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QUINAZOLINE ALKALOIDS IN NATURE

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This review generalizes information on the distribution in the plant and animal kingdoms of all types of quinazoline alkaloids known at the present day.

The main structural element of the class of quinazoline alkaloids is the heterocyclic skeleton of quinazoline, which has not hitherto been detected in living Nature and was obtained synthetically in 1895 [1]. The quinazoline alkaloids form a small group of secondary natural compounds. At the present time (up to and including 1995), more than 140 substances of this type are known. The chemistry of the quinazoline alkaloids had its origin in 1888, with the discovery of the first natural representative of them — (+)-peganine (known in the foreign literature as vasicine). The beginning of the 20th century (namely, in 1909 and 1915) saw the isolation of two of the most important parents of other structural types of quinazoline bases — tetrodotoxin and rutecarpine. Then followed the first lull, and only in the mid-1940's and, especially, in the 1950's did a vigorous development of the chemistry of the quinazoline alkaloids begin. It must be mentioned that, in parallel with work on the isolation of this group from various natural sources and the determination of their structures, investigations on their synthesis and the determination of their biological activities were intensively developed, and today the number of synthetic quinazoline derivatives many times exceeds the number of natural quinazoline bases. Correspondingly, the number of publications on this subject is considerable. In view of this, we have limited ourselves to a consideration of the distribution of quinazoline compounds in living Nature.

A number of publications of review nature [2-5] have been devoted to the chemistry of the quinazoline alkaloids; however, in our opinion, they do not give a general picture of the distribution of this class of compounds in the plant and animal kingdoms. Thus, for example, in some publications a particular structural type is considered [6, 7]; in others there is information not only on the natural alkaloids but also on their numerous synthetic analogs [8, 9]; a third group gives the chemical composition of only one plant [10]; and, finally, another group consists of simple lists of facts accumulated over a definite time interval [11-13]. Furthermore, there are no generalizing papers on individual groups of quinazolines. We have attempted to bring together the available information on the quinazoline alkaloids and to show their place in the plant and animal kingdoms.

The distribution in Nature of bases of the quinazoline series is not restricted by the frameworks of any one or more taxonomic units. These alkaloids, unlike many others, are found not only in higher plants (both monocotyledons and dicotyledons) but also in lower plants (fungi and microorganisms) and in the most diverse classes of animals (mainly dwellers of the seas and oceans).

Table 1 gives information on the distribution of quinazoline alkaloids in the plant and animal kingdoms. It must be mentioned that in its compilation we strove to follow strictly the principle of the evolutionary development of living material from simple to complex. All the taxons in which representatives of the quinazoline bases have been detected are arranged in just this sequence. The classification of plant and animal taxons is given in accordance with the schemes adopted in two fundamental monographs [14, 15].

In accordance with the classification of the quinazoline alkaloids by structural types adopted at the present time, we propose to distinguish the following groups within this class of compounds: I) simple (bicyclic) quinazolines; II) tricyclic quinazolines; III) quinazolinocarbolines; IV) tryptoquivalines; V) tetrodotoxins; and VI) quinazolines with various structures. In accordance with this scheme, we shall consider each group individually.

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TABLE 1. Distribution of Quinazoline Alkaloids in Nature

Biological species	Literature ref.	Structural type
Lower Plants (bacteria and fungi)		
I. Spirillaceae		
Vibrio alginolyticus and other marine species of the *Vibrio* genus	113, 121, 123	V
II.Pseudomonadaceae		
Pseudomonas aeruginosa, P.fluorescens, P.putida	11, 13, 14, 17, 18, 19	I
Other marine species of the *Pseudomonas* genus (marine species)	113, 121, 123	V
Bacillus (marine species)	113, 121, 123	V
Plesiomonas (marine species)	121	V
III. Bacteriaceae		
Klebsiella pneumoniae	43	II
IV. Sacharomycetaceae		
Candida lipolytica	139, 141	VI
V.Deuteromycetes (Imperfect Fungi)		
Alternaria citri	2, 25	I
Cladobotryum varium	2	I
Colletotrichum lagenarium	2	I
VI. Ascomycetes (Ascomycetous Fungi)		
Aspergillus alliaceus	126, 127, 128, 129, 130	VI
A.clavatus	93, 94, 95, 96, 99, 111	IV
A.fischeri	125, 132, 133	VI
A.flavipes	140	VI
A.fumigatus	96, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 143, 144, 145	IV, VI
Corynascus setosus	97, 98, 142	IV, VI
Fusarium culmorum	2	I
Neosartorya fischeri	142	VI
Penicillium aurantiogriseum	131	VI
P.chrysogenum	2, 25	I
Penicillium sp.	134, 135, 136, 137	VI
Higher Plants		
I.Polygonaceae		
Polygonum tinctorium	141	VI
II. Brassicaceae (Cruciferae)		
Isatis tinctoria	139, 141	VI
III. Malvaceae		
Sida acuta, S.cordifolia, S.humilis, S.rhombifolia, S.spinosa	35, 37, 60	II
IV. Saxifragaceae		
Dichroa febrifuga	12, 21, 22, 23	I
Hydrangea macrophylla	22, 23	I
H.umbellata	12, 22, 23	I
V. Fabaceae (Leguminosae)		
Galega officinalis	37, 46, 48, 61	II
G.orientalis	60	II
VI. Lecythidaceae		
Couroupita guianensis	141	VI
VII. Rutaceae		
Araliopsis tabouensis	75, 82	III
Euxylophora paraensis	66, 74, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92	III
Evodia meliaefolia	70, 76, 82	III
E. rutaecarpa	67, 68, 70, 71, 72, 73, 76, 77, 80, 82	III

