CHAPTER II

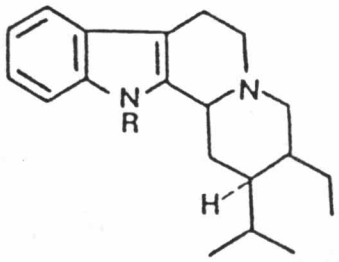
THE ALKALOIDS OF STRYCHNOS SPECIES

Classification of Strychnos Alkaloids

The majority of the isolated alkaloids from Strychnos species belongs to the group of Terpenoid indole alkaloids. A basis for the classification of the indole alkaloids is proposed by Kompis et al.(27) and Kisakurek and Hesse (28). The alkaloids can be divided into 8 types according to their characteristic skeletons. These types are (Figure 4) Corynanthean (C-type),Vincosan (D-type), Vallesiachotaman (V-type), Strychnan (S-type), Aspidospermatan (A-type), Plumeran (P-type), Eburnan (E-type) and Ibogan (J-type). In addition, the combination between the two units of the same or the different indole alkaloid types would generate the bisindole alkaloid skeletons.

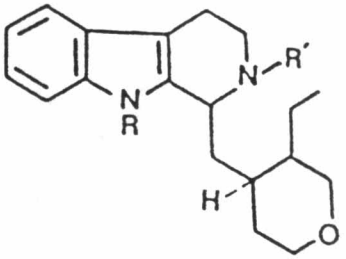
The indole alkaloids belonging to the Strychnos species are comprised with 5 types of alkaloids, they are the C-, D-, V-, S- and A-types. The most abundant alkaloids in the genus are of the S-type and the lesser ones are of the C-type (2).

Figure 4 The Indole alkaloids skeletons



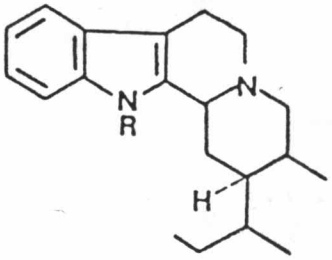
Corynanthean

(C-type)



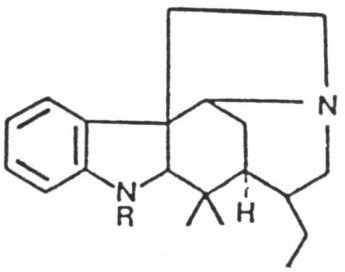
Vincosan

(D-type)



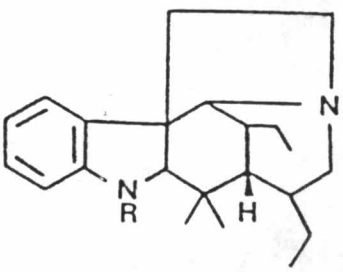
Vallesiachotaman

(V-type)



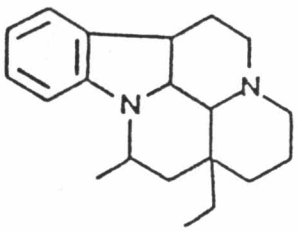
Strychnan

(S-type)



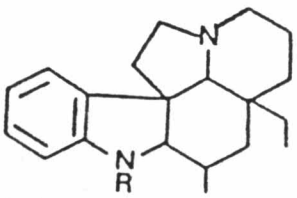
Aspidospermatan

(A-type)



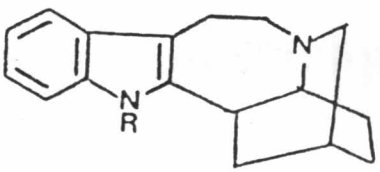
Eburnan

(E-type)



Plumeran

(P-type)



Ibogan

(J-type)

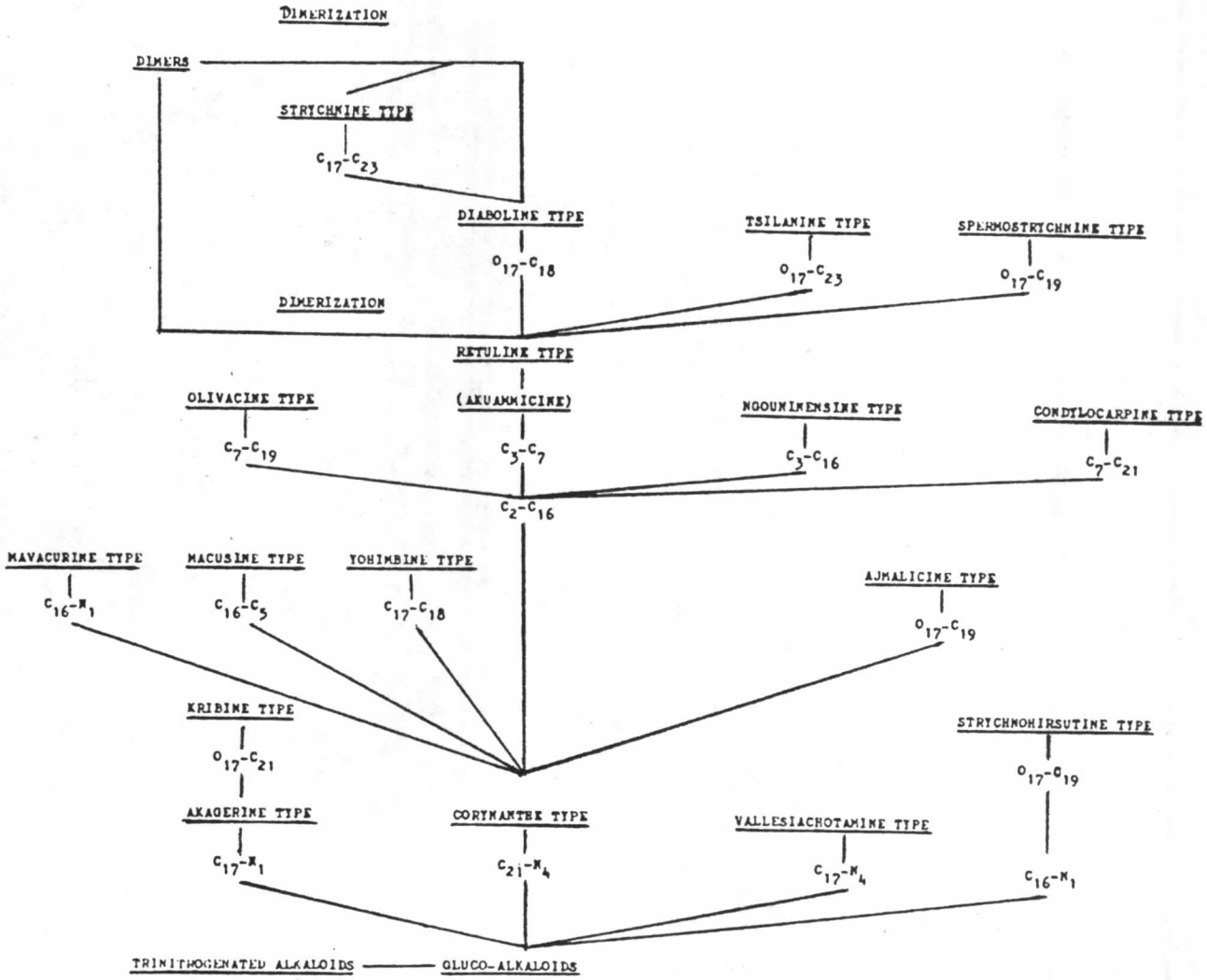


Figure 5 Biogenetic classification of Strychnos alkaloid (5,29)

Ohiri et al. (5) on dealt with African Strychnos species subclassified Strychnos alkaloids into groups corresponding to the Coune proposal (29). This biogenetic classification (See Figure 5 page 20)is set out for arranging Strychnos alkaloids according to the sites of bond migrations and the sites of ring formation of the various metabolic products during the processes of the biosynthesis leading to the individual skeletons.

According to the above classifications (2,5,29) Strychnos alkaloids could be arranged into 2 main classes; monomeric indole alkaloids and bisindole alkaloids. Furthermore, monomeric indole alkaloids are subdivided into 6 types, five of which can be cleary differentiated while the rest is put in the miscellaneous alkaloids (M-type) (See Table 2 page 22). Bisindole alkaloids which including the various combination products of monomeric indole alkaloids are subdivided into 2 types, there are symmetric bisindole alkaloids of the Strychnan-Strychnan type (S-S type) and asymmetric bisindole alkaloids of Strychnan-Corynanthean (S-C type). All types of Strychnos alkaloids (as shown in Table 2) are further subdivided into two or more groups which are designed especially for the alkaloids of this genus. Basing on this division, it is hoped to give a more information covering their chemotaxonomic significant.

Table 2

Subdivision of the Main Types of Strychnos Alkaloids

Class	Subdivision
Class 1 Monomeric indole alkaloids	
Type 1 Corynanthean (C-type)	
	Group C_1 : E-seco indole group
	Group C_2 : Ajmalicine group
	Group C_3 : Yohimbine group
	Group C_4 : Akagerine group
	Group C_5 : Mavacurine group
	Group C_6 : Sarpagine group
	Group C_7 : Oxindole group
Type 2 Vincosan (D-type)	
	Group D_1 : Strictosidine group
	Group D_2 : Decussine group
Type 3 Vallesiachotaman (V-type)	
	Group V_1 : Antirhine group
	Group V_2 : Angustine group
Type 4 Strychnan (S-type)	
	Group S_1 : Retuline group
	Group S_2 : Diaboline group
	Group S_3 : Isostrychnine group

Table 2 (continued)

Class	Subdivision
Type 4 (continued)	
	Group S_4 : Strychnine group
	Group S_5 : Spermostrychnine group
	Group S_6 : Tsilanine group
Type 5	Aspidospermatan (A-type)
	Group A_1 : Condylocarpine group
Type 6	Miscellaneous (M-type)
	Group M_1 : Ngouniensine group
	Group M_2 : Olivacine group
Class 2	Bisindole alkaloids
Type 1	Strychnan - Strychnan (S-S type)
	Group B_1 : Retuline-Retuline (S_1 - S_1) group
	Group B_2 : Diaboline-Diaboline (S_2 - S_2) group

Table 2 (continued)

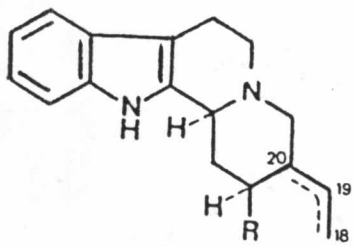
Class	Subdivision
Type 1 (continued)	
	Group B_3 : Retuline-Diaboline
	$(S_1 - S_2)$ group
	Group B_4 : Isostrychnine-Isostrychnine
	$(S_3 - S_3)$ group
Type 2	Strychnan - Corynanthean (S-C type)
	Group B_5 : Diaboline - E-seco indole
	$(S_2 - C_1)$ group

Various skeletons of Strychnos alkaloids together with their representatives are listed as follows (see also Table 2).

Class 1 Monomeric indole alkaloids

Type 1 Corynanthean type

Group C (E-seco indole)
1



Geissoschizine and others

1 Geissoschizine

(R = $-C(CO\ CH_3)=CHOH$; △ 19,20)

2 De-carbomethoxy-geissoschizine

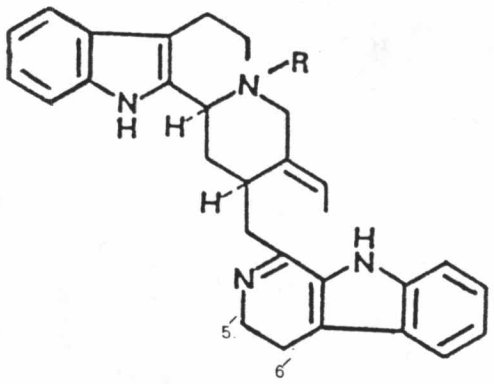
(R = $-CH=CHOH$; △ 19,20)

3 Geissoschizal

(R = $-CH_2-CHO$; △ 19,20)

4 Normelinonine B

(R = $-CH_2-CH_2OH$; △ 18,19)



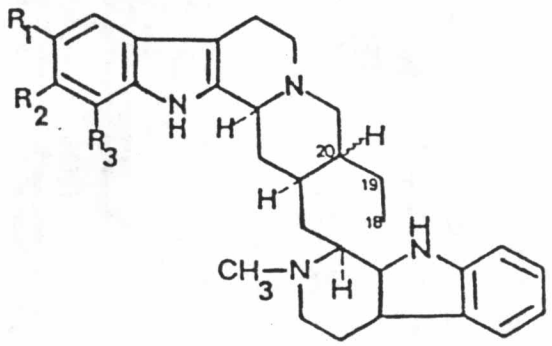
Usambarensine and other

5 Usambarensine

(R = H ; Δ 5′,6′)

6 N$_b$-Methyl-usambarensine

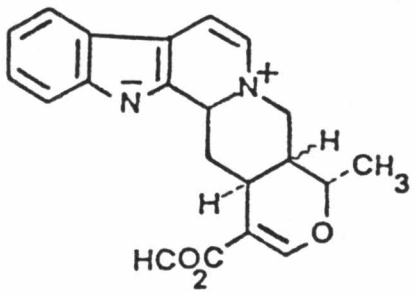
(R = CH$_3$; Δ 5′,6′)



7 Usambarine

(R$_1$ = R$_2$ = R$_3$ = H ; 20-β-H ; Δ18,19)

Group C_2 (Ajmalicine)



