the amino group of this ring, and on the tropolone ring C.

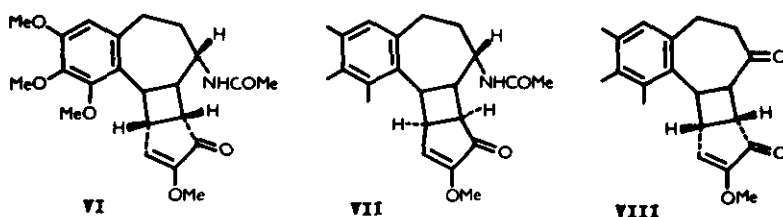
In 1924, Windaus²⁴ assigned a phenanthrene skeleton with oxo-methoxymethylene substituents on ring C to colchicine. Cook et al.²⁵ and, a short time later, Dewar²⁶ assigned to it the correct structure with the seven-membered tropolone ring C. In 1955, the position of the substituents on this ring C was corrected²⁷ and this new colchicine structure was confirmed by X-ray analysis.²⁸ Margulis²⁹ as well as Lessinger and Margulis³⁰ studied the conformation of colchicine and isocolchicine by X-ray crystallography. Silverton³¹ elucidated the structure of colchiceine (If).



Scheme 1

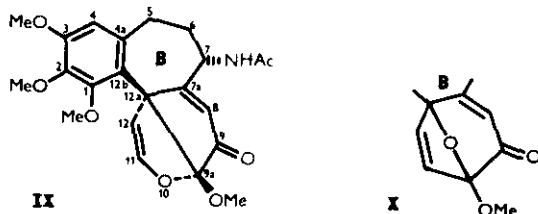
The methoxyl group of the tropolone ring can be easily saponified with dilute acids or sodium hydroxide to give colchiceine (If). Its further saponification affords trimethylcolchiceinic acid (= correctly deacetylcolchiceine (IIb)). Colchiceine is a mixture of colchiceine (If) and isocolchiceine (Iff). Methylation with diazomethane yields colchicine (Ia) and isomeric isocolchicine (Iaa)³² (Scheme 1). The methoxyl group can be replaced by the amino group to give the already known colchiceinamides,^{33,34} or by the thio groups (SH or SCH₃) (V).^{34,35}

This methoxyl group of the tropolone ring can be removed by the action of hydrogen with acetone-deactivated Raney nickel to give colchicide (XI).³⁶ Grewe³⁷ converted colchicine into the α -, β -, and γ -lumiderivatives. The β - (VI) and the γ - (VII) lumiderivatives were found in all the parts of the Yumbasoidae.^{16,38} These two lumiderivatives were prepared from the majority of the isolated tropolone alkaloids.³⁹⁻⁴³ Mass spectrometry has revealed that α -lumicolchicine is a dimer which on thermic reaction is converted into β -lumicolchicine and then, through the effect of sunlight into γ -lumicolchicine. The last two derivatives are stereoisomers on the rings C and D.⁴³

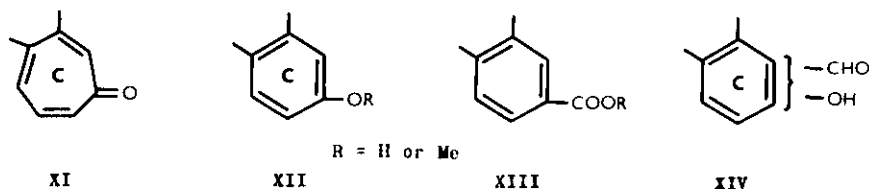


From the corms of Gloriosa superba, Canonica et al.⁴¹ have isolated β -lumicolchicone (VIII) with a keto group instead of an acetamido group at the C₁₀-position.