TABLE 1 (continued)

Biological species	Literature ref.	Structural type
Glycosmis arborea	1, 5, 6, 7	I
G.pentaphylla	1, 5, 8	I
Hortia arborea	76, 78, 79	III
H.badinii	76, 79	III
H.brasiliana	78	III
H.longifolia	79	III
H.regia	76	III
Tetradium glabrifolium	66	III
Vepris loisii	66, 69	III
Zanthoxylum arborescens	15, 16	I
Z.budrunga	1, 75, 76	I, III
Z.limonella, Z.pluviatile	76	III
Z.oxyphyllum	75	III
Z.rhetsa	75, 81, 82	III
VIII. Biebersteiniaceae		
B.multifida	37	II
IX. Peganaceae		
Peganum harmala	32, 37, 38, 46, 47, 48, 49, 50, 57, 58, 59, 60, 62	II
P.nigellastrum	37, 46, 48, 60	II
X. Nitrariaceae		
Nitraria komarovii	38, 46, 48, 53, 54, 55, 56	II
N. sibirica	37, 46	II
XI. Araliaceae		
Mackinlaya klossii, M.subulata	64, 65	II
M.macrosciadia	41, 46, 64, 65	II
XII. Rubiaceae		
Galium aparine	37, 38, 42, 44	II
XIII. Scrophulariaceae		
Linaria transiliensis,	37, 46, 60	II
L. vulgaris	37, 60	II
L.alpina, L.anticaria, L.avenaria, L.dalmatica, L.genistifolia, L.popovii, L.pseudo-laxiflora, L.purpurea, L.repens, L.triornithophora, L.ventricosa, L.vulgariformis and some other species of the *Linaria* genus	60	II
XIV. Acanthaceae		
Adhatoda beddomei	35, 37, 46, 59	II
A.vasica	27, 28, 29, 32, 33, 34, 35, 36, 37, 39, 40, 45, 48, 51, 59, 60	II
Anisotes sessiliflorus	29, 30, 31, 45, 60, 63	II
Strobilanthes cusia	21, 24, 139, 141	I, VI
XV. Asteraceae (Compositae)		
Echinops echinatus	4, 26	I
XVI. Poaceae (Gramineae)		
Arundo donax	46	II
XVII. Arecaceae (Palmae)		
Daemonorops draco	52	II
Animals		
I. Anthozoa (Corals)		
Anemonia sulcata	121	V
II. Turbellaria		
Planocera multitentaculata	121	V
III. Nemertini		
Lineus fuscoviridis	113, 121, 123	V
Tubulanus punctatus	113, 121	V

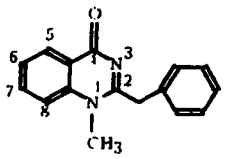
TABLE 1 (continued)

Biological species	Literature ref.	Structural type
IV. Bryozoa		
Hincksinoflustra denticulata	138	VI
V. Gastropoda		
Babylonia japonica	121	V
Charonia sauliae	113, 121, 123	V
Monodonta labio	20	I
Natica lineata	113, 121	V
Niotha clathrata	121	V
Tutufa lissostoma	121	V
Zeuxis siquijorensis	121	V
VI. Cephalopoda		
Octopus maculosus	113, 121, 123	V
VII. Crustacea		
Atergatis floridus	113, 121	V
Zosimus aeneus	121	V
VIII. Merostomata		
Androctonus australis	121	V
Carcinoscorpius rotundicauda	121	V
IX.Myriapoda		
Glomeris marginata	9, 10	I
X. Asteroidea (Starfish)		
Astropecten latespinosus, A.polyacanthus, A.scoparius	121	V
XI. Ascidiacea		
Pyura sacciformis	3	I
XII. Pisces (Fish)		
a) Gobiidae		
Gobius criniger	121	V
b) Tetraodontidae		
Amblyrhynchotes hypselogenion	121	V
Arothron nigropunctatus	116, 118, 119,121, 123,124	V
A.stellatus	121	V
Fugu alboplumbeus, F.oblongus, F.stictonotus	121	V
F.niphobles	116, 118, 121, 124	V
F.pardalis, F.poecilonotus	113, 116, 118, 120, 121, 123, 124	V
F.rubripes	113, 120, 121, 123	V
F.vermicularis	113, 121	V
Lagocephalus lunaris	121	V
Pugilina ternatana	121	V
XIII. Amphibia		
a) Ambystomatidae		
Ambystoma tigrinum	121, 124	V
b) Brachycephalidae		
Atelopus ambulatorius, A.oxyrhynchus, A.senex, A.varius	121	V
A.chiriquiensis	121, 122	V
Brachycephalus ephippium	121	V
c) Salamandridae (True salamanders)		
Cynops ensicauda	112, 113, 114, 116, 117, 121, 123, 124	V
C.marmorata	121	V
C.pyrrogaster	116, 121, 124	V
C.viridescens	121, 124	V
Paramesotriton hongkongensis	121	V
Taricha granulosa	115, 116, 121	V
T.rivularis, T.torosa	121	V
Triturus alpestris	116, 121, 124	V
T.oregon	116, 121	V
T.vulgaris	121, 124	V

I. Simple (Bicyclic) Quinazolines

The simple (bicyclic) quinazoline alkaloids are very widely distributed in living Nature. They have been detected in bacteria (*Pseudomonas*), fungi (*Alternaria, Cladobotryum, Colletotrichum, Fusarium, Penicillium*), in higher plants of the families Saxifragaceae (*Dichroa, Hydrangea*), Rutaceae (*Glycosmis, Zanthoxylum*), Asteraceae (*Echinops*), and Acanthaceae (*Strobilanthes*), and in gastropod mollusks (*Monodonta*), Myripoda (*Glomeris*), and ascidians (*Pyura*). At the present time, 26 representatives of this group of alkaloids are known.