Ajmalicine and others

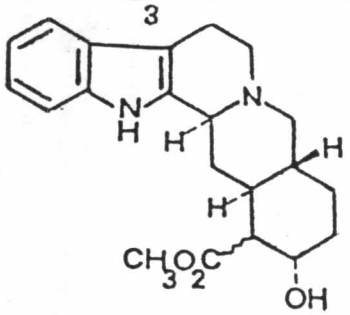
8 Alstonine

(20- α -H)

9 Serpentine

(20- β -H)

Group C_3 (Yohimbine)



Yohimbine and others

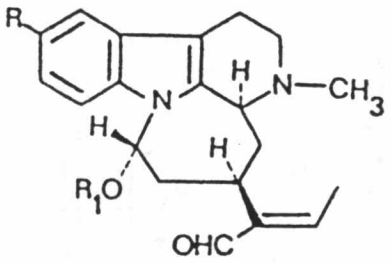
10 α -Yohimbine

(16- α -$COOCH_3$)

11 β -Yohimbine

(16- β -$COOCH_3$)

Group C (Akagerine)
4



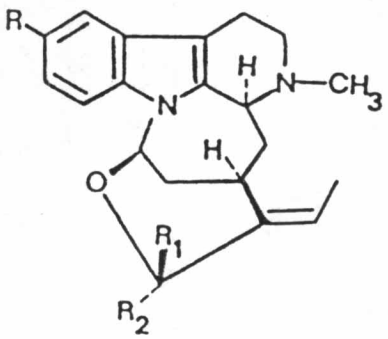
Akagerine and others

12 Akagerine

(R = R = H)
1

13 17-O-Methyl-akagerine

(R = H, R = CH)
1 3



Kribine and others

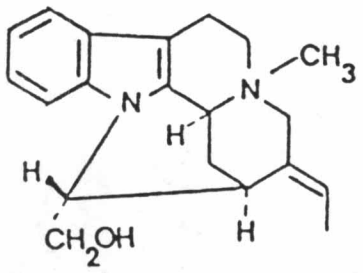
14 Kribine

(R =R = H ; R = OH)
2 1

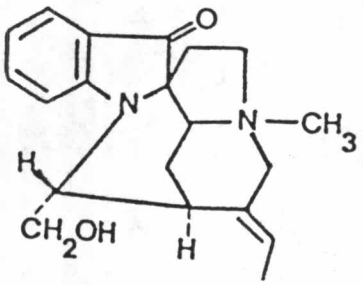
15 21-O-Methyl-kribine

(R = R = H ; R = OCH)
2 1 3

Group C (Mavacurine)



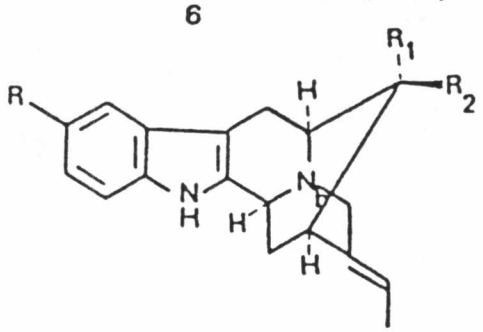
16 Mavacurine



17 C-Fluorocurine

(Pseudoindoxyl-mavacurine)

Group C (Sarpagine)
6



Sarpagine and others

18 Sarpagine

(R_1 = OH, R_2 = H, R_3 = CH_2OH)

19 Macusine B

(R_1 = R_2 = H, R_3 = CH_2OH; $\underline{N}^+_b$ - CH_3)

20 Normacusine B

(R_1 = R_2 = H, R_3 = CH_2OH)

21 O-Methylmacusine B

(R_1 = R_2 = H, R_3 = CH_2OCH_3; $\underline{N}^+_b$ - CH_3)

22 16-Epi-O-methyl macusine B

(R_2 = R_1 = H, R_3 = CH_2OCH_3; $\underline{N}^+_b$ - CH_3)

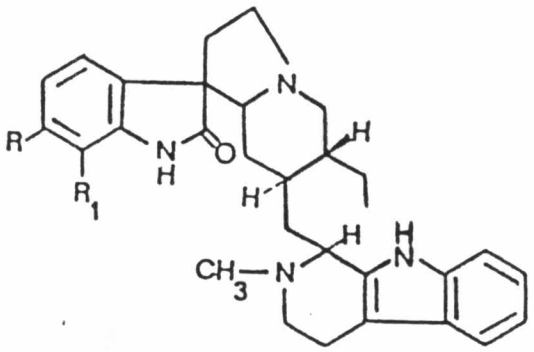
23 Akuammidine

(R_1 = H, R_2 = CH_2OH, R_3 = CO_2CH_3)

24 Polyneuridine

(R_1 = H, R_2 = CO_2CH_3, R_3 = CH_2OH)

Group C (Oxindole)
7



Strychnofoline and others

25 Strychnofoline

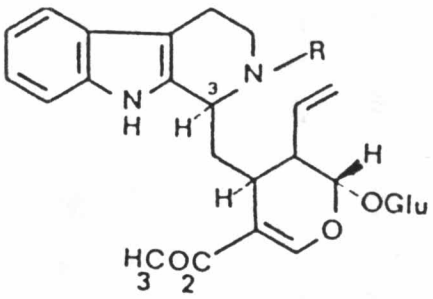
(R = OH, R = H ; Δ 18,19)
1

26 Oxindole I 7R

(R = R = H ; 19R)
1

Type 2 Vincosan (D-type)

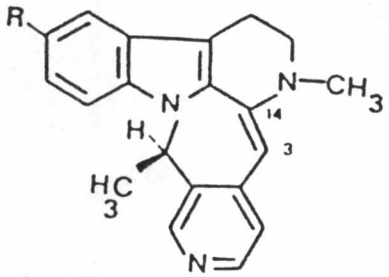
Group D_1 (Strictosidine)



27 Dolichantoside

(R = CH_3 ; 3-α-H)

Group D_2 (Decussine)



Decussine and others

28 Decussine

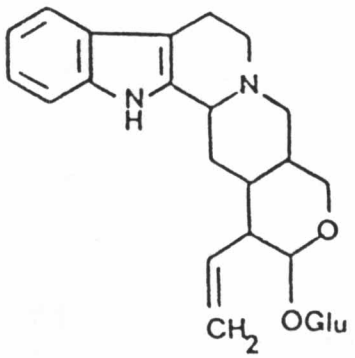
(R = H)

29 3,14-Dihydro-decussine

(R = H ; 3,14-dihydro)

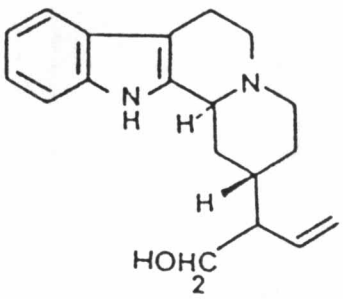
Type 3 Vallesiachotaman (V-type)

Group V_1 (Gluco alkaloids)



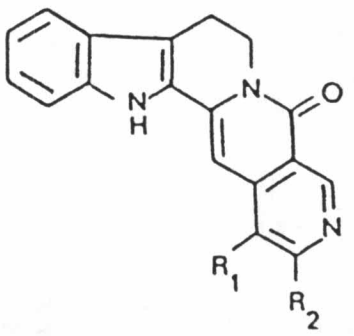
30 Strychnos decussata glucoalkaloid

Group V_2 (Antirhine)



31 Antirhine

Group V (Angustine)
3



Angustine and others

32 Angustine

(R_1 = H, R_2 = $-CH=CH_2$)

33 Angustidine

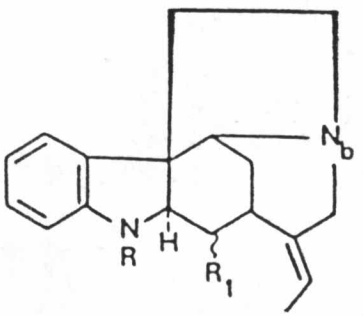
(R_1 = CH_3, R_2 = H)

34 Angustoline

(R_1 = H, R_2 = $-CH(OH)-CH_3$)

Type 4 Strychnan (S-type)

Group S$_1$ (Retuline)



normal series

35 Retuline

(R = COCH$_3$, R$_1$ = α-CH$_2$OH)

36 Isoretuline

(R = COCH$_3$, R$_1$ = β-CH$_2$OH)

37 Acetyl-reluline

(R = COCH$_3$, R$_1$ = α-CH$_2$-OCOCH$_3$)

38 Retuline N-oxide

(R = COCH$_3$, R$_1$ = β-CH$_2$OH; N$_b$ → O)

39 Akaummicine

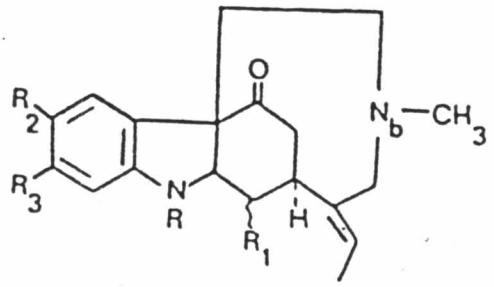
(R = H , R$_1$ = CO CH$_2$ CH$_3$)

40 18-Desoxy-Wieland-Gumlich aldehyde

(R = H ; R$_1$ = CHO ; Δ 2,16 ; 19,20-dihydro)

41 Fluorocurarine

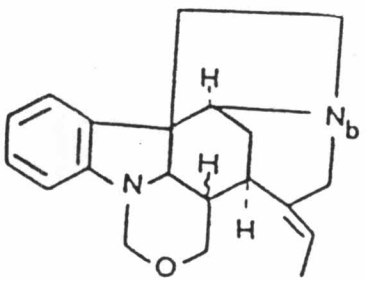
(R = H, R$_1$ = CHO; Δ 2,16 ; $\overset{+}{N}_b$-CH$_3$)



$\underline{N}_b$-methyl-<u>sec</u>-pseudo series

<u>42</u> Strychnosilidine

($R_2 = R_3 = OCH_3$, $R_1 = \alpha$-$CH_2CO_2CH_3$, $R = COCH_3$)



Rosibiline and isomer

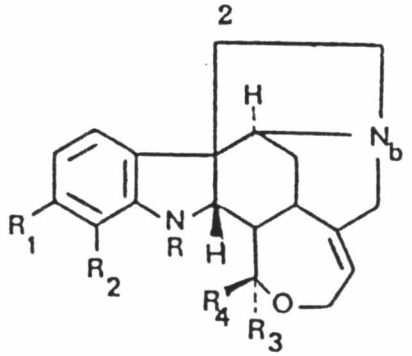
<u>43</u> Rosibiline

(16-β-H)

<u>44</u> Isorosibiline

(16-α-H)

Group S (Diaboline)



Diaboline and others

45 Wieland-Gumlich aldehyde (WGA)

($R_1 = R_2 = R_3 = R_4 = H$, R = OH)

46 Condensamine

(R_3 = COCH, R_1 = OCH, $R_2 = R_4 = H$, R_3 = -OCOCH)

47 Diaboline

(R_3 = COCH, $R_1 = R_2 = R_3 = H$, R_4 = OH)

48 Ethyldiaboline (Diaboline ethyl ether)

48a (R_3 = COCH, $R_1 = R_2 = R_3 = H$, R_4 = 17- α -OEt)

48b (R_3 = COCH, $R_1 = R_2 = R_4 = H$, R_3 = 17- β -OEt)

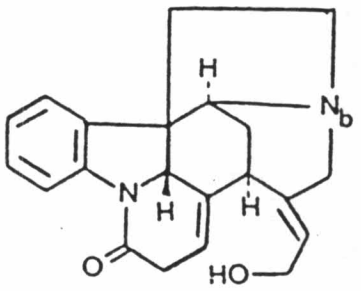
49 11-Methoxydiaboline

(R_3 = COCH, R_1 = OCH, $R_2 = R_3 = H$, R_4 = OH)

50 O-Acetyl diaboline

(R_3 = COCH, $R_1 = R_2 = R_3 = H$, R_4 = -OCOCH)

Group S$_3$ (Isostrychnine)



Isostrychnine and others

51 Isostrychnine

(Δ 19,20)

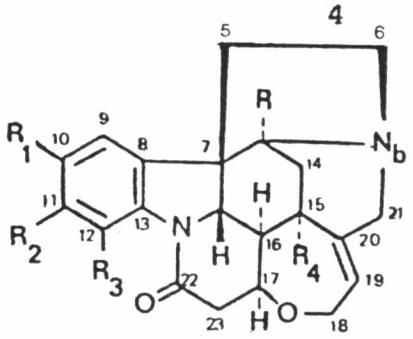
52 19,20-Dihydroisostrychnine

(19,20 dihydro)

53 Protostrychnine

(16-α- , 17-β-dihydro, 17-β-OH)

Group S (Strychine)



[N→O] = N-oxide series

3- α -H = normal series

3-α-OH = pseudo series

normal and pseudo series

54 Strychnine

(R = R = R = R = R = H)
1 2 3 4

55 Brucine

(R =R = R = H , R = R = OCH)
3 4 1 2 3

56 α-Colubrine

(R = R = R = R = H, R = OCH)
1 3 4 2 3

57 β-Colubrine

(R = R = R = R = H, R = OCH)
2 3 4 1 3

58 10-Hydroxystrychnine

(R = R = R = R = H, R = OH)
2 3 4 1

59 12-Hydroxystrychnine

(R = R = R = R = H, R = OH)
1 2 4 3

60 15-Hydroxystrychnine

(R = R = R = R = H, R = OH)
1 2 3 4

61 12-Hydroxy-11-methoxystrychnine

(R = R = R = H,R = OCH , R = OH)
1 4 2 3 3

62 Strychnine N-oxide

($R_1 = R_2 = R_3 = R_4 = H$; $N_b \rightarrow O$)