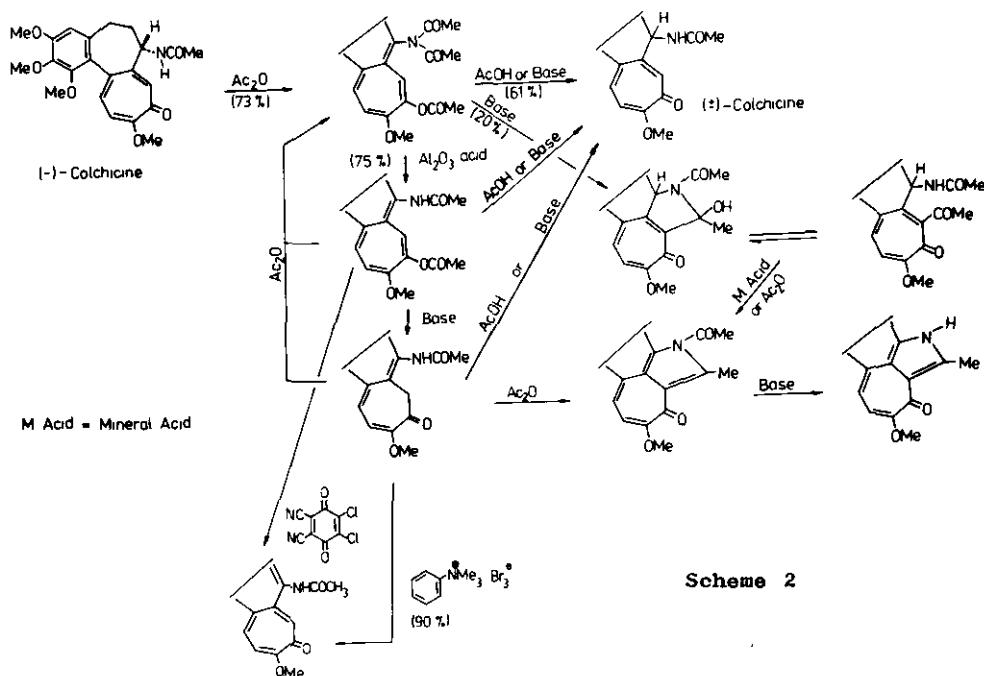
Zeisel and Friedrich⁴⁴ prepared 10,12a-oxycolchicine (X). This substance is readily obtained from colchicine by treatment with chromium trioxide in acetic acid. Preparative experiments and physical methods have shown⁴⁵⁻⁴⁷ that on boiling with acids, this substance is converted into colchiceine (If).



By treatment with potassium hypiodide⁴⁸ or hydrogen peroxide in alkaline medium²⁷ the seven-membered tropolone ring of colchiceine (If) can be rearranged into colchinole (XII) with a benzene ring C. On treatment with sodium methanolate, colchicine (Ia) is converted into colchicineic acid (= allocolchiceine) (XIIIa) or its methylester (= allocolchicine) (XIIIb) in ca. 100% yield.⁴⁹⁻⁵¹ This reaction is often used to study the constitution and biosynthesis of alkaloids with tropolone ring. Sadykov et al. found allocolchicine and allocolchiceine derivatives in plant material.⁵²



While carrying out the racemization of colchicine and thiocolchicine with acetic acid anhydride, Bladé-Font prepared a new series of colchicine derivatives^{53,54} (Scheme 2).



Racemization of colchicine with the Schiff-base afforded racemic N-deacetyl-colchiceine, 7-oxo-deacetamidocolchicine, and 7-oxo-deacetamidisocolchicine.⁵⁵ Biotransformation of colchicine carried out with microsomal fractions of animal liver gave colchinale (XIV).^{56,57} Battersby et al.⁵⁸ elucidated the constitution of the alkaloid speciosine (IIk) which was isolated from C. speciosum by Kiselev.⁵⁹ On heating, this alkaloid was converted into demecolcine (colchamine) (IIIf).⁶⁰ Capraro and Brossi described a simple conversion of colchicine into demecolcine.⁶¹ The French authors⁶² reported the isolation of a tropolone alkaloid with glucose on the ring A (Ie) and an alkaloid containing a sulphur atom on the ring C. There was also prepared

colchicine with various substituents at C₄-position⁶³ and, with the help of microorganisms, 1-demethylcolchicine which has not been found in nature as yet.⁶⁴ Hufford et al.⁶⁵ screened a number of microorganisms for their ability to bio-transform colchicine, and Streptomyces spectabilis and S. griseus were chosen for preparative scale fermentation. Both organisms produced C₂ and C₃ demethylcolchicine.