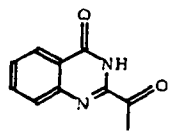
From the chemical point of view these compounds are represented by a quinazoline nucleus, which may contain substituents in positions 1, 2, 3, 4, and 7. These may be methyl, ethyl, hydroxyl, hydroxymethyl, benzyl, carbonyl, carboxyl, amide, bromine, or acetyl. In addition, more complex groupings are often found in position 3. For example, in the ascidian *Pyura sacciformis* an alkaloid containing bromine — 7-bromoquinazoline-2,4-dione — has been detected, which is a fairly rare occurrence.



1. ARBORINE

Glycosmis arborea [16], G.pentaphylla [17], Zanthoxylum budrunga [18]
$C_{16}H_{14}N_2O$: 250.2990
mp .: 155–156°
{ picr. 174° (dec.) n-chl. 215°, h.b. 76°, h-i. 96°, nitr. 117°, picrol. 171°, m-i. 126–127°}

UV: 227, 268, 277, 306, 315 (4.25, 3.68, 3.72, 3.94, 3.87) [188]
IR: 1645, 1603, 1531, 1502, 1456 [189]
Mass: 250, 249, 133, 132, 105, 104
PMR: 3.60 (3H, s, NCH_3); 4.26 (2H, s, $PhCH_2$); 7.10–7.90 (8H, m, H–Ar); 8.30 (1H, q, J=8, 2, H-5) [190]



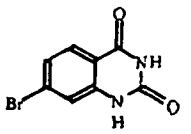
2. 2-ACETYLQUINAZOLIN-4(3H)-ONE

Alternaria citri [22], Cladobotryum varium [23], Colletotrichum lagenarium [24], Fusarium culmorum [25], Penicillium chrysogenum [26]
$C_{10}H_8N_2O_2$: 188.1846
mp: 205° (e-a) [24], 200–201° (acetonitrile) [193]

UV: 229, 303 (3.38, 3.13) [23]
IR: 3165, 3065, 1710, 1600
Mass: 188(M^+, 100), 160(17), 146 (46), 119 (28) [23]
PMR: 2.70 (3H, s, CH_3); 7.40–7.90 (3H, m, H–Ar); 8.20 (1H, m, H–Ar); 12.20 (1H, br.s, NH) [193]
^{13}C NMR [193]

C-9	194.0 (s)	C-7	134.7 (d)	C-5	126.1 (d)
4	159.9 (s)	6	128.8 (d)	4a	123.6 (s)
1a	147.3 (s)	8	128.5 (d)	10	24.7 (q)
2	147.1 (s)				

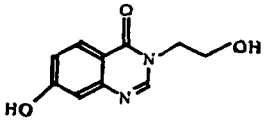
3. 7-BROMOQUINAZOLINE-2,4-DIONE



Pyura sacciformis [33]
$C_8H_5BrN_2O_2$: 241.0429
mp .: >330° (meth.)
UV: 225, 310
IR: 1730, 1680

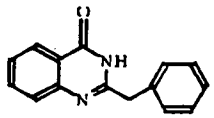
Mass: 242 (99), 240 (M^+, 100), 199 (70), 197 (69), 172 (41), 170 (48)
PMR: 7.36 (1H, dd, J -2.0, 8.9); 7.39 (1H, d, J=2.0); 7.89 (1H, d, J=8.9)

4. 7-HYDROXYECHINOZOLINONE



Echinops echinatus [27]
$C_{10}H_{10}N_2O_3$: 206.1994

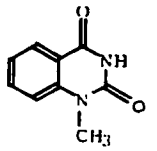
5. GLYCOSMININE



Glycosmis arborea [28], G.pentaphylla [29]
$C_{15}H_{12}N_2O$: 236.2722
mp.: 249°
UV: 225, 265, 303, 312 (4.44, 3.95, 3.66, 3.57) [188]

IR: 3440, 3356, 1676, 1613, 770, 748, 713
Mass: 236 (M^+), 235, 119, 92, 91, 90, 78, 77
PMR: 4.08 (CH_2); 7.50 (8H, H-Ar); 8.26 (d, H-5); 10.25 (NH) [189]

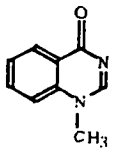
6. GLYCOSMICINE



Glycosmis arborea [19]
$C_9H_8N_2O_2$: 176.1736
mp.: 270–271° (meth. chl.-meth.)
UV: 219, 244, 311 (4.70, 3.97, 3.64)
IR: 1701, 1661, 1605, 1484, 1399 [189]

Mass: 176 (M^+), 133, 132, 105, 104, 92, 90, 78, 77
PMR: 3.58 (NCH_3); 7.72 (3H, H-6, H-7, H-8); 8.22 (1H, d, H-5); 8.59 (NH)

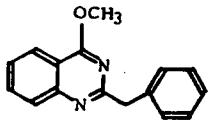
7. GLYCORINE



Glycosmis arborea [19]
$C_9H_8N_2O$: 160.1746
mp.: 145–147°
h-chl. 242° (dec.) picr. 249° (dec.)
UV: 230, 269, 278, 306, 317 (4.08, 3.59, 3.66, 3.91, 3.84) [188]