63 12-Hydroxystrychnine N-oxide

($R_1 = R_2 = R_4 = H$, $R_3 = OH$; $N_b \rightarrow O$)

64 Brucine N-oxide

($R_3 = R_4 = H$, $R_1 = R_2 = OCH_3$; $N_b \rightarrow O$)

65 Pseudostrychnine

($R = OH$, $R_1 = R_2 = R_3 = R_4 = H$)

66 Pseudobrucine

($R = OH$, $R_1 = R_2 = OCH_3$, $R_3 = R_4 = H$)

67 N-Methylstrychninium

($R_1 = R_2 = R_3 = R_4 = H$; $N_b^+ - CH_3$)

68 3,12-Dihydroxystrychnine

($R_3 = OH$, $R_1 = R_2 = R_4 = H$)

69 3,12-Dihydroxy-11-methoxy strychnine

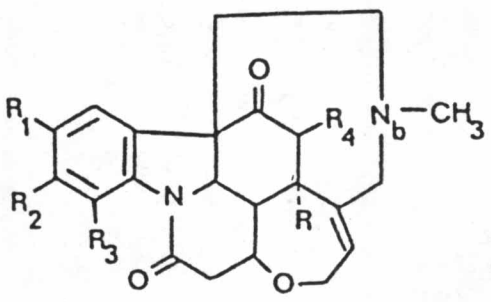
($R_3 = OH$, $R_1 = R_4 = H$, $R_2 = OCH_3$)

70 Pseudo-α-colubrine

($R = OH$, $R_1 = R_3 = R_4 = H$, $R_2 = OCH_3$)

71 Pseudo-β-colubrine

($R = OH$, $R_1 = OCH_3$, $R_3 = R_2 = R_3 = R_4 = H$)



[$\underset{b}{N}$ - CN] = $\underset{b}{N}$ -cyano series

N-methyl-sec-pseudo series (3 keto-group)

72 Icajine

($R_1 = R_2 = R_3 = R_4 = H$)

73 Novacine

($R_3 = R_4 = H$, $R_1 = R_2 = OCH_3$)

74 Vomicine

($R_1 = R_2 = R_4 = H$, $R_3 = OH$)

75 14-Hydroxyicajine

($R_1 = R_2 = R_3 = H$, $R_4 = OH$)

76 14-Hydroxynovacine

($R_3 = H$, $R_1 = R_2 = OCH_3$, $R_4 = OH$)

77 15-Hydroxyicajine

($R_1 = OH$, $R_2 = R_3 = R_4 = H$)

78 15-Hydroxy novacine

($R_1 = OH$, $R_2 = R_3 = OCH_3$, $R_4 = H$)

79 11-Methoxyicajine

($R_1 = R_3 = R_4 = H$, $R_2 = OCH_3$)

80 N-Methyl-sec-pseudo-β-colubrine

($R_2 = R_3 = R_4 = H$, $R_1 = OCH_3$)

81 Icajine N-oxide

($R_1 = R_2 = R_3 = R_4 = H$, $N_b \rightarrow O$)

82 12-Hydroxy-11-methoxy-N-methyl-sec-pseudostrychnine

($R_1 = R_4 = H$, $R_2 = OCH_3$, $R_3 = OH$)

83 N-cyano-sec-pseudo-colubrine

($R_2 = R_3 = H$, $R_1 = OCH_3$; N_b-CN), or

($R_1 = R_3 = H$, $R_2 = OCH_3$; N_b-CN)

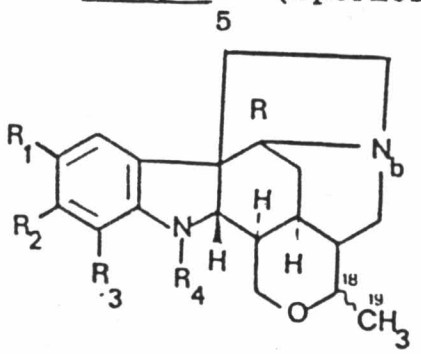
84 N-cyano-sec-pseudostrychnine

($R_1 = R_2 = R_3 = H$; N_b-CN)

85 N-cyano-sec-pseudobrucine

($R_3 = R_4 = H$, $R_1 = R_2 = OCH_3$; N_b-CN)

Group S (Spermostrychnine)



normal and pseudo series

86 Spermostrychnine

($R_1 = R_2 = R_3 = H$, $R_4 = COCH_3$; 18-β-CH_3)

87 Strychnospermine

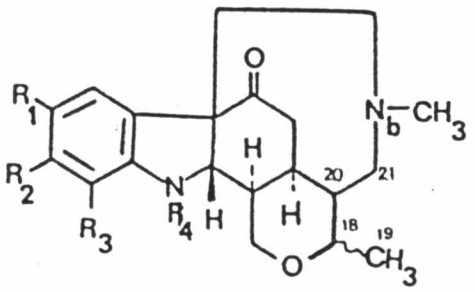
($R_1 = R_2 = H$, $R_3 = OCH_3$, $R_4 = COCH_3$; 18-β-CH_3)

88 Strychnosplendine

($R_1 = OH$, $R_2 = R_3 = R_4 = H$; 18-β-CH_3)

89 Isostrychnosplendine

($R_1 = OH$, $R_2 = R_3 = R_4 = H$; 18-α-CH_3)



N-methyl-sec-pseudo series

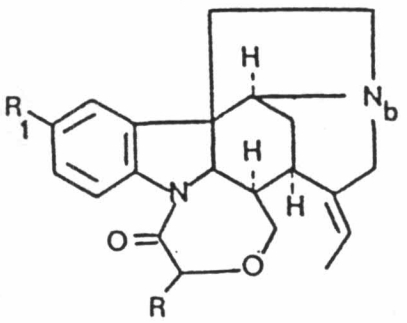
90 Strychnofendlerine

($R_1 = R_2 = R_3 = R_4 = H$; 18- β -CH_3)

91 Strychnobrasiline

($R_1 = R_2 = R_3 = R_4 = H$; 18- β -CH_3 ; Δ 20,21)

Group S (Tsilanine)
6



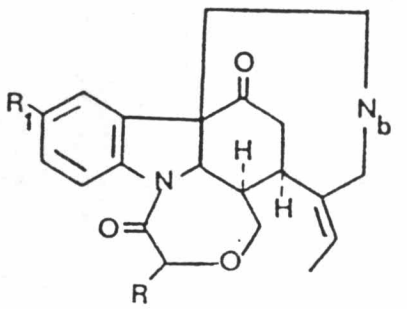
normal series

92 Tsilanine

(R = OCH , R = H)
3 1

93 10-Methoxytsilanine

(R = R = OCH)
1 3



N-methyl-sec-pseudo series

94 Holstiine

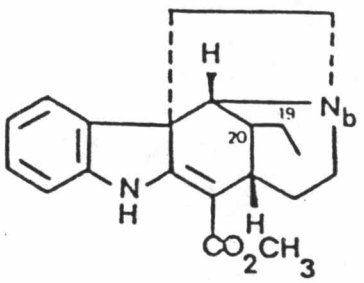
(R = OH, R = H)
1

95 Rindline

(R = R = OCH)
1 3

Type 5 Aspidospermatan (A-type)

Group A (Condylocarpine)
1



Condylocarpine and others

96 Condylocarpine

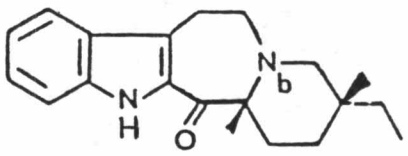
(△ 19,20)

97 Tubotaiwine

(19,20 dihydro)

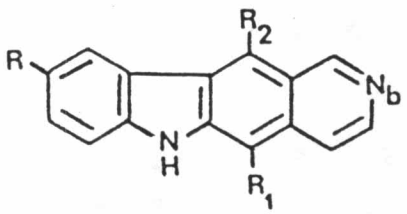
Type 6 Miscellaneous (M-type)

Group M_1 (Ngouniensine)



98 Ngouniensine

Group M_2 (Olivacine)



Ellipticine and Others

99 Ellipticine

($R = H$, $R_1 = R_2 = CH_3$)

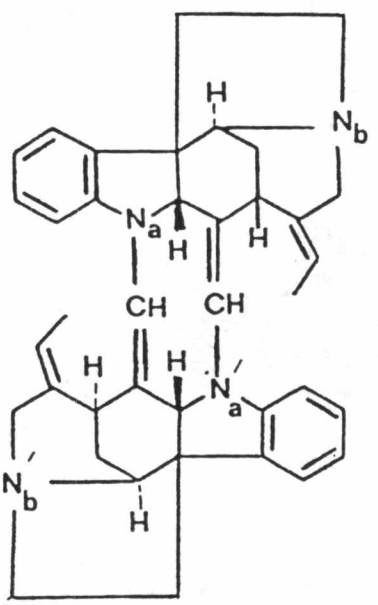
100 Ellipticine N_b-oxide

($R = H$, $R_2 = R_3 = CH_3$, $N_b \rightarrow O$)

Class II Bisindole alkaloids

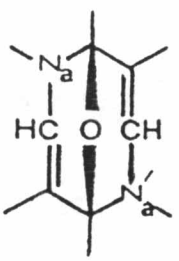
Type 1 Strychnan - Strychnan (S-S type)

Group B (Retuline-Retuline) (S - S)

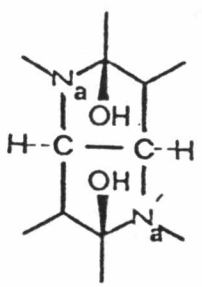


Dihydrotoxiferine and derivatives (101-105)

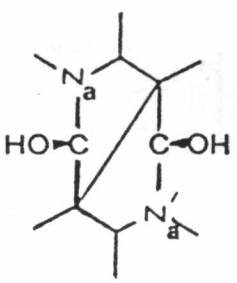
Only the part indicating the difference among the representatives alkaloids (106 - 110) will be shown here



C-Curarine and derivatives (106-108)

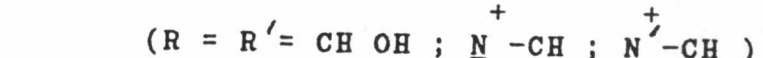


C-Calebassine (109)

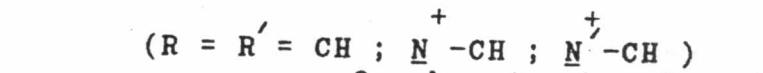


Bisnor-C-Alkaloid D (110)

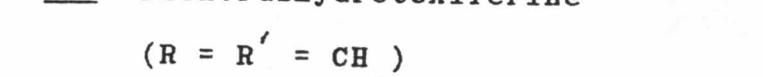
101 Toxiferine



102 Dihydrotoxiferine



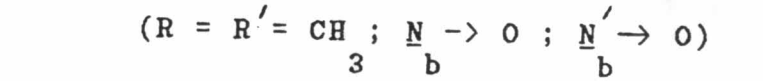
103 Bisnordihydrotoxiferine



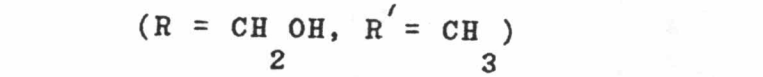
104 Bisnordihydrotoxiferine

di $\underset{b}{N}$ -oxide

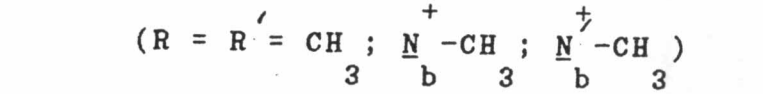
105 Bisnor-C-alkaloid H



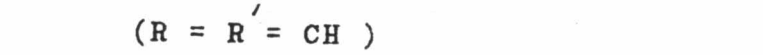
106 C-Curarine



107 Bisnor-C-Curarine

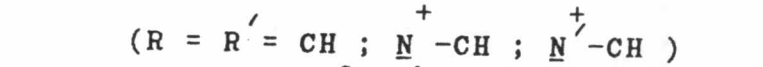


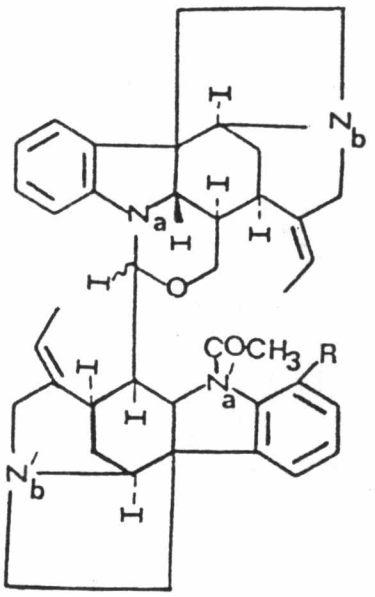
108 C-alkaloid E



109 C-Calebassine

110 Bisnor-C-alkaloid D





Strychnobiline and others (111-112)

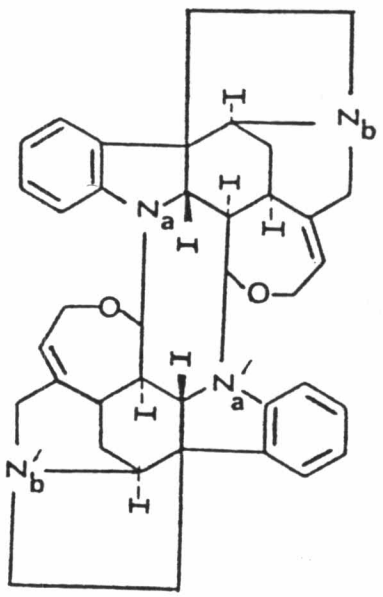
111 Strychnobiline

(R = H, 17 - β - H)