Corrodi and Hardegger studied the stereochemistry of the acetamido group of colchicine.^{66,67} They isolated N-acetyl-L-glutamic acid after exhaustive ozonization of colchicine. Several authors studied this problem by optical rotatory dispersion and circular dichroism.^{68,69} Colchicine and its natural derivatives have the S-configuration. The ¹H-NMR measurements have shown that the amido group of the colchicine compounds is in equatorial position.⁷⁰

During the past three decades, the newly isolated alkaloids were identified by polarography, ultraviolet, infrared, mass spectra, ¹H- and ¹³C-NMR data, and photophysical processes.^{41,65,71-80,161}

In 1959 and in the following years, colchicine and some of its derivatives were synthesized by Eschenmoser et al.⁸¹ in Switzerland, Tammelen et al.⁸² and Woodward et al.⁸³ in the USA, by Nakamura et al.,⁸⁴ by Kotani et al.⁸⁵ and by Kato et al.⁸⁶ in Japan, and by Martel et al.⁸⁷ in France. Scott et al.⁸⁸ synthesized colchicine on the basis of the biogenetic theory postulating that the rings A and C are coupled by phenolic oxidation. Evans et al. synthesized colchicine by application of new alternatives to oxidative phenolic coupling.⁸⁹ Wallace published the synthetic approaches to morphine and colchicine alkaloid analogs.⁹⁰

II. Alkaloids without tropolone ring

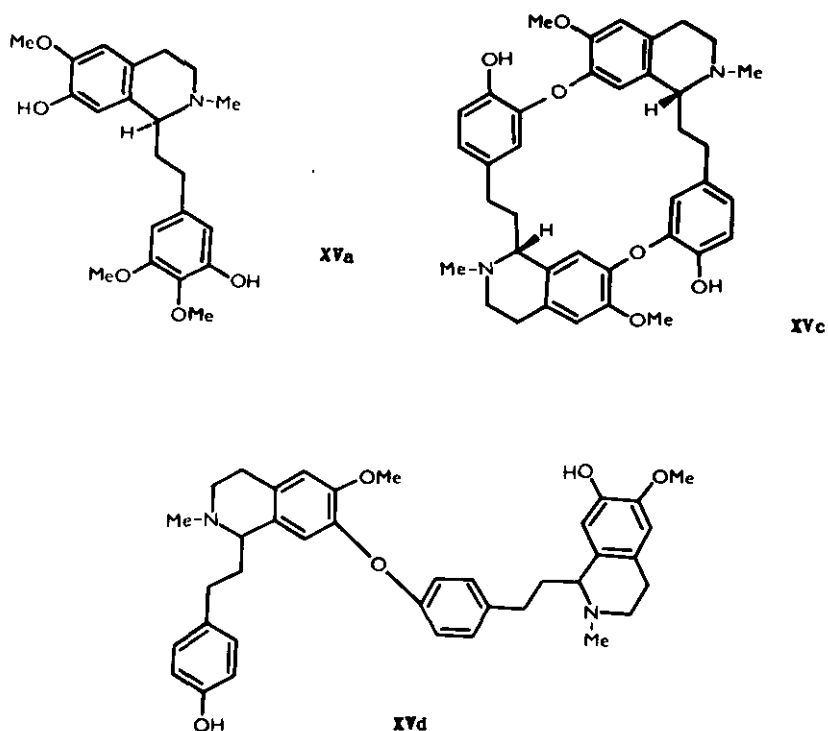
These substances form other groups of alkaloids of the plants of the sub-family Wurmbaeoideae. Androcymbine (XVIa), melanthioidine (XVc), colchicine (Ia), and demecolcine (IIIf) were isolated from the leaves of the South African plant Androcymbium melanthioides.⁹¹ The structures of androcymbine and melanthioidine were elucidated in the years between 1962 and 1968. The Tables C to G show the other isolated alkaloids without tropolone ring. All of them can be derived^{91b} from phenethyltetrahydroisoquinoline - autumnaline (XVa) - on the basis of the phenolic ortho-para or para-para oxidative coupling in the same way as in the Papaver alkaloids,^{92,93} which are derived from benzyltetrahydroisoquinoline.