UV (H^+) 282, 295, 304 (3.68, 3.73, 3.69) [189]
IR: 3113, 3067, 3022, 1704, 1652, 1635, 1620, 1540, 1498, 1382, 758
Mass: 160 (M^+), 133, 132, 105, 104, 92, 90, 78, 77
PMR (DMSO-d_6): 3.83 (NCH_3); 7.35 (H-8); 7.49 (H-6); 7.73 (H-7); 8.25 (H-2), 8.35 (H-5) [189]

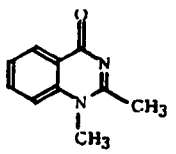
8. GLYCOPHYMOLINE



Glycosmis pentaphylla [35]
$C_{16}H_{14}N_2O$: 250.2990
mp.: 165°
UV: 230, 268, 276, 302, 312 (4.35, 3.85, 3.78, 3.50, 3.45)

IR: 1618, 1610, 1545, 1208
Mass: 249 (M^+-1), 235, 119, 91
PMR: 3.70 (3H, OCH_3); 4.23 (2H, CH_2); 7.25 (5H, H-Ar); 7.50–7.80 (3H, H-Ar); 8.10 (1H, H-5)

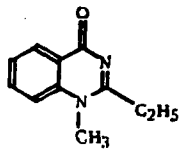
9. GLOMERINE



Glomeris marginata [20, 21]
$C_{10}H_{10}N_2O$: 174.0793
mp.: 198–200° [20]; 204–205° (e-a.) [21]
UV: 230, 265, 275, 305, 315
Mass: 174 (M^+), 146, 145, 133, 105, 104

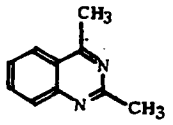
PMR: 2.63 (3H, s, CH_3); 3.76 (3H, s, NCH_3); 7.20–7.86 (3H, m, H-Ar); 8.23 (1H, dd, J=3, 7, H-5) [191]

10. HOMOGLOMERINE



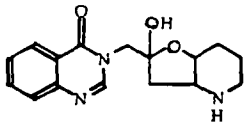
Glomeris marginata [20, 21]
$C_{11}H_{12}N_2O$: 188.0948
mp.: 145–147° [20]
149° (e-a) [192]
UV: 230, 265, 275, 305, 315
Mass: 188 (M^+), 160, 133, 105
PMR: 1.41 (3H, t, J=8, CH_2CH_3); 2.90 (2H, q, J=8, CH_2CH_3); 3.75 (3H, s, NCH_3); 7.33–7.80 (3H, m, H-Ar); 8.33 (1H, dd, J=3, 7, H-5) [191]

11. 2,4-DIMETHYLQUINAZOLINE



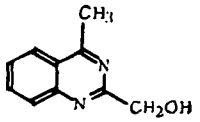
Pseudomonas aeruginosa, P.fluorescens, P.putida [36]
$C_{10}H_{10}N_2$: 158.2024
mp.: 63–64°

12. ISOFEBRIFUGINE* [227 a]



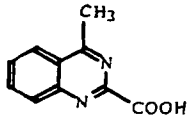
Dichroa febrifuga [37, 38], Hydrangea umbellata [39]
mp: 138–139° (ac.)
$[\alpha]_D$ +121° (chlf.) [226]
IR: 1695–1678, 1613, 1105, 1055 [226]

13. 2-HYDROXYMETHYL-4-METHYLQUINAZOLINE



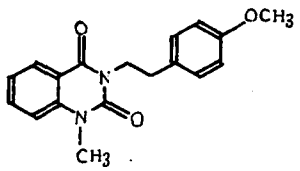
Pseudomonas aeruginosa, P. fluorescens, P.putida [36]
$C_{10}H_{10}N_2O$: 174.2014

14. 2-CARBOXY-4-METHYLQUINAZOLINE



Pseudomonas aeruginosa, P.fluorescens, P.putida [36]
$C_{10}H_8N_2O_2$: 188.1846

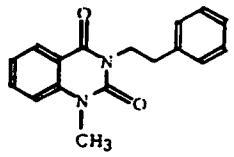
15. 3-(2′-[4″-METHOXYPHENYL)ETHYL]-1-METHYL-1H,3H-QUINAZOLINE-2,4-DIONE



Zanthoxylum arborescens [34]
$C_{18}H_{18}N_2O_3$: 310.1317
mp: 133–134° (e-a-pet.eth.)

UV: 222, 242, 276, 283, 310 (61000, –, 3200, 3200, 4100)
IR: 1700, 1660, 1620
Mass: 311 (10), 310 (M^+ 45), 155 (11), 135 (100), 134 (52), 121 (75), 119 (54), 58 (20), 57 (16)
PMR: 2.87 (2H, m, CH_2); 3.58 (3H, s, NCH_3); 3.77 (3H, s, OCH_3), 4.44 (2H, m, CH_2); 6.90, 7.20 (A_2B_2 system); 8.12 (1H, q, H-6)

16. 1-METHYL-3-(2′-PHENYLETHYL)-1H,3H-QUINAZOLINE-2,4-DIONE



Zanthoxylum arborescens [34]
$C_{17}H_{16}N_2O_2$: 280.1211
mp.: 100–102° (e-a-pet.eth.)
UV: 221, 240, 310 (61000, –, 4100)
IR: 1702, 1655, 1620