112 Isostrychnobiline

(R = H, 17 - α - H)

Group B (Diaboline-Diaboline) (S_2 - S_2)



Caracurine and others

113 Caracurine V

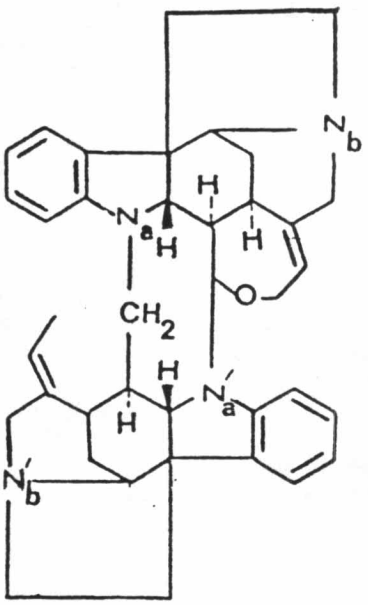
114 Caracurine V mono N-oxide

($N_b \rightarrow O$)

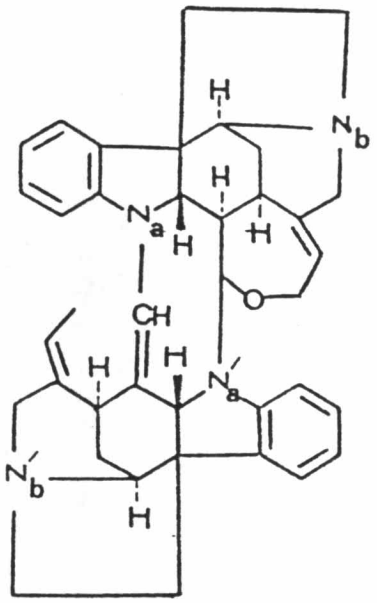
115 Caracurine V di N-oxide

($N_b \rightarrow O$, $N_b' \rightarrow O$)

Group B (Retuline-Diaboline) (S_1-S_2)
3



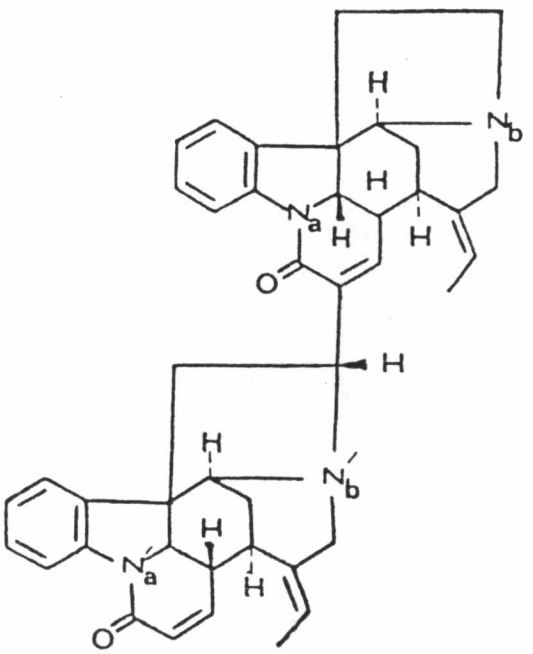
116 Dolichocurine



117 Dolichothyrine

Group B (Isostrychnine-Isostrychine)
4

(S_3 - S_3)

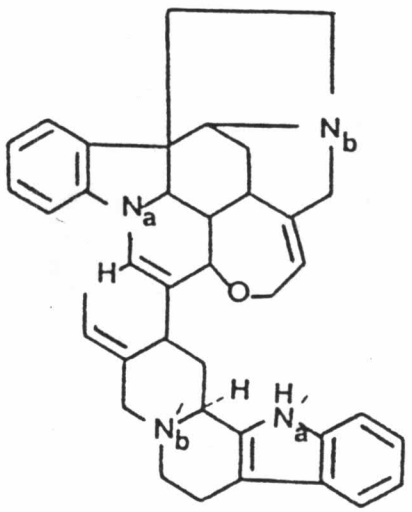


118 Sungucine

Type 2 Strychnan - Corynanthean (S - C type)

Group B (Diaboline - E-seco indole)

(S - C 5 2 1)



119 Longicaudatine

Alkaloids of Thai Strychnos species

The chemical investigations of various Strychnos species known to occur in Thailand have been carries out. The alkaloid contents of those species are summarized in Table 3, page 55.

In Table 3, the isolated alkaloids are arranged according to the biogenetic classifications which have been set out in Table 2. The parts of plants from which the alkaloids have been isolated together with the appropriate literature references are also presented.

Table 3

Lists of alkaloids of Strychnos species growing in Thailand

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
Section I : Strychnos				
S. ignatii Berg.	fr, l	Diaboline 47	S_2	30,31
	l,peri,rb,rw, s,sb,tw	Brucine 55	S_4	20,32
	l,s,sb,tw	Brucine N-oxide 64	S_4	20,32
	l,s	α-Colubrine 56	S_4	20
	l,s	β-Colubrine 57	S_4	20
	sb	N-cyano-sec-pseudo brucine 85	S_4	32,33
	sb	N-cyano-sec-pseudo colubrine 83	S_4	32,33
	sb	N-cyano-sec-pseudo strychnine 84	S_4	32,33
	l,peri,s,tw	Icajine 72	S_4	20
	l,s	12-Hydroxystrychnine 59	S_4	20
	l,peri,s,tw	Novacine 74	S_4	20
	l,peri,s,sb, tw	Pseudobrucine 66	S_4	20,32

Table 3 (continued)

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S.ignatii (continued)	l,peri,s,sb, rb,rw,tw	Pseudostrychnine 65	S 4	20,32
	fr,l,peri,rb, rw,s,sb,tw	Strychnine 54	S 4	20,31, 32
	l,s,rb,rw,sb	Strychnine N-oxide 62	S 4	20,32
	l,peri,s,tw	Vomicine 74	S 4	20
	rb	Longicaudatine 119	B 5	34,35
S.lucida R.Br.	sb	Akuammidine 23	C 6	34
	br,l,rb,sb	Normacusine B 20	C 6	20,34
	l	Sarpagine 18	C 6	20
	br,fr,l,s,sb	Diaboline 47	S 2	20,34
	sb	Ethyldiaboline 48	S 2	34
	br,fr,l,peri, rb,s,sb,tw	Brucine 55	S 4	20,30, 34
	br,l,peri,s, sb,tw	Brucine N-oxide 64	S 4	20,34
	fr,s,sb	α-Colubrine 56	S 4	20,34
	fr,l,rb,s,sb	β-Colubrine 57	S 4	34
	l,tw	Icajine 72	S 4	20
	fr,l,peri,s, tw	Novacine 73	S 4	20

Table 3 (continued)

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S. lucida (continued)	br,fr,l,rb, sb,tw	Pseudobrucine 66	S 4	20,34
	l	Pseudostrychnine 65	S 4	34
	br,l,rb,sb	Strychnine 54	S 4	20,30, 34
	l,peri,s,tw	Strychnine N-oxide 62	S 4	20
	rb	Longicaudatine 119	B 5	34,35
S. nux-blanda A.W.Hill	unknown	Diaboline 47	S 2	30
	l,s	Brucine 55	S 4	20
	l	Brucine N-oxide 64	S 4	20
	l	Icajine 72	S 4	20
	l	Novacine 73	S 4	20
	l,s	Pseudobrucine 66	S 4	20
	l,s	Strychnine 54	S 4	20
	l,s	Strychnine N-oxide 62	S 4	20
	l	Vomicine 74	S 4	20
S. nux-vomica Linn.	Ys	Decarbomethoxy-geissoschizine 2	C 1	36,37
	Ys	Geissoschizal 3	C 1	36,37
	Ys	Geissoschizine 1	C 1	36,37

Table 3 (continued)

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S.nux-vomica	rb	Normelinonine B 4	C 1	37,38
(continued)	rb	C-Mavacurine 16	C 5	31,39
	rb	16-Epi-O-methyl macusine B 22	C 6	36,38
	rb	O-methylmacusine B 21	C 6	36,38
	l,rb	Normacusine B 20	C 6	36,38, 40
	Ys	Wieland-Gumlich aldehyde 45	S 2	37
	l	19,20-Dihydro-isostrychnine 52	S 3	38
	l,rb,s,Ys	Isostrychnine 51	S 3	37,38, 40,42
	rb	Protostrychnine 53	S 3	38,40
	b,fr,l,peri, rb,rw,s,sb, sw	Brucine 55	S 4	38,39, 40,41, 43
	b,fr,l,peri, rb,rw,s	Brucine N-oxide 64	S 4	20,38, 41
	b,peri,s	α-Colubrine 56	S 4	20,41
	b,peri,rb,s	β-Colubrine 57	S 4	20,38,41
	l	3,12-Dihydroxy-11-methoxystrychnine 69	S 4	38

Table 3 (continued)

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S. nux-vomica (countinued)	l	3,12-Dihydroxy-strychnine 68	S 4	38
	l,rb	10-Hydroxystrychnine 58	S 4	38
	b,fr,l,peri, rb,s	12-Hydroxystrychnine 59	S 4	20,38, 40,41
	l	12-Hydroxystrychnine N-oxide 63	S 4	38
	l,rb	12-Hydroxy-11-methoxy strychnine 61	S 4	38,40
	s	15-Hydroxystrychnine 60	S 4	44
	b,fr,l,peri, s	Icajine 72	S 4	20,41, 43
	peri	N-Methyl-sec-pseudo - β -colubrine 80	S 4	41
	s	11-Methoxyicajine 79	S 4	45
	b,fr,l,peri, s	Novacine 73	S 4	20,41, 43
	b,fr,l,peri, rb,rw,s,sb, sw	Pseudobrucine 66	S 4	20,38, 41

Table 3 (continued)

Plants	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S.nux-vomica (continued)	s	Pseudo- α-colubrine 70	S 4	30,42
	s	Pseudo- β-colubrine 71	S 4	30,42
	b,fr,l,peri, rb,rw,s,sb, sw	Pseudostrychnine 65	S 4	20,38, 41
	b,fr,l,peri, rb,rw,s,sb, sw	Strychnine 54	S 4	20,31, 38,39, 41,43
	b,fr,l,peri, rb,rw,s,sb, sw	Strychnine N-oxide 62	S 4	20,38, 41
	b,fr,l,peri, s	Vomicine 74	S 4	20,38, 39,41, 46
	Ys	Condylocarpine 96	A 1	37
S.rupicola Pierre ex Dop	l	Angustidine 33	V 3	20
	l	Angustine 32	V 3	20
	l	Angustoline 34	V 3	20
	s	Brucine 55	S 4	20

Table 3 (continued)

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S.rupicola (continued)	s	Brucine N-oxide 64	S_4	20
	s	Icajine 72	S_4	20
	s	Strychnine 54	S_4	20
	s	Novacine 73	S_4	20
S.wallichiana Steud. ex DC.	l	Angustidine 33	V_3	20
	l	Angustine 32	V_3	20
	l	Angustoline 34	V_3	20
	rb	Condensamine 46	S_2	47
	rb	11-Methoxydiaboline 49	S_2	47
	br,l,r,rb, rw,s,sb, sm br,sw	Brucine 55	S_4	20,48, 49
	l,s	Brucine N-oxide 64	S_4	20,48, 49
	s	α-Colubrine 56	S_4	20,49
	s	β-Colubrine 57	S_4	20,49
	l	N-Cyano-sec-pseudo brucine 77	S_4	20,33, 48
	l	N-Cyano-sec-pseudo strychnine 78	S_4	20,33, 48

Table 3 (continued)

Plant	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S.wallichiana (continued)	l,r,s,st	12-Hydroxystrychnine 59	S 4	48,49
	l,s	12-Hydroxy-11-methoxy -N-methyl-sec-pseudo strychnine 82	S 4	20,49
	l,s	12-Hydroxy-11-methoxy pseudostrychnine 67	S 4	20
	s	12-Hydroxy-11-methoxy strychnine 61	S 4	49
	l	14-Hydroxyicajine 75	S 4	20,49
	l	14-Hydroxynovacine 76	S 4	20,49
	br,l,s,rb, rw,sb,sm br, st	Icajine 72	S 4	20,48, 49
	l	Icajine N-oxide 81	S 4	20,48
	l	N-Methyl-sec-pseudo - β -colubrine 80	S 4	20,48
	br,l,s,sm br	Novacine 73	S 4	20,48, 49

Table 3 (continued)

Plants	Plant Part[a]	Isolated Alkaloid	Group	Ref.
S.wallichiana (continued)	l,rb,s,sb	Pseudobrucine 66	S 4	20,48
	b,l,r,s,sb	Pseudostrychnine 67	S 4	20,33, 48,49
	br,l,r,rb,rw, s,sb,sm br, st,sw	Strychnine 54	S 4	20,48, 49
	l,r,rb,rw,s, st,sw	Strychnine N-oxide 62	S 4	20,48
	l,rb,s,sb,st	Vomicine 74	S 4	49
	rb	Bisnor-dihydro toxiferine 102	B 1	47
	rb	Longicaudatine 119	B 5	47
Section II : Penicillatae				
S.axillaris	l	Spermostrychnine 86	S 5	20
Colebr.	l	Strychnospermine 87	S 5	20
Section III : Brevitubae				
S.vanprukii	l	Angustidine 33	V 3	20,50
Craib	l	Angustine 32	V 3	20,50
	l	Angustoline 34	V 3	20,50

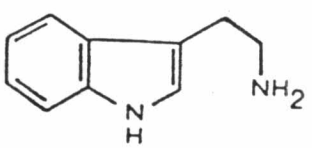
Table 3 (continued)

Plants	Plant Part[a]	Isolated Alkaloid	Group	Ref.
Section IV :				
Lanigerae				
S.minor	l	Angustidine 33	V[3]	20,50
Dennst.	l	Angustine 32	V[3]	20,50
	l	Angustoline 34	V[3]	20,50
	l	O-Acetyldiaboline 50	S[2]	20
	l	Diaboline 47	S[2]	20
	l	Methoxydiaboline 49	S[4]	20
	fr	Brucine 55	S[4]	20
	fr	Brucine N-oxide 64	S[4]	20
	fr	Novacine 73	S[4]	20
	fr	Strychnine 54	S[4]	20
	fr	Strychnine N-oxide 62	S[4]	20

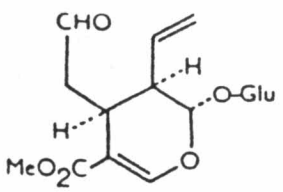
[a] The abbreviations for the Plant Part are listed as follows : b = bark, br = branch, fr = fruit, l = leaf, peri = pericarp, rt = root, rb = root bark, rw = root wood, s = seed, sb = stem bark, sm br = small branch, sw = stem wood, tw = twig, Ys = Yung seedling.