The isolation of this new group of alkaloids has revealed how the whole group of colchicine alkaloids with tropolone ring arises. There are, however, not yet known the biological effects of any of the alkaloids of these groups of precursors or minor alkaloids since they are present in the plants only in traces.

(1) Phenethyltetrahydroisoquinoline bases (XV)

Melanthioidine (XVc) was the first isolated representative of this group.⁹¹ Its molecular weight showed it to be a dimer.^{94,95} ¹H-NMR Spectroscopy revealed symmetry of the molecule and therefore overlapping of the signals of the protons of its two halves. Reduction with sodium in liquid ammonia gave four derivatives^{95,96} which were identified as phenethyltetrahydroisoquinoline derivatives.

Table C. (1) Phenethyltetrahydroisoquinoline bases



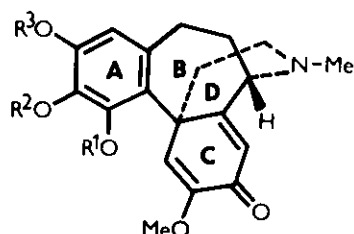
XVa S-(+)-Autumnaline (opt. antipode
= Alkaloid CC-22)^{14,58,102-107}

XVb Base m.p. 222°¹⁰⁵

XVc R-(-)-Melanthioidine^{91,94-96,107}

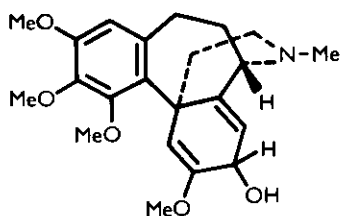
XVd Jolantinine^{97,98}

Table D. (2) Homopromorphinanane bases (XVI)

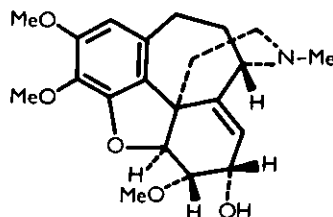


XVIa	$R^1=R^3=Me; R^2=H$	$\sim S-(-)$ -Androcymbine ^{91,103,108-112,115,116,124,129}
XVIb	$R^1=R^2=R^3=Me$	$\sim S-(-)$ -O-Methylandrocymbine ^{102,109,110,127b}
XVIc	$R^1=H; R^2=R^3=Me$	$\sim S-(-)$ -Collutine (= Alkaloid L-7) ¹¹³
XVId	$R^1=R^2=R^3=Me$	$\sim R-(+)$ -Krokiflorine (= Alkaloid K-2) ⁸
XVIE	$R^1=R^2=Me; R^3=H$	$\sim R-(+)$ -Alkaloids CC-3a and CC-10 ^{102,103}
XVIf	$R^1=Me; R^2+R^3=CH_2$	$\sim R-(+)$ -Alkaloid CC-20 ^{102,103}
XVIg	$R^1=Me; R^2+R^3=CH_2$	$\sim S-(-)$ -Alkaloid AM-3 ^{110,111}

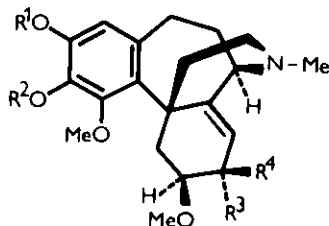
Table E. (3) Dihydro- and tetrahydrohomopromorphinanane bases (XVII-XIX)



XVII $\sim S-(-)$ -Szovitsidine¹¹⁴
(= Alkaloid OGG-2?)¹¹¹



XVIIIa $\sim S-(-)$ -Kreysiginine¹¹⁷⁻¹²²
XVIIIb $\sim R-(+)$ -Alkaloid CC-21^{102,103,109}
XVIIIc $(+)$ -Floramultinine⁷¹¹⁷



XIXa $R^1=R^4=H; R^2=Me; R^3=OH$ $\sim R-(+)$ -Alkaloid CC-3b^{102,103}
XIXb $R^1+R^2=CH_2; R^3=H; R^4=OH$ $\sim R-(+)$ -Alkaloid CC-2^{102,103,125}

Battersby et al.⁹⁵ used Ullman's double reaction to synthesize melantheidine from the phenolic bromophenethyltetrahydroisoquinoline compound. Consequently, the alkaloid is a bisphenethyltetrahydroisoquinoline base.