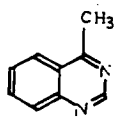
Mass: 280 (M^+, 67), 189 (28), 177 (35), 176 (100), 134 (27), 133 (28), 132 (15), 105 (40), 104 (77), 91 (15), 78 (17), 77 (27), 56 (15)

PMR: 2.93 (2H, m); 3.55 (3H, s, NCH_3); 4.40 (2H, m, CH_2); 7.80 (J=7, H–Ar); 8.12 (1H, q, H-6)

^{13}C NMR:

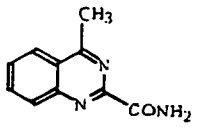
C-2	140.4	C-8	134.9	C-13	138.6
4	161.4	9	113.3	16	126.4
5	115.4	10	150.7	17	128.4*
6	128.9	11	34.0	18	128.9*
7	122.8	12	43.2	NCH_3	30.6

17. 4-METHYLQUINAZOLINE



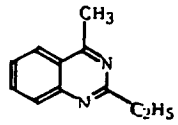
Pseudomonas aeruginosa, P.fluorescens, P.putida [36]
$C_9H_8N_2$: 144.1756
mp.. 36–37°

18. 4-METHYLQUINAZOLINE-2-CARBOXAMIDE



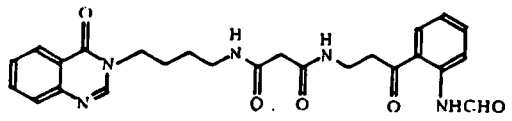
Pseudomonas aeruginosa, P.fluorescens, P.putida [36]
$C_{10}H_9N_3O$: 187.2002

19. 2-ETHYL-4-METHYLQUINAZOLINE



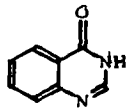
Pseudomonas aeruginosa, P.fluorescens, P.putida [36]
$C_{11}H_{12}N_2$: 172.2292

20. MONODONTAMIDE F



Monodonta labio [40]
$C_{25}H_{27}N_5O_5$: 477.5168

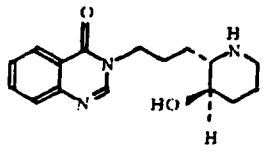
21. 4-OXOQUINAZOLINE



Dichroa febrifuga [30], Strobilanthes cusia [194]
$C_8H_6N_2O$: 146.1478
mp: 212–213° (alc.)
h-chl. 247° (eth.)

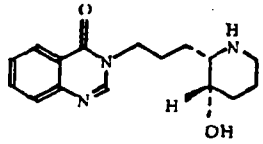
UV: 223, 265, 300, 313 (4.36, 3.81, 3.60, 3.54) [188]
IR: 1664, 1608 [197]
Mass: 146 (M^+) [221]

22. *trans*-FEBRIFUGINE



Hydrangea macrophylla [195]
$C_{16}H_{21}N_3O_2$: 287.3600

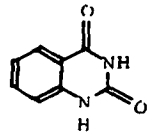
23. *cis*-FEBRIFUGINE* [227 b]



Dichroa febrifuga [37, 38], Hydrangea macrophylla [195], H.umbellata [39]
$C_{16}H_{21}N_3O_2$: 287.3600
mp. 158–160° (chlf.-pet. eth.)
$[\alpha]_D$+16° (alc.)

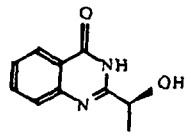
h-chl. 232-233° (meth.-HCl, dec.)
$[\alpha]_D$-12.8 (water)} [226]
IR: 1727, 1695–1678, 1613 [226]

24. QUINAZOLINE-2,4-DIONE



Strobilanthes cusia [194]
$C_8H_6N_2O_2$: 162.1468
mp.: 350°

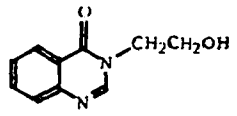
25. CHRYSOGINE



Alternaria citri [22], Penicillium chrysogenum [31]
$C_{10}H_{10}N_2O_2$: 190.2004
mp.: 190–192° (e-a)
$[\alpha]_D$–41° (alc.) [193]; –24° [31]
UV: 225, 230, 265, 271, 305, 316 (27500, 25500, 8250, 7500, 4200, 3450)

IR: 3370, 3120, 2875, 1675, 1625, 1605, 1050 [222]
PMR: [31]

26. ECHINOSOLINONE



Echinops echinatus [32]
$C_{10}H_{10}N_2O_2$: 190.2004
mp.: 150° (chlf.-meth.)
UV: 230, 265, 270, 319 (4.39, 3.67, 3.68, 3.77)
IR: 3320, 2920, 2880, 1665, 1620, 1572, 1555, 1495, 1212, 1050, 925, 840

Mass: 190 (M^+), 172, 146, 119, 91
PMR(CD_3OD): 3.20 (CH_2OH); 4.12 (2H, NCH_2); 7.40–7.65 (m,H-6, H-7, H-8); 8.00 (1H, H-5); 8.80 (H-2)

II. Tricyclic Quinazolines

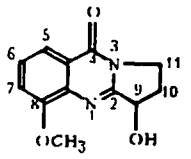
The tricyclic quinazoline alkaloids are found only in higher plants of the following families: Malvaceae (*Sida*), Fabaceae (*Galega*), Biebersteiniaceae (*Biebersteinia*), Peganaceae (*Peganum*), Nitrariaceae (*Nitraria*), Araliaceae (*Mackinlaya*), Rubiaceae (*Galium*), Scrophulariaceae (*Linaria*), Acanthaceae (*Adhatoda, Anisotes*), Poaceae (*Arundo*), and Arecaceae (*Daemonorops*). An exception is formed by 8-hydroxydeoxyvasicinone, isolated from a culture of the bacterium *Klebsiella pneumoniae* var. *oxytoca (Bacteriaceae)*. The tricyclic quinazolines are very numerous. At the present day, 39 compounds of this type are known. The richest sources of them are *Adhatoda vasica* (16 bases isolated), *Peganum harmala* (13 bases), and *Nitraria komarovii* (8 bases).