Biosynthesis of Indole Alkaloids

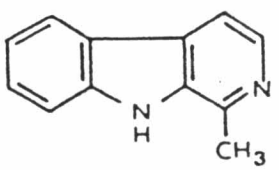
The structures of indole alkaloids were typically derived from the condensation between the nitrogen-containing moiety, tryptamine 120 and a C-9 or C-10 monoterpenoid moiety, secologanin 121 or other modified secologanin unit (27). Thus is different from simple indole alkaloids such as harman 122 and koenigine 123 which were not the products of the tryptamine-monoterpene condensation.



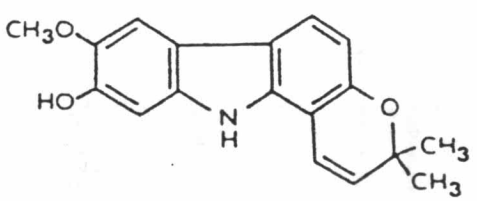
120 Tryptamine



121 Secologanin



122 Harman

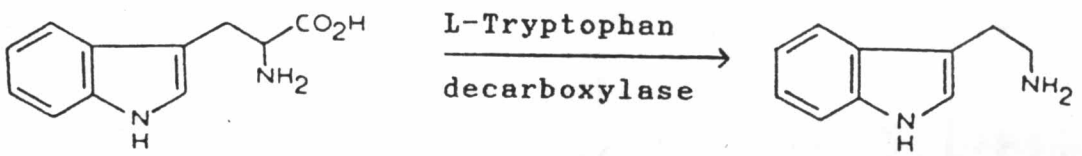


123 Koenigine

The biogenesis of indole alkaloids involved two important pathways,one of which lead to the non-terpenoid moiety and the other lead to the terpenoid moiety. In order to gain more informations about the whole process of indole alkaloid biosynthesis, many works have been carried out by using the cell-free system (51-55).

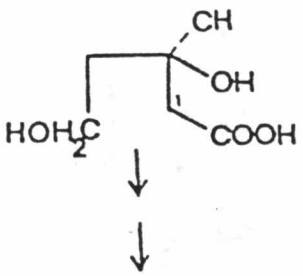
1) The Non-Terpenoid Moiety

The non-terpenoid moiety of the indole alkaloids originated from an amino acid, L-tryptophan 124 via its decarboxylation product, tryptamine 120, which is the more direct biogenetic precursor (51). The enzyme, L-tryptophan decarboxylase was indicated to involve in the biosynthesis of indole alkaloids (52,53) (See Figure 6). However, the general characteristics of this enzyme are still uncleared and more investigation details seem to be necessary (1).

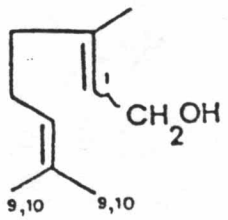


124 L-Tryptophan 120 Tryptamine

Figure 6 Formation of tryptamine 120

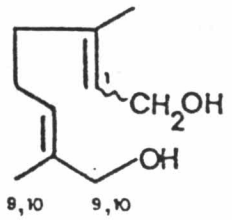


128 Mevalonic acid



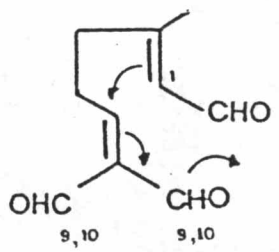
126 Geraniol (E-isomer)

127 Nerol (Z-isomer)

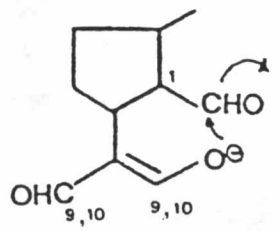


129 10-Hydroxy geraniol (E-isomer)

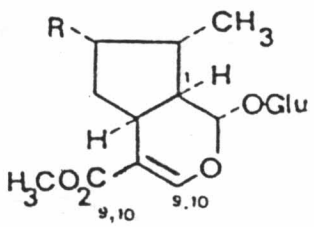
130 10-Hydroxy nerol (Z-isomer)



131 Trialdehyde

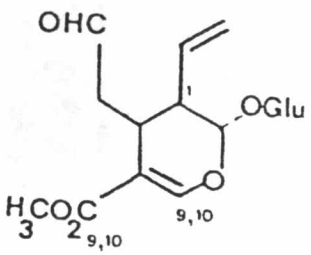


132



133 7-Deoxyloganin (R=H)

125 Loganin (R=OH)



121 Secologanin

Figure 7 Hypothetical pathway for the conversion of geraniol 127 and nerol 128 to loganin 126 and secologanin 121

2) The Terpenoid Moiety

The terpenoid moiety of indole alkaloids was proved to be the C-9 or C-10 monoterpene (27). The possible biosynthetic relationship between the monoterpenes and the indole alkaloids was first postulated by Thomas (56) and Wenkert (57) and recently confirmed by feeding or enzymatic experiments (58-61). The result demonstrated that secologanin 121 was a sole direct presursor for the monoterpenoid moiety. Loganin 125 was established as a key precursor of secologanin 121. The studies of the biosynthesis of loganin 125 have proved that its C-10 skeleton derived specifically from geraniol 126 or its cis-isomer, nerol 127 (58).Mevalonic acid 128 was available for the formation of geraniol 126 which could be established by using liver and yeast system (58, 62). The conversion of geraniol 126 or nerol 127 into loganin 125 involved unknown sequences including the oxidations of the C-9 and C-10 methyl groups and the oxidation of the C-1 position to the aldehydic state, the saturation of the Δ 1,2-olefinic residue and the formation of the cyclopentane ring (60,63).

The hydroxylation at C-10 to form 10-hydroxy geraniol 129 and 10-hydroxy nerol 130 might be the primary step beyond the Geraniol stage (60, 61). The following stages are proceeded through the oxidation of the hydroxyl groups at C-1 and C-10 and also the

oxidation of C-9 to form a trialdehyde functions 131 which after cyclization gives rise to the possible intermediate, 132 and the cyclopentane, units 133 and 125 (61). The intermediacy of deoxyloganin 133 in the biosynthetic process leading to loganin 125 as well as indole alkaloids is well documented (59). The final cleavage of the iridoid skeleton of loganin 125 directly gives rise to its corresponding seco-derivatives, secologanin 121 (25,64). The overall veiw of the biosynthetic pathway to secologanin 121 is accommodated in Figure 7 page 67.

3) The Key Role Intermediate "Strictosidine"

The condensation of tryptamine 120 with secologanin 121 was demonstrated by Battersby et al.(51) and Staunton (65) (See Figure 8 page 70). The reaction resulted in the formation of two epimeric- β-carboline gluco-alkaloids; Strictosidine (isovincoside) 134 with 3α-(S)-configuration and vincoside 135 with 3β-(R)-configuration. Recent works (54-55, 66-69) have defined strictosidine 134 but not vincoside 135 as being the true precursor of the various types of indole alkaloids. The crucial enzyme catalysing the condensation was named strictosidine synthase (70).

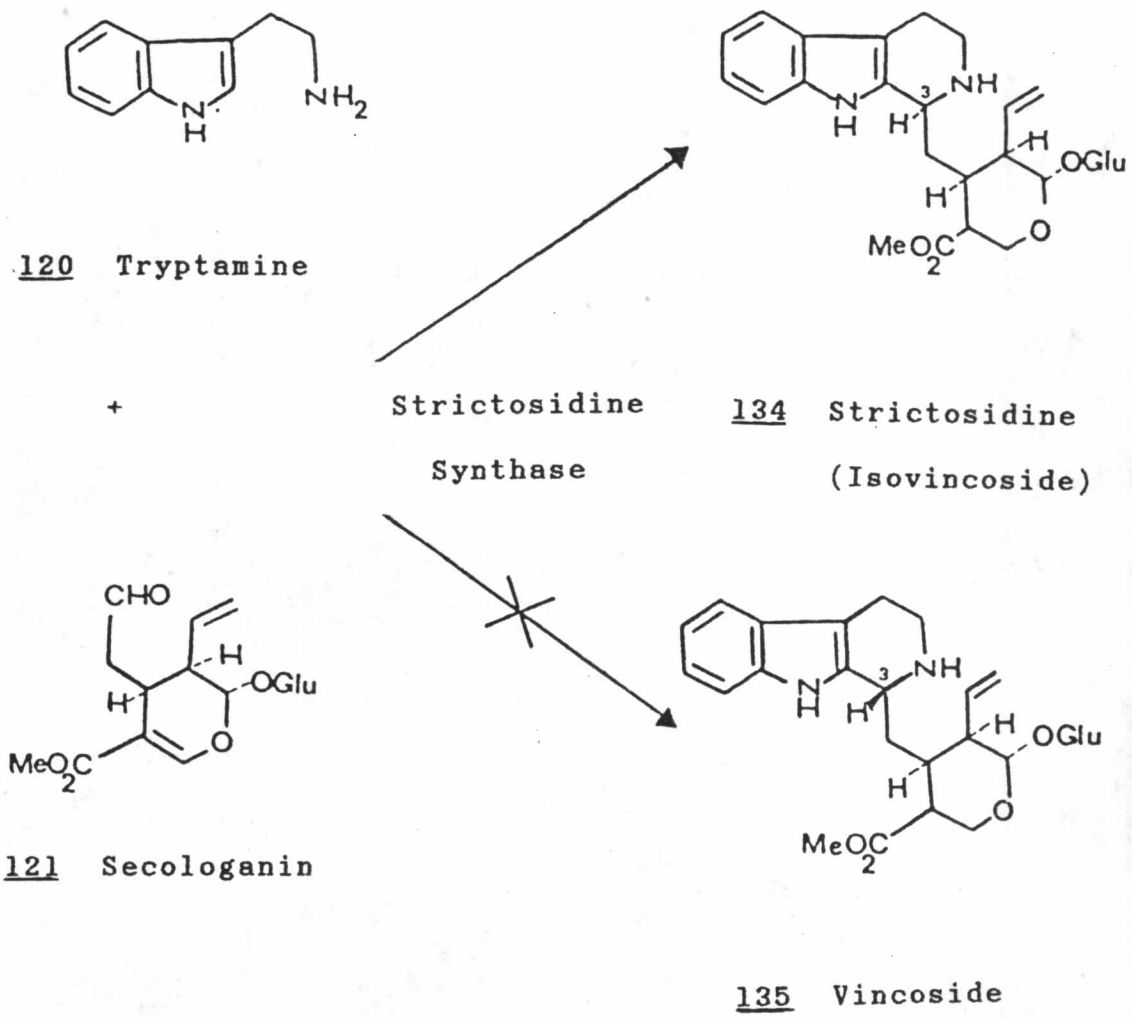


Figure 8 Formation of strictosidine 134 from tryptamine 120 and secologanin 121

Strictosidine 134 can be regarded as the universal precursor of monoterpenoid indole alkaloids (54-55, 65-69). The various types of monoterpenoid indole alkaloids and their relationships with strictosidine 134 are demonstrated (54) in Figure 9 page 72.