Jolantinine is another dimer alkaloid of this group.^{97,98}

Kametani et al.⁹⁹⁻¹⁰¹ used Ullman's double reaction to synthesize some other derivatives in addition to melantheidine and they decomposed racemic melantheidine into its antipodes. Kametani's school also studied the enzymatic phenolic oxidation of this series of compounds.¹⁰⁰

Battersby^{14,58} and Šantavý et al.¹⁰² isolated the phenethyltetrahydroisoquinoline alkaloid autumnaline (= alkaloid CC-22) (XVa). The synthesis and the physico-chemical properties of this base and of its homologues were studied by Battersby,^{14,58,95,103,104} Kametani,⁹⁹ Brossi,^{105,106} and by DeAngelis.¹⁰⁷

Types (2) and (3) of the homopromorphinane group

There have been isolated 13 homopromorphinane alkaloids. They differ in the number of double bonds in the ring C, in the presence or absence of the methoxyl group of this ring, and in the substituents of the ring A. This group is subdivided into two subgroups:

The substances of the androcymbine group (XVI)

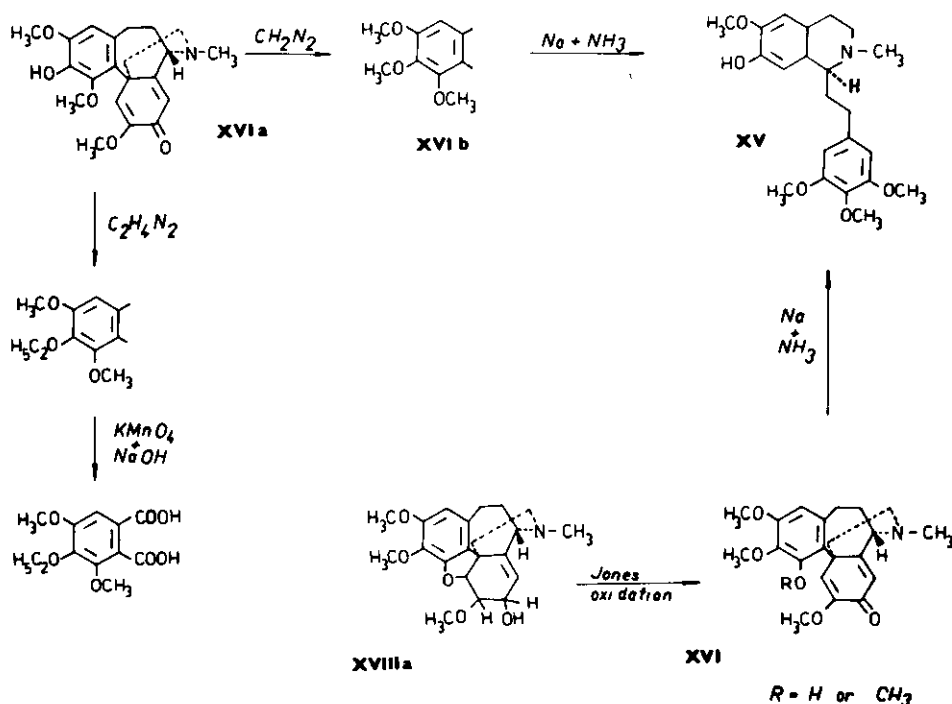
The constitution of androcymbine (XVIa) (Table D), which resembles that of the promorphinane alkaloid salutaridine, was elucidated^{103,108-112} by classical degradation (Scheme 3), spectroscopic and other physico-chemical methods.¹¹²

The substances of the dihydro- and tetrahydroandrocymbine group (XVII-XIX)

The first representative of this group is kreysiginine (XVIIIa) (Table E) which has an oxygen bridge between the rings A and C. Its constitution and the absolute configuration were elucidated by X-ray and ¹H-NMR analysis.^{109,117-121} The dihydro- and the tetrahydrohomopromorphinane alkaloids were converted¹⁰³ into bases of the androcymbine type by Jones's oxidation. The absolute S-configuration of kreysiginine at C₇ is identical with that of androcymbine (XVIa), szovitsidine (XVII), and colchicine alkaloids with tropolone ring.