From the chemical point of view, this group is extremely inhomogeneous. Here it is possible to distinguish "classical" tricyclic quinazoline alkaloids having substituents in position 4 (keto group, hydroxyl, acetone residue), 6 (hydroxyl), 8 (methoxyl, hydroxyl), 9 (hydroxyl), and 11 (hydroxyl). These compounds are mainly characteristic for plants of the genera *Adhatoda, Sida, Peganum, Galium, Galega,* and *Linaria*). There are a number of alkaloids containing in position 9 a residue of methyl or ethyl anthranilate or N-methylanthranilate and also of N-dimethylaniline (alkaloids of the *Adhatoda* and *Anisotes* genera). There is one representative in each case with the cleavage of ring B (vasicol) and ring C (pegamine). N-oxides of tricyclic quinazoline bases have been isolated from *Nitraria komarovii* quite recently [78-80]. This is the first case of the reliable detection of compounds with groupings of this type among the quinazoline alkaloids. A single indirect mention of this is contained in [88], which also reports the finding of peganine and vasicinone glycosides in an aqueous extract from *Adhatoda vasica*. However, these glycosides were not isolated in the individual state and their structures remain unsubstantiated, for which reason we do not give them.

Quinazolines with a six-membered ring *C* and cleavage of the bond between rings *B* and *C* have been isolated from plants of the Australian genus *Mackinlaya*. And, finally, dimers (dipegine and nordine) have ben detected among compounds of the group under consideration.

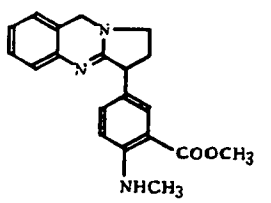
Some alkaloids of this group are narrowly specialized products of secondary metabolism (for example, the above-mentioned *Anisotes* and *Mackinlaya* alkaloids), while others, conversely, are widely distributed in the vegetable kingdom. For example, (±)-vasicinone is found in plants of 8 genera and 15 species, deoxyvasicinone in 7 genera and 9 species, and (±)-peganine in 6 genera and 24 species. Furthermore, in a number of cases, tricyclic quinazolines have been isolated from families that, according to some workers [89, 90], cannot in any way be called alkaloid-bearing (Malvaceae, Araliaceae, Arecaceae).

27. ADHAVACINONE



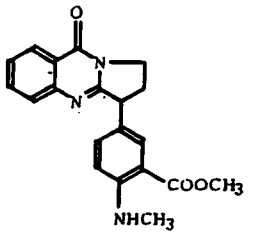
Adhatoda vasica [41]
$C_{12}H_{12}N_2O_3$: 232.2372
mp : 230–232°
$[\alpha]_D \pm 0°$
UV : (meth): 214, 238, 284, 314, 326 (4.60, 4.01, 4.21, 3.80, 3.62)
IR . 3260 1670, 1627, 1570, 1480, 1260, 850
Mass . 232 (M^+), 217 ($M-15)^+$
PMR . 2.35 (2H, m, H-2); 3.88 (3H, s, OCH_3); 4.25 (2H, m, H-1); 5.20 (1H, t, J=7, H-3); 7.20–7.40 (2H, m, H-6, H-7); 7.90 (1H, dd, J=8, 2, H-8)

28. ADHATODINE



Adhatoda vasica [83]
$C_{20}H_{21}N_3O_2$: 335.4040
mp .: 183°
UV: 225, 262, 300, 361 (4.51, 4.03, 3.86, 3.70)
IR (chlf.): 3378, 1678, 1626, 1608, 1575, 1439
IR 3385, 1685, 1630, 1598, 1575, 770
Mass: 335 (M^+, 100), 334 (78), 302 (11), 277 (14), 276 (14), 248 (10), 247 (11), 246 (12), 218 (9), 171 (28), 150.5 (21), 136.5 (14)

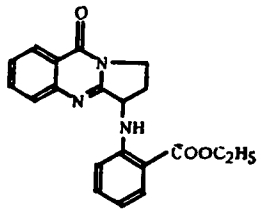
29. ANOSITINE



Adhatoda vasica [83], Anisotes sessiliflorus [69]
$C_{20}H_{19}N_3O_3$: 349.3872
mp .: 189–190° (ac.-hx.) [69]; 186° [83]
(3-hydroxy 185–187° (meth.)
UV: 212, 226, 259, 301, 312, 356 (37700, 54100, 14800, 4900, 4500, 5400)
IR: 2.99μ, 6.09μ, 5.95μ
Mass: 349 (M^+), 348, 317, 316, 290, 262, 185, 158.5

PMR (τ-scale): 1.73 (bd, J=9, H-8); 2.17 (d, J=3, H-2'); 3.36 (d, J=9, H-5'); 5.40–6.10 (3H, H-3, H-5); 6.20 (s, OCH_3); 7.12 (s, NCH_3); 7.20–8.00 (m, H-4) [69]