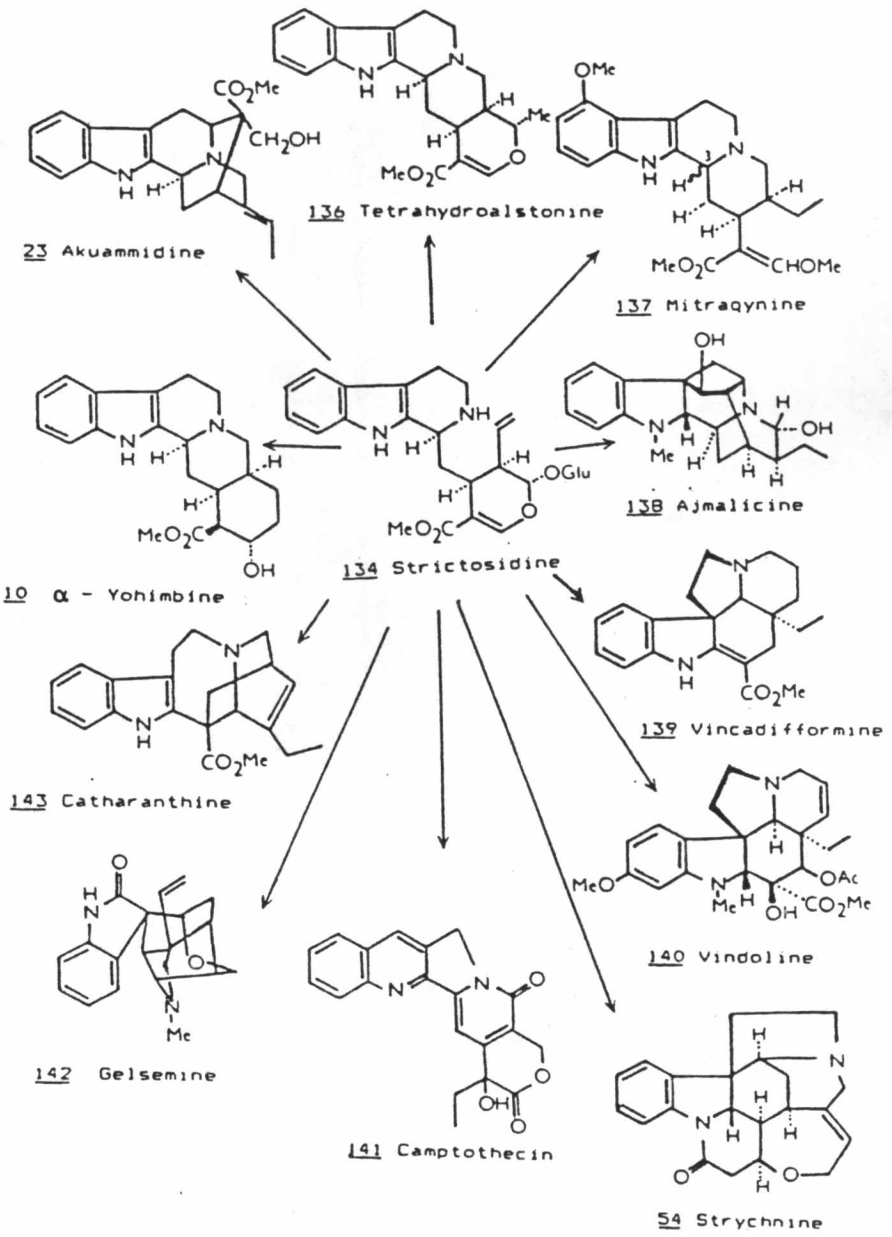


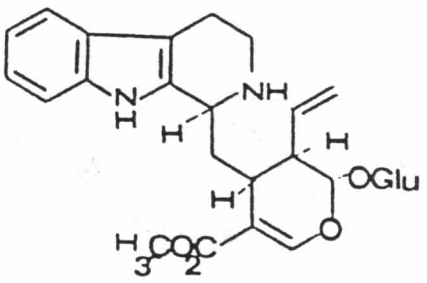
Figure 9 Strictosidine 134 as a key role intermediate in indole alkaloids biosynthesis.

Biosynthesis of Strychnos Alkaloids

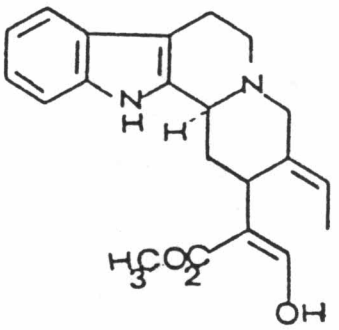
Like other terpenoid indole alkaloids, the biogenetic pathway of Strychnos alkaloids is starting from tryptamine 120 and secologanin 121. The typical route of the alkaloid biosynthesis in Strychnos species has been indicated by Heimberger and Scott (37). The overall pathway has proceeded via strictosidine 134, geissoschizine 1, dehydropreakuamicine 144 and Wieland-Gumlich aldehyde 45.

The important veiw of strictosidine 134 as being the key role intermediate of the biosynthetic pathway is emphasized by the isolation of N_b-methyl strictosidine, dolichantoside 145 from the root bark of African S.gossweileri Exell. (71).

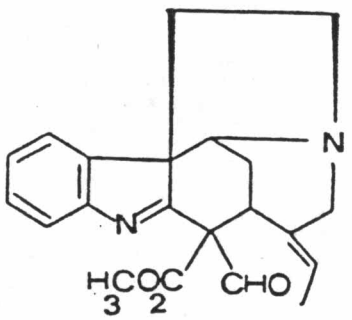
The role of geissoschizine 1 in the sequence of the heteroyohimbine alkaloids and several types of alkaloids biosynthesis have been demonstrated (27,72). However,more recent works (54,68,73-76) reveal that geissoschizine 1 seems to involve in the biosynthesis after two intermediates, 4,21-dehydrocorynantheine aldehyde 146 and 4,21- dehydrogeissoschizine 147. The alkaloid, 4,21-dehydrogeissoschizine 147 has been found naturally in Guettarda eximia Baill. (74) as well as isolate in a radioactive form from the incubations of [1-^{14}C] tryptamine 120 and secologanin 121 (75).



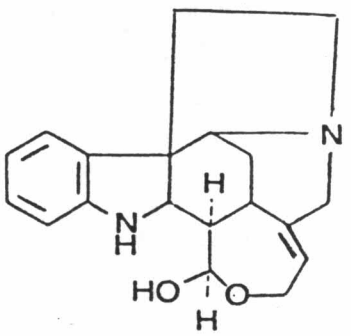
134 Strictosidine



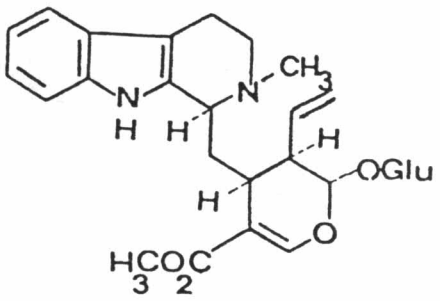
1 Geissoschizine



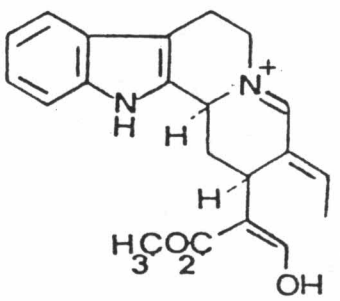
144 Dehydropreakuammicine



45 Wieland-Gumlich aldehyde



145 Dolichantoside



147 4,21-Dehydrogeissoschizine

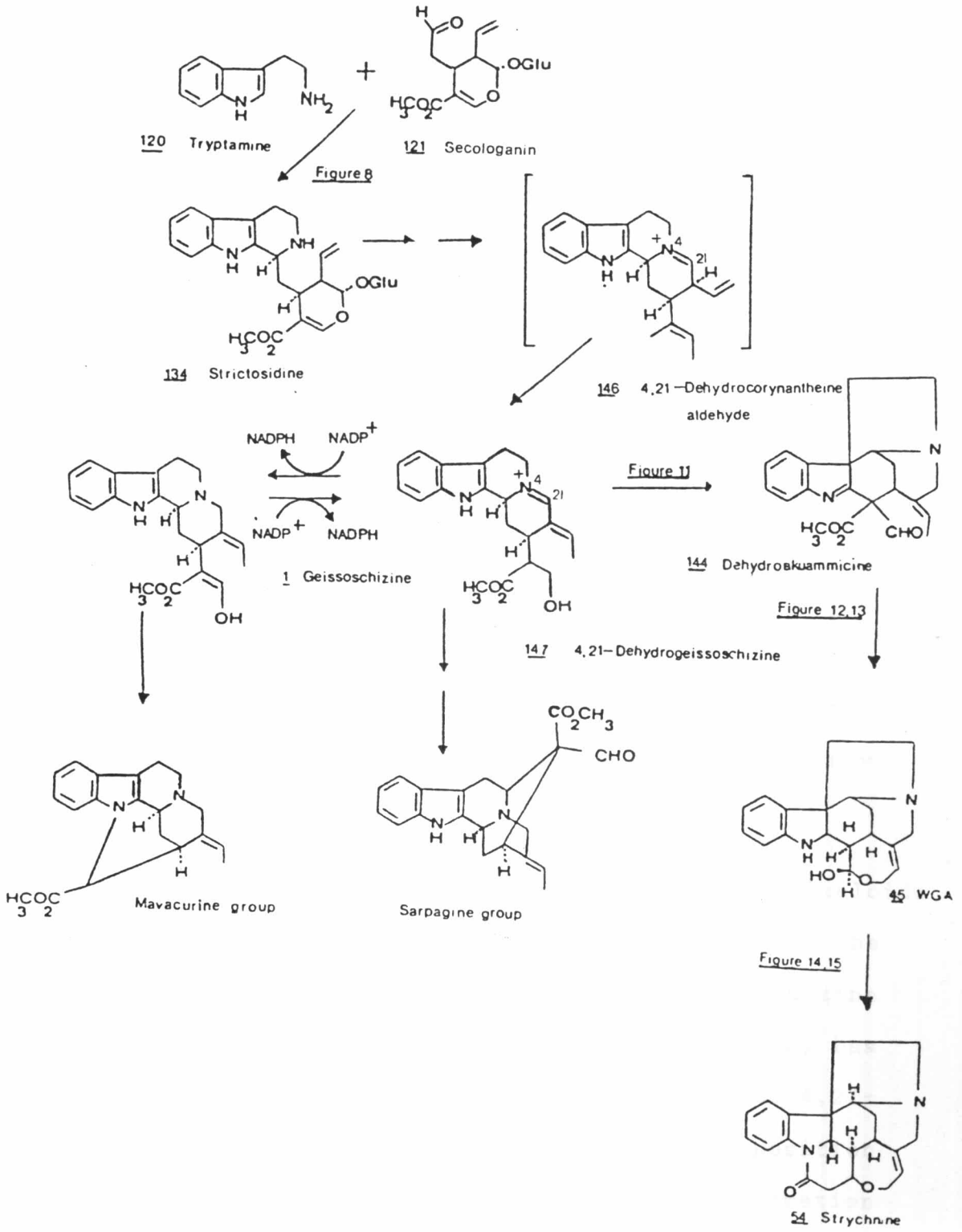
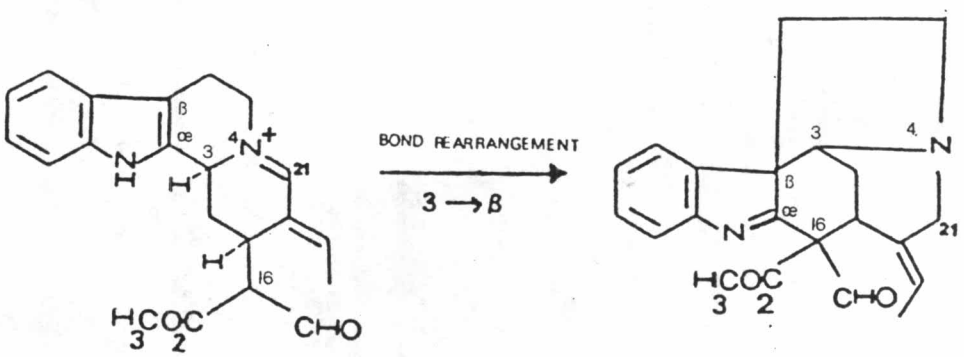


Figure 10 Overall veiw of the biosynthesis of Strychnos alkaloids.

4,21-Dehydrogeissoschizine 147 is considered as the important branch point intermediate (75-76) in the biosynthesis of the Corynanthean, Ibogan, Aspidospermatan and also Strychnan type alkaloids. The relationships among the pathway intermediates in the biosynthesis of Strychnos alkaloids are demonstrated in Figure 10 page 75. Geissoschizine 1 is converted from 4,21-dehydro-geissoschizine 147 under NADPH-regenerating conditions (69).

The C-mavacurine group (C_3) of the corynanthean type alkaloid seems to be derived from 4,21-dehydro geissoschizine 147 via geissoschizine 1 by $C_{16} \longrightarrow N_a$ ring closure (77) (see Figure 10). It is generally accepted that 4,21-dehydrogeissochizine 146 produced the sarpagine group (C_6) alkaloids, however the pathway to form $C_{16} \longrightarrow C_5$ bridge of sarpagine group is not clearly understood (76-78).

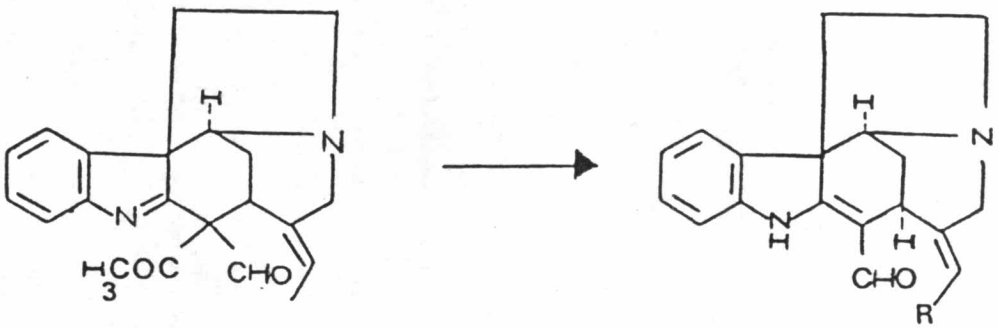
In the biosynthetic of strychnan type alkaloids (S-type), dehydropreakaummicine 144 is presumed to be the next stage intermediate after 4,21-dehydrogeissoschizine 147. The formation of dehydropreakuammicine 144 (52) has designed via the rearrangement of the C-3 bond of 4,21-dehydrogeissoschizine 147 from the α - to the β -position in the indole portion, follows by the bond formation between the α -position and C_{16} (see Figure 11 page 76).