The alkaloids of this group are a twin group of promorphinane and morphinane alkaloids^{92,93} with the difference that the homopromorphinane alkaloids have an additional CH₂-group in the ring B.

Kametani et al.^{115,116,127} studied the biogenetical synthesis of androcymbine



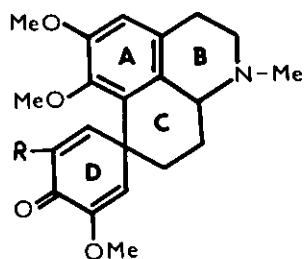
Scheme 3

and of some of its derivatives. Photolysis of 1-(2-bromo-4-hydroxy-3,5-dimethoxyphenethyl)-1,2,3,4-tetrahydro-7-hydroxy-6-methoxy-2-methylisoquinoline in the presence of sodium iodide gave racemic androcymbine (XVIa). When photolysis was carried out without sodium iodide, it afforded rac. multifloramine (XXIXc).¹²⁹

(4) Homoproaporphine alkaloids (XX-XXVIII)

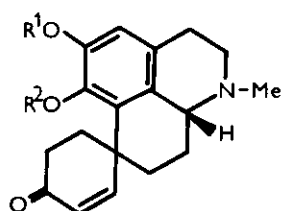
This group comprises several types of compounds (Table F). They differ in the number of double bonds in the ring D and consequently in the ultraviolet, infrared, and ¹H-NMR spectroscopic properties. When there is a keto group at the C₁₂ or C₁₃ atom of the ring D, it may form a cyclic half-acetal bridge with a phenolic group at C₁. The half-acetal hydroxyl can be free or etherified with a methyl group. Moreover, the double bond in the ring D can be in the cis- or the trans-configuration to the hydrogen at C_{6a}. The proaporphine alkaloids have similar properties.^{92,93} The mass spectra of all the proaporphine and homoproaporphine alkaloids exhibit^{109,126} the characteristic peaks M-1⁺ (100%) and M-43.¹⁶¹

Table F. (4) Homoproaporphine bases (XX-XXVIII)



XXa R=H Kreysiginone (Dienone I, m.p. 194° and Dienone II, m.p. 202° 104,119,122-124c,176

XXb R=OMe S-(+)-1-Hydroxy-12-methoxy-kreysiginone¹⁰⁵

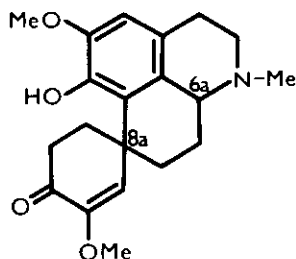


XXIIa R¹=Me; R²=H 6aR, 8aS-(+)-Bulbo-codine¹⁴⁴ (= (+)-Jolantamine = Alkaloid K-8)^{126,145}

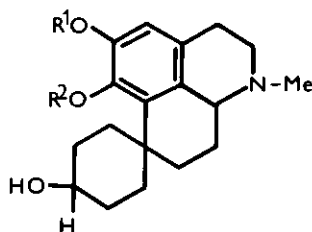
XXIIb R¹=R²=Me R-(+)-Krokiflorinone (= Alkaloid K-16)¹⁴⁶ (= Umtaline = Strumozine)^{111,130}