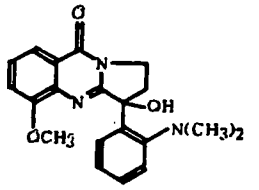
30. ANISESSINE



Anisotes sessiliflorus [69]
$C_{20}H_{19}N_3O_3$: 349.3872
mp .: 170–171° (meth.)
UV: 207, 225, 253, 300, 311, 340 (36600, 54100, 14700, 4900, 4200, 6300)
IR: 2.95μ, 6.05μ, 5.95μ
Mass: 349 (M^+), 303, 302, 275, 200, 183

PMR (τ-scale): 1.73 (bd J=4, H-8); 2.00 (dd, J=4.1, H-3'); 3.10 (d, J=4, H-6'); 3.27 (t, J=4, H-4'); 4.97 (1H, m, H-3); 5.30–6.20 (m, H-5); 7.10–7.84 (dm H-4)

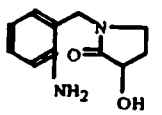
31. ANIFLORINE



Anisotes sessiliflorus [69]
$C_{20}H_{21}N_3O_3$: 351.1403
mp .: 195–197° (meth.)
UV: 207, 235, 286, 312, 324 (31300, 19900, 7000, 6600, 5800)
UV (H^+): 207, 236, 291, 312, 324 (30500, 16100, 6200, 7700, 7500)
IR: 2.90μ, 6.02μ

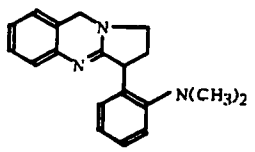
Mass: 351 (M^+), 318, 303, 231, 191, 161, 132
PMR (τ-scale): 2.05 (dd, J=8.1, H-8); 2.70–2.95 (H-3', H-4', H-5', H-6'); 5.40–5.90 (m, H-5); 6.12 (s, OCH_3); 7.20 (s, NCH_3); 7.00–7.50 (m, H-4)

32. VASICOL* [227 c]



Adhatoda vasica [81], Peganum harmala [82]

33. VASICOLINE



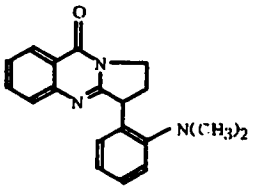
Adhatoda vasica [83]
$C_{19}H_{21}N_3$: 291.1395
mp .: 135° (ac.-heptane)
UV: 212, 224, 293 (4.10, 4.07, 3.81)
IR (chlf.): 1621, 1592, 1572
IR: 1652, 1590, 1570, 770, 720

Mass: 291 (M^+), 276, 259, 247, 185, 171, 169, 144, 130
PMR: 1.60–2.10 (2H, m, H-4); 2.67 [s, $N(CH_3)_2$]; 2.25–3.80 (2H, m, H-4); 3.10–3.40 (2H, m, H-5); 4.50 (1H, t, J=9, H-3); 4.60 (2H, s, H-7); 6.80–7.30 (8H, m, H-Ar)

^{13}C NMR [198]

164.9	127.6	50.0
153.1	124.5	47.6
143.6	123.7	46.0 (2C)
137.6	120.8	43.8
128.9	119.3	29.8
128.2		

34. VASICOLINONE



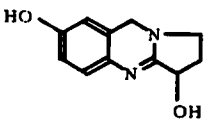
Adhatoda vasica [83]
$C_{19}H_{19}N_3O$: 305.3782
mp .: 152° (hx.) [83]; 155–156° [196]
UV: 227, 268, 305, 317 (4.33, 3.91, 3.52, 3.42)
IR (chlf.): 1664, 1618 [83]; 1665, 1615 [196]
IR: 1705, 1670, 1620, 785, 765
Mass: 305 (M^+), 290, 273, 261, 185, 144, 77

PMR: 1.90–2.90 (2H, m, H-4); 4.00–4.55 (2H, m, H-5); 5.04 (1H, t, J=9, H-3); 7.05–7.70 (7H, m, H-Ar); 8.31 (1H, bd, J=9, H-8) [83]

^{13}C NMR [198]

161.7	129.1	121.6
161.2	128.4	120.4
153.2	127.2	46.0 (2C)
149.5	126.2	45.6
136.7	126.0	45.0
133.8	125.0	29.7

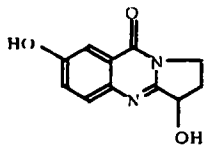
35. VASICINOL



Adhatoda beddomei [42], A.vasica [43], Sida acuta, S.humilis, S.rhombifolia, S.spinosa [44], S.cordifolia [45]
$C_{11}H_{12}N_2O_2$: 204.2272
mp .: 272–273°

$[\alpha]_D$+46° (e-a)
{6-OMe. 210°}

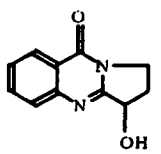
36. VASICINOLONE



Adhatoda vasica [46]
$C_{11}H_{10}N_2O_3$: 218.2104
mp .: 279°
{di-Ac. 204°}
UV(meth) 225, 276, 325
IR: 3400, 1670, 1624, 1600, 1490

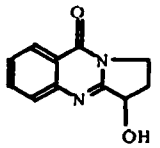
Mass: 218 (M^+, 100), 217 (7.7), 190 (5.9), 162 (83.3), 135 (53.1), 131 (13.4), 119 (16.4), 106 (14.2), 69 (57.5)
PMR (CD_3COOD): 2.40 (2H, m, H-2); 4.20 (2H, m, H-1); 5.60 (1H, t, H-3); 7.60 (3H, m, H-5, H-6, H-8)

37. (–)-VASICINONE* [227 d]