147 4,21-Dehydrogeissoschizine 144 Dehydropreakuammicine

Figure 11 Transformation of 4,21-Dehydrogeissoschizine 146 to Dehydropreakuammicine 144

By lossing the carbomethoxy group of dehydro preakuammicine 144 would lead to the next recognized intermediate for rather complicated grid, nor-C-fluorocurarine 148 which then would hydroxylate to 18-hydroxy-nor-C-fluorocurarine 149 (1) (see Figure 12)



144 Dehydropreakuammicine

148 Nor-C-fluorocurarine

R = CH_3

149 18-Hydroxy-nor-C-fluorocurarine

R = CH_2OH

Figure 12 Alkaloids derived from Dehydropreakuammicine 144

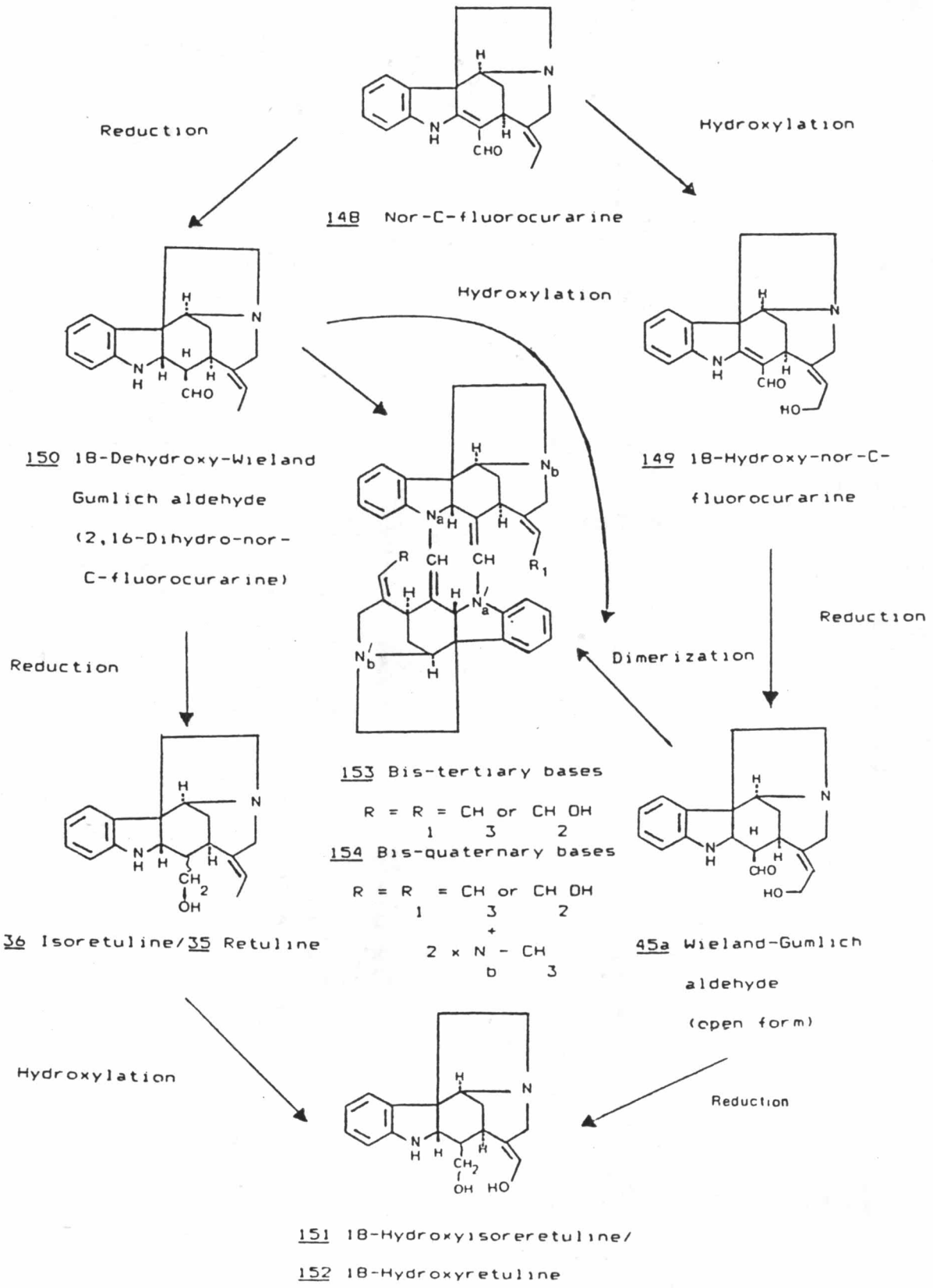
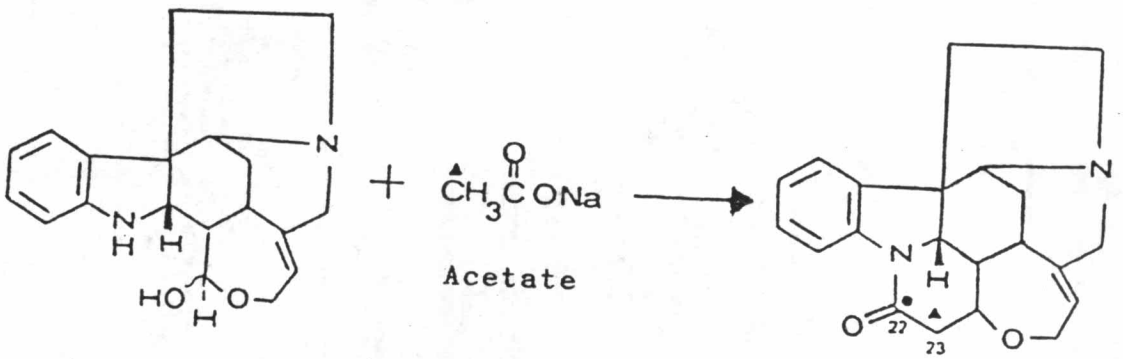


Figure 13 Alkaloids derived from Nor-C-fluocurarine 148

The reduction of these two compounds, nor-C-fluorocurarine 148 and 18-hydroxy-nor-C-fluorocurarine 149 (1) would produce 18-dehydroxy Wieland-Gumlich aldehyde 150 and Wieland-Gumlich aldehyde (open form) 45a, respectively. These two aldehydes, 150 and 45a are the precursors of monomeric Strychnos alkaloids such as isoretuline 36, retuline 35, 18-hydroxyisoretuline 151 and 18-hydroxy retuline 152 as well as bis-tertiary 153 or bis-quaternary 154 alkaloid (see Figure 13 page 79). In conclusion, it is possible to indicate that 18-dehydroxy Wieland-Gumlich aldehyde 150 is hydroxylated to give Wieland-Gumlich aldehyde (open form) 45a and then the two molecules of either the same or different aldehydes of 150 and 45a are condensed to form bis-tertiary base 153 and also bis-quaternary base 154.

Heimberger and Scott (37), have proved that Wieland-Gumlich aldehyde 45 (close form) is a precursor of heptacyclic bases exemplified by strychnine 54. Although the N_a-acetyl derivative of Wieland-Gumlich aldehyde, diaboline 47 has been supposed to involve in the biosynthetic pathway to strychnine 54, it is failed to incorporate into strychnine 54 during the feeding experiment (37). This negative result leads to the suggestion that an extra two carbon atom C_{22} and C_{23} of strychnine 54 might be come from an acetate unit rather than the ring closure between C_{17} and N_a-acetyl group of diaboline 47. The condensation of the acetate unit at C_{17}

and subsequent ring closure at N_a of Wieland-Gumlich aldehyde 45 to produce strychnine 54 have been proved (79). (See Figure 14).



45 ▲, • = labelled 54

Figure 14 Formation of Strychnine 54 from Wieland-Gumlich aldehyde 45 and acetate unit

In addition, Heimberger and Scott (37) have predicted that there will be an aldol-acid compound called prestrychnine 155 which is placed at the last step in the biosynthesis next to strychnine 54. This proposal is supported by the isolation of protostrychnine 53 from the root bark of S.nux-vomica Linn. (40). Finally, protostrychnine 53 would be dehydrated to give strychnine 54. The metabolic grid at the final stage of the biosynthesis pathway to strychnine 54 has shown in Figure 15 (page 83).

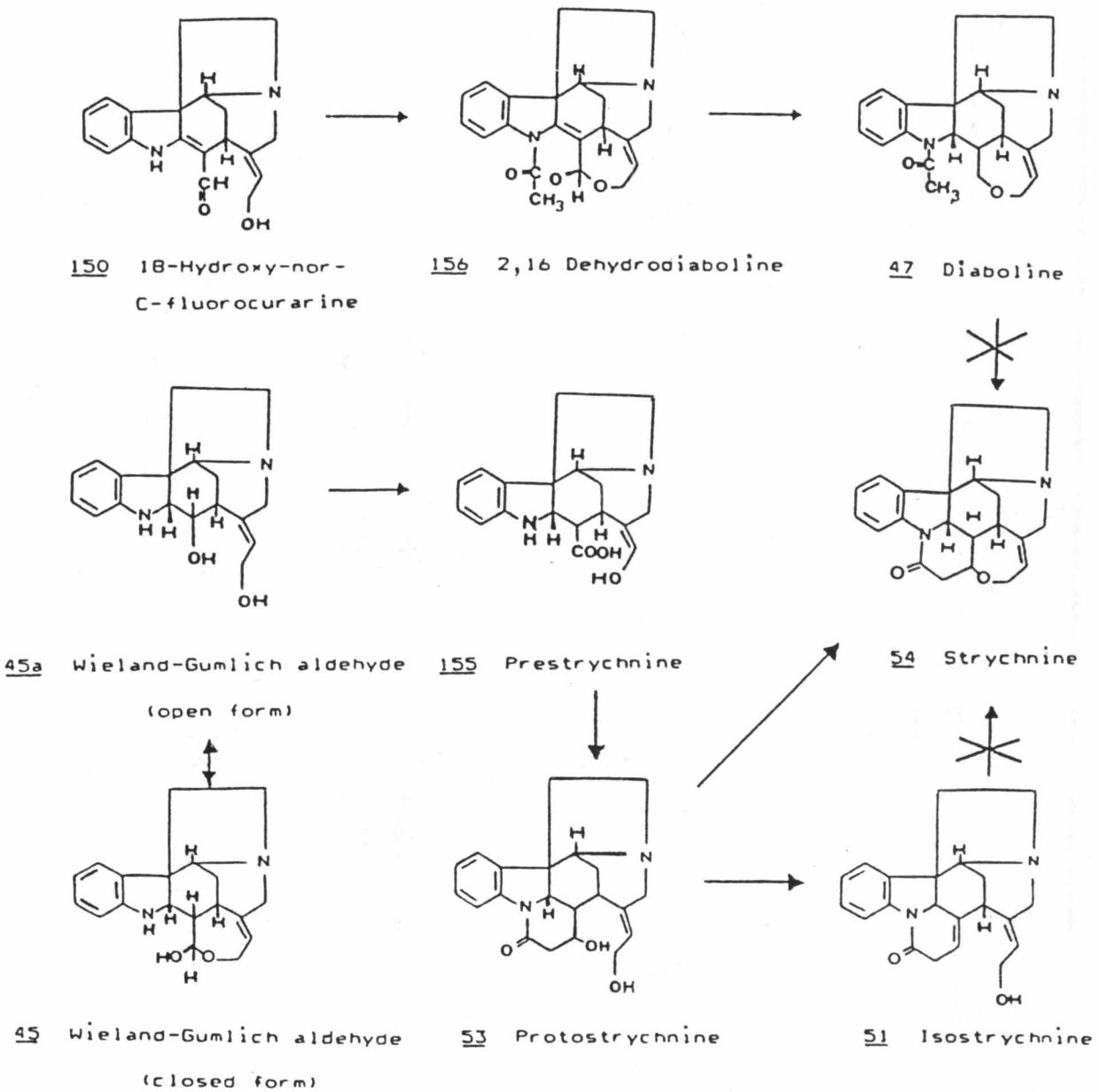


Figure 15 The final stage in the biosynthesis pathway of Strychnine 54.

Strychnos Alkaloids and Pharmacological Relationships

Strychnos alkaloids are well-known in possessing both muscle relaxant and central nerveous system stimulant action (5,11-12,15-17). In addition, a number of other pharmacological activities which have been demonstrated are antimicrobial (80,82), antitumour and anticancers activities (83,84), hypotensive effect (12, 85-88), reserpine like activities (35),cardiac depressant action (83) and cardiotoxic effect (89).

The strong central nerveous system stimulant action of Strychnos alkaloids is the major cause of clonic and tonic convulsions. Clonic convulsion occurs when having an alternating contraction and relaxation of the muscles, whereas a sustained rigidity of the muscles occurs (5) in tonic convulsion.

Muscle relaxant effect may also be subdivided into truly curarizing and muscle relaxant activities (5). Curarizing activity represents by the neuro-muscular blockage of impulse transmission of the motor end-plates as a result of inhibition of acetylcholine. The result possesses the complete paralysis of the skeletal or striated muscle apparatus. It is generally accepted that inhibitors of neuro-muscular transmission exerts their principal action either presynaptically or postsyn aptically or a combination of both, while muscle relaxant activity refers to the term of being only a weak

action on neuro-muscular junctions.

In general, non-polar fractions of the crude alkaloids from Strychnos spp., always show strong convulsant activity of the both clonic and tonic types while the polar fractions show the muscle relaxant activity (17).