XXIIc Jolantine = Jolantaminemethohydroxide¹⁴⁷

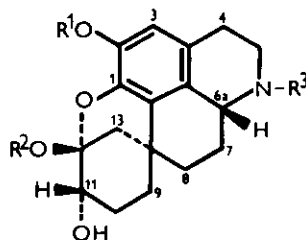
XXIIId Alkaloid OGG-3 ?^{111,148}



XXI Dihydrokreysiginone^{112,123,124b,142}



XXIII R¹=Me; R²=H R-(+)-Trigamine¹⁴⁹



XXIVa R¹=H; R²=R³=Me R-(+)-Kesselringine^{150,151}

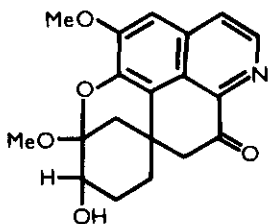
XXIVb R¹=R²=H; R³=Me S-(-)-Kesselridine (= Alkaloid K-10)¹⁵²

XXIVc R¹=R²=R³=Me R-(+)-Regeline (= Alkaloid K-15)¹⁵³

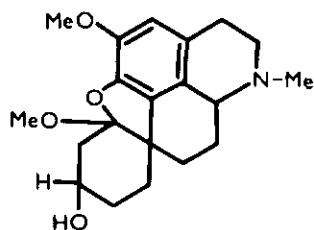
XXIVd R¹=R³=Me; R²=H R-(+)-Regelamine^{126,154}

S-(-)-Alkaloid G-2^{111,155}

XXIVe R¹=R³=H; R²=Me R-(+)-Luteine (= Alkaloid L-1)¹⁵⁶



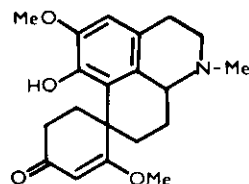
XXV Regelinone (= Alkaloid K-14)¹⁵⁷



XXVI (+)-Luteicine (= Alkaloid L-3)¹⁵⁸

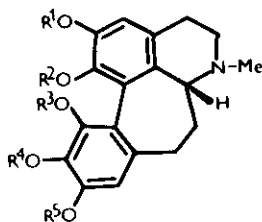


XXVII (+)-Jolantimine (= Luteinone)^{98,145}



XXVIII (-)-Luteidine (= Alkaloid L-2)^{8,135,135b}

Table G. (5) Homoaporphine alkaloids (XXIX)



XXIXa $R^1=R^3=R^4=R^5=Me; R^2=H$

$\sim$ R-(-)-Kreysigine (= Alkaloid CC-1)^{14,102,117,123,124,127c,144}

XXIXb $R^1=R^3=R^5=Me; R^2=R^4=H$

$\sim$ R-(-)-Floramultine (optical antipode S-(+)-Bechuanine) (= (+)-Merenderine)^{14,102,117,118,122,123,130-132,159}

XXIXc $R^1=R^3=R^4=Me; R^2=R^5=H$

$\sim$ R-(-)-Multifloramine^{14,105,122-124,129}

XXIXd $R^1=R^2=R^4=R^5=Me; R^3=H$

$\sim$ S-(+)-Szovitsamine¹³³

XXIXe $R^1=R^4=R^5=Me; R^2=R^3=H$

$\sim$ R-(-)-Alkaloid CC-24^{102,103}

XXIXf $R^1=R^3=H; R^2=R^4=R^5=Me$

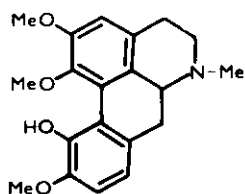
Szovitsinine¹⁶⁰

XXIXg $R^1=R^2=R^3=R^4=R^5=Me$

$\sim$ R-(-)-O-Methylkreysigine¹⁶¹

(5) Homoaporphine alkaloids (XXIX)

Kreysigia multiflora¹¹⁷ gave three alkaloids ((-)-kreysigine (XXIXa), (-)-floramultine (XXIXb), and O-methylkreysigine (XXIXg)), whereas Colchicum cornigerum¹⁰² the two alkaloids (alkaloids CC-1 (XXIXa) and CC-24 (XXIXe)) which belong to this group of compounds (Table G). The alkaloid bechuanine (optical antipode of floramultine) was isolated¹³⁰ from Iphigenia bechuanica, the alkaloid merenderine from Merendera raddeana,^{131,132} the alkaloid szovitsamine (XXIXd)¹³³ from Colchicum szovitsii, and the alkaloid isocorydine (XXX) from Camptorrhiza strumosa.¹³⁰ Isocorydine was derived from the benzyltetrahydroisoquinoline compound reticuline like the other alkaloids of the family Papaveraceae.^{92,93} These alkaloids can be converted into O-methylkreysigine (XXIXg) by methylation with diazomethane. It was found that on isolation or crystallization the alkaloids without tropolone ring are very easily racemized.



XXX

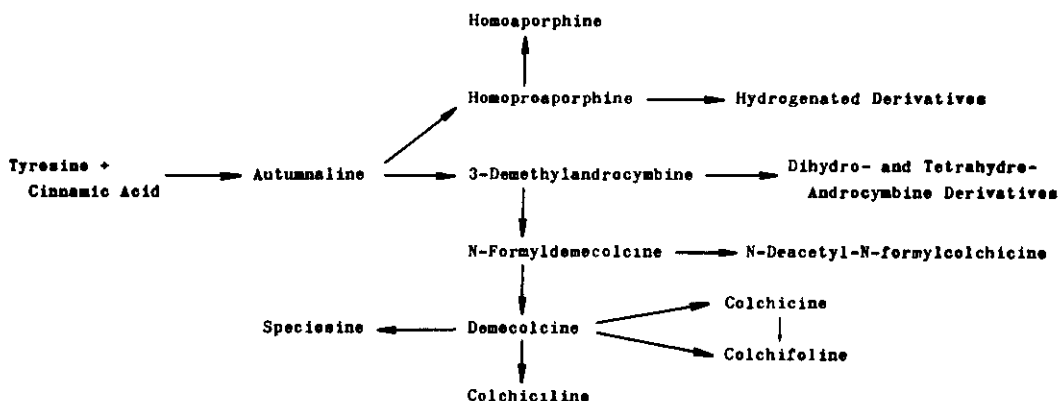
For the homoaporphine alkaloids see also papers.^{14,105,123,124,128,129,138-143,176}

Table H. Unclassified alkaloids without tropolone ring

Floramultinine ¹¹⁷	Alkaloid X-1	163
Alkaloid O ¹⁶²	Alkaloid CL-1	164
Alkaloid AM-4 ¹¹¹	Alkaloid CL-2	164
Alkaloid G-1 ¹⁵⁵	Alkaloid G-4	155
Crociflorine (Alkaloid K-2)	}	8,134-137
Regelinine (Alkaloid K-6)		
Regelidine (Alkaloid K-7)		
Crociflorinine (Alkaloid K-9)		
Crocifloridine (Alkaloid K-11)		

III. The biosynthesis of alkaloids with and without tropolone ring

Battersby et al.,^{165,166} Leete et al.,¹⁶⁷ Hill and Unrau,¹⁶⁸ and also Trozyan et al.¹⁶⁹ studied the biosynthesis of colchicine alkaloids and its minor derivatives by using labeled phenylalanine, tyrosine, cinnamic acid, methionine, and acetic acid. According to them the ring A and the carbon atoms 5, 6, 7 and 12 of colchicine (Ia) originate from phenylalanine (or tyrosine) and cinnamic acid. Radioactive acetic acid participates only in the formation of the acetamido group.^{169b} Battersby et al.¹⁷⁰⁻¹⁷⁵ found that widening of the benzene ring A of phenethyltetrahydroisoquinoline (autumnaline (XVa)) gave rise to a tropolone ring, and phenolic oxidation to a linkage between the rings A and C of colchicine. The intermediate step of the biosynthesis of colchicine was formed by the alkaloids of androcymbine type (XVI). Consequently, autumnaline is the basic compound for the biosynthesis of homomorphinan (XVI) and tropolone alkaloids (I-V) and, moreover, for the homoproaporphines (XX-XXVIII) and homoaporphines (XXIX)^{104,123} (Scheme 4).



Developmental series of phenethyltetrahydroisoquinoline (autumnaline) alkaloids

Scheme 4

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