The chemical structures of these alkaloids can be related to their pharmacological activities (12,90) and the arrangements of the Strychnos alkaloids structures are recently described (5,80-86) to correlate either to convulsant or muscle relaxant activities. However, only some structural types of Strychnos alkaloids can be related to this arrangement due to the insufficient pharmacological investigation of these alkaloids (5,34).

Alkaloids with Convulsant Activity

1. Strychnan type alkaloids (S-type)

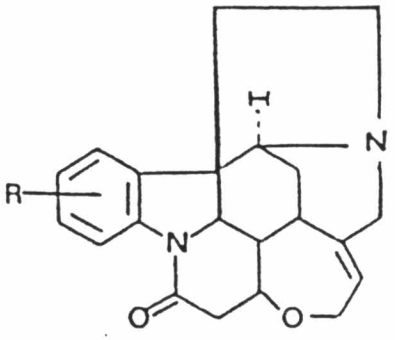
The alkaloids having the strychnan type skeleton are the major components responsible for possessing the convulsant activity. Sanberg and Kristiansson (91) made a comparative study of the convulsant effect of strychnan type alkaloids and divided them into 4 groups according to their extencity such as:-

1.1) Alkaloids of the normal and pseudo series

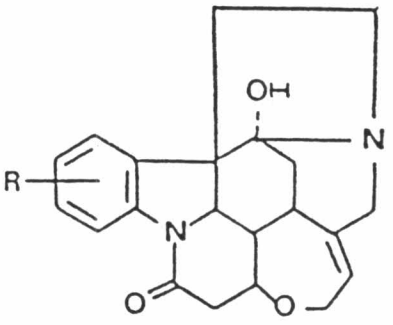
1.2) Alkaloids of the N-methyl-sec pseudo series

1.3) Diaboline group

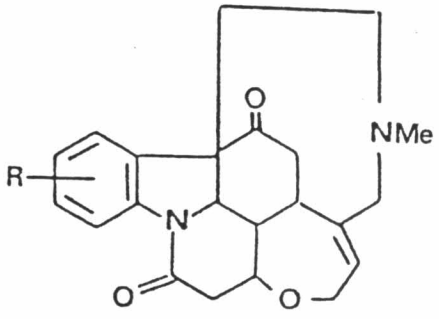
1.4) Spermostrychnine group



normal series

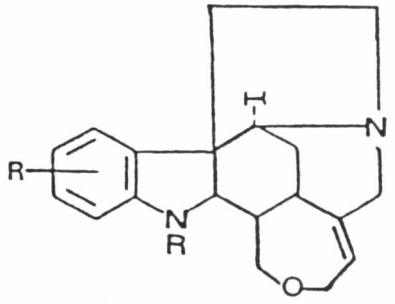


pseudo series

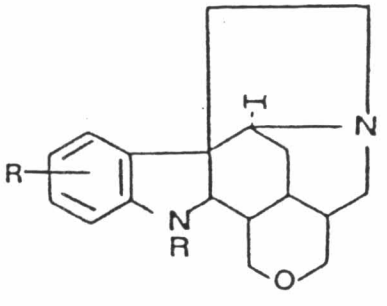


N-methyl-sec-pseudo series

Strychnine group (S_4)



Diaboline group (S_2)

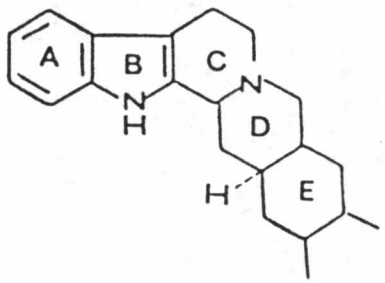


Spermostrychnine type (S_2)

Each groups of the alkaloids possess the convulsant activities to a lesser or greater extent related to their characteristic structures. The normal and pseudo series of the strychnine group (S_4) are characterized to possess the tonic convulsion. The extension phase is thus typical for the strychnine skeleton. Strychnine 54 and 12-hydroxystrychnine 59 which belong to the normal series possesses strongest activity . The pseudo series are slightly less active than strychnine 54 because of their 3 α -hydroxyl groups get a lesser fitness with the specific receptor.

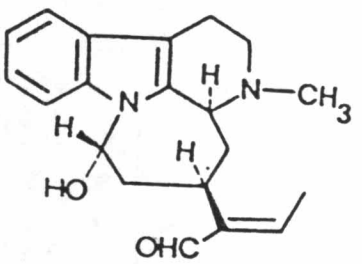
The N-methyl-sec-pseudo series of the strychnine group (S_4) have the analogous activity but are less active than strychnine 54. The explanation is that the ring containing the 3-keto group extrudes from the back of the molecule causing a less satisfactory fitness with the receptor.

The diaboline group (S_2) and the spermostrychnine group (S_5) alkaloids have the sum of changes introduced to the molecules with respect to strychnine 54. The opening of the amide lactam ring in the both groups will produce a marked decreasing in potency and toxicity. These last two groups have the same convulsant activity but only clonic convulsion are observed.



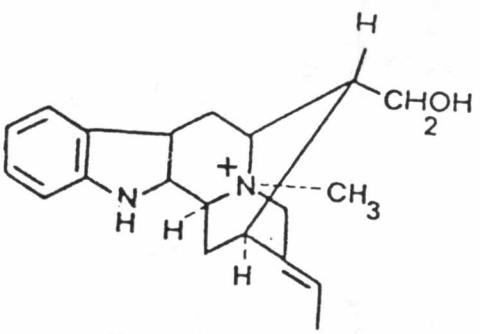
Corynanthean type

(C-type)



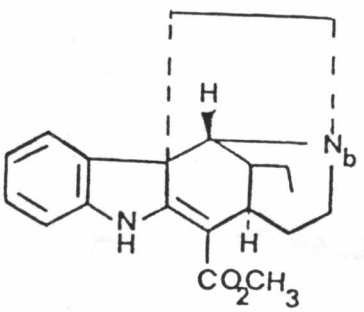
Akagerine group (C4)

12 Akagerine



Sarpagine group (C6)

19 Macusine B



Aspidospermatan type

(A-type)

97 Tubotaiwine

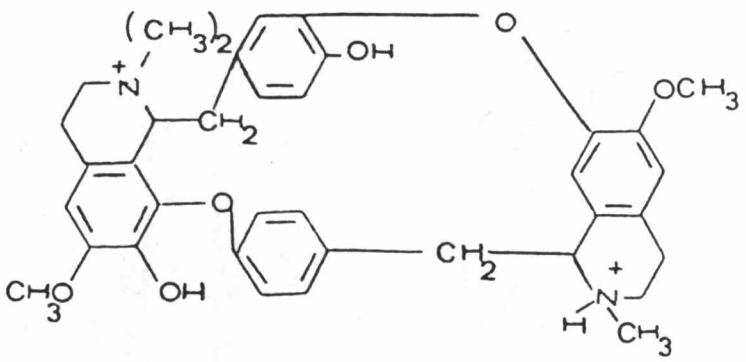
2. Other alkaloid types

Some alkaloids of the corynanthean type alkaloids (C-type) also possess convulsant activity. In subsequence studies (94-96), akagerine group (C_4) alkaloids, akagerine 12 and its congeners are the potent convulsant agents. They also possess the tonic convulsion effect which is less activity than strychnine 54. The sarpagine group (C_6) alkaloids such as macusine B 19 show clonic convulsant effect in vivo (87). Tubotaiwine 97, the alkaloid of the aspidospermatan type (A-type) also shows only weak clonic convulsion in vivo (97).

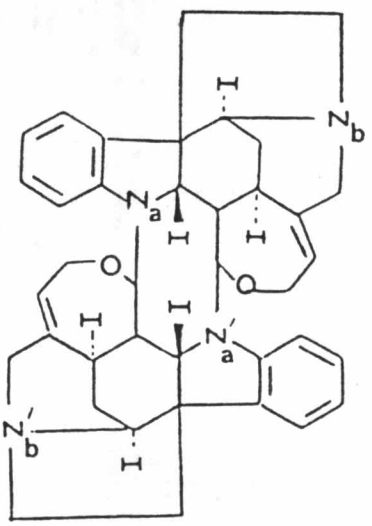
Alkaloids with Muscle-relaxant Activity

1. Bisindole type alkaloid (B-type)

The bisindole alkaloids are known to have a muscle-relaxant activity (11). The action is similar to the well-known bis-benzylisoquinoline alkaloid, D-tubocurarine 156. D-tubocurarine 156 was isolated from the tube curare and from Chondrodendron tomentosum Ruiz. et Pav. of the family Menispermaceae.



156 d - Tubocurarine



113 Caracurine v

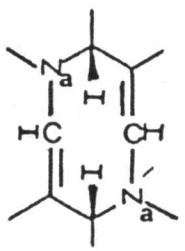
The bisindole alkaloids exhibit their potency activities which are related to their skeletons. The tertiary bisindole alkaloid, Caracurine V 113 shows a weak muscle relaxant activity while the quaternary ones exhibit potent curarizing effect. The presence of two quaternary nitrogens in a single molecule is responsible for a strong activity and the optimal activity depends on the distance between the quaternary nitrogens. For optimal activity, the distance must be about 14 A° whereas the distance decreases, the activity decreases (5). The presences of hydroxyl group at C-18 induce a stronger curarizing activities (12,87).

The bisindole alkaloids may be divided into 3 groups according to the transformation at the central eight membered ring of the molecules which base on the toxiferine 101 skeleton (5,12).

1.1) Toxiferine group

This group shows slowly progressive onset of paralysis but the effect is long duration. The representatives of the group are toxiferine 101, C-dihydrotoxiferine 102 and C-alkaloid H 157 (see Figure 16 page 92). Toxiferine 101 is the most potent member of this group which possesses even more potent than d-tubocurarine 156.

Figure 16 The chart indicates those members of the three bisindole alkaloid skeletons which respect to their central 8-membered ring

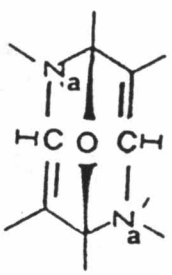


Toxiferine group

101 Toxiferine; R = R´ =OH

102 C-Dihydrotoxiferine ; R = R´ = H

157 C-Alkaloid H; R = H, R´ = OH

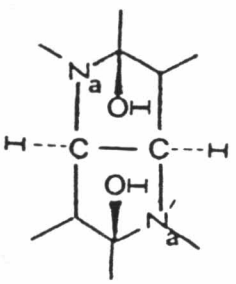


Curarine group

108 C-Alkaloid E ; R = R´ OH

106 C-Curarine ; R = R´ = H

158 C-Alkaloid G; R = H, R´ = OH



Calebassine group

159 C-Alkaloid A ; R = R´ = OH

109 C-Calebassine ; R = R´ = H

160 C-Alkaloid F ; R = H , R´ = OH

1.2) Curarine group

The representatives of this group are C-curarine 106, C-alkaloid E 108 and C-alkaloid G 158. C-curarine 106 is the most potent member of this group and being more potent than d-tubocurarine 156. However, the effect is sustained in moderate duration.

The most active effect of the Curarine group possesses by an ether oxygen in the central eight membered ring (see Figure 16 page 92).

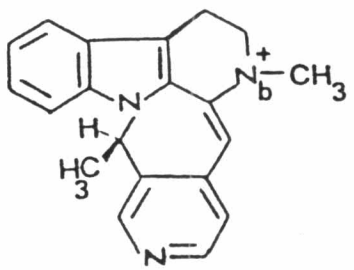
1.3) Calebassine group

The alkaloids of this group are less potent than d-tubocurarine 156 and the effect is short duration. The low activity may be explained by the fact that the presence of the C-C bridge in the central eight-membered ring such representative by C-calebassine 109, C-alkaloid A 159 and C-alkaloid F 160 would reduce the distance between the two quaternary nitrogens down to 8.6 A° (see Figure 16 page 92).

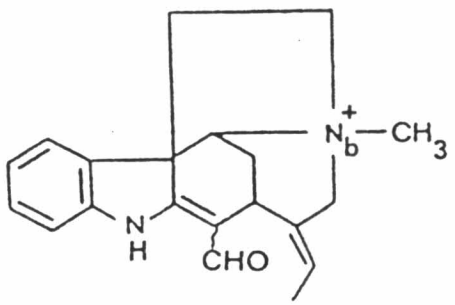
2. Other alkaloid types

Decussine 28, the alkaloid of the vincosan type(D-type) had pronounced muscle-relaxant effect. It is probably dued to the 13,14 double bond of the molecule being responsible for their muscle relaxant activity (99-100).

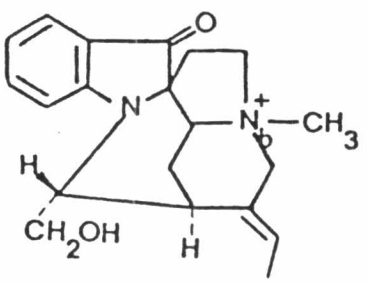
Some monoquaternary alkaloids, fluorocurarine 41, C-fluorocurine 17 and C-mavacurine 16 give only a weak curare activity too (87).



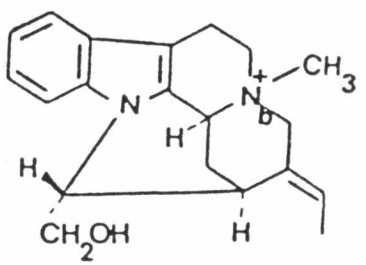
28 Decussine



41 Fluorocurarine



17 C-Fluorocurine



16 C-Mavacurine