Adhatoda beddomei [42], A.vasica [47], Biebersteinia multifida [48], Galega officinalis [49], Galium aparine [50], Linaria transiliensis [51], L.vulgaris [52], Nitraria sibirica [53], Peganum harmala [54], P.nigellastrum [55], Sida acuta, S.humilis, S.rhombifolia, S.spinosa [44], S.cordifolia [45]

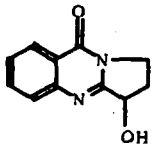
38. (±)-VASICINONE* [227 e]



Galium aparine [50], Nitraria komarovii [56], Peganum harmala [57]

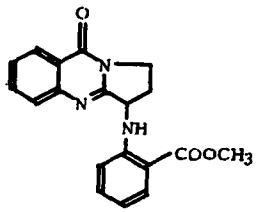
PMR: 2.26 (1H, J=13.4, 8.4, 7.2, 6.8, H-10e); 2.63 (1H, J=13.4, 7.6, 7.3, 4.7, H-10a); 4.03 (1H, J=12.3, 8.4, 4.7, H-11e); 4.33 (1H, J=12.3, 7.6, 7.2, H-11a); 5.16 (1H, J=7.3, 6.8, H-9); 7.51 (1H, J=8.1, 6.8, 1.3, H-6); 7.71 (1H, J=8.2, 1.3, 1.2, H-8); 7.78 (1H, J=8.2, 6.8, 1.3, H-7); 8.28 (1H, J=8.1, 1.3, 1.2, H-5) [117]

39. (+)-VASICINONE



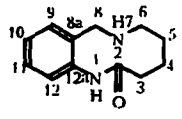
Adhatoda vasica [58]
$C_{11}H_{10}N_2O_2$: 202.2114
mp.: 201–202° (chlf.-e-a)
$[\alpha]_D$+148° (alc.)
{Ac. 135°, $[\alpha]_D$+10° (chlf.)

40. VASNETINE



Adhatoda vasica [84]
$C_{19}H_{17}N_3O_3$: 335.3604

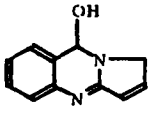
41. 3,4,5,6,7,8-HEXAHYDRO-1,7-BENZODIAZEPIN-2(1H)-ONE



Mackinlaya macrosciadia [86]
$C_{12}H_{16}N_2O$: 204.2708
mp.: 92.5–93.5° (CCl_4)
Mass: 204 (M^+)

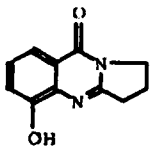
PMR: 1.65–1.85 (4H, m, H-4, H-5); 2.35–2.45 (2H, m, H-3); 3.17–3.28 (2H, m, H-6); 4.65 (2H, m, H-1, H-7); 4.50 (2H, s, H-8); 6.58–7.15 (4H,m, H-9, H-10, H-11, H-12)

42. (−)-8-HYDROXY-2,3-DEHYDRODEOXYPEGANINE



Galium aparine [50]
$C_{11}H_{10}N_2O$: 186.2124
mp: amorph.
$[\alpha]_D$−44°

43. 8-HYDROXYDEOXYVASICINONE

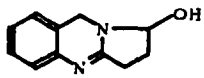


Klebsiella pneumoniae [187]
$C_{11}H_{10}N_2O_2$: 202.2035
mp.: 157° [187]; 158–160° [199]
UV (meth.) 205, 235, 242, 284, 315, 327 (22100, 22100, 18900, 5880, 5830, 5020)

IR (NaCl): 1660, 1620
Mass: 202.0735 (M^+, 100), 201 (45), 174.0792 ($C_{10}H_{10}N_2O$, 11), 145.0764 ($C_9H_9N_2$, 24), 145.0524 (C_9H_7NO), 145.0404 ($C_8H_5N_2O$), 106.0289 (C_6H_6NO, 17), 69.0578 (C_4H_7N, 18)
PMR (meth. chl.) :$XCH_2CH_2CH_2Y$ (2.23, quintet; 3.12, τ; 4.13, t; J=7.4, 8.2); arom. ABX system (H_a 7.22, H_b 7.35, H_x 7.64, J_{AB}=7.83, J_{BX}=8.49, J_{AX}=1.83)
^{13}CNMR:

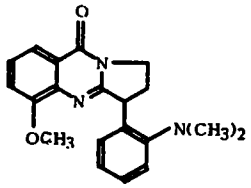
160.5	126.7	46.5
158.5	120.4	32.1
151.1	116.9	19.4
137.5	116.6	

44. (−)-1-HYDROXYDEOXYPEGANINE



Galium aparine [50]
$C_{11}H_{12}N_2O$: 188.2282

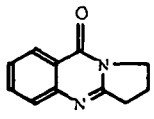
45. DEOXYANIFLORINE



Adhatoda vasica [83], Anisotes sessiliflorus [69]
$C_{20}H_{21}N_3O_2$: 335.4040
mp.: 168–172° (meth.)
UV: 211, 232, 285, 315, 330 (33000, 23100, 8600, 6900, 5800)
UV (H^+): 211, 237, 285, 315, 320(33000, 20300, 7700, 6900, 5700)
Mass: 335 (M^+), 320, 304, 215, 200, 144

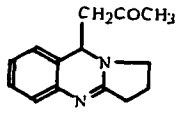
PMR (τ-scale) : 2.12 (dd, J=8.1, H-8), 2.70–3.10 (H-3', H-4', H-5', H-6'); 5.05 (dd, J=10.6, H-3); 5.60–5.95 (m H-5); 6.15 (s, OCH_3); 7.41 (s, NCH_3); 7.10–8.15 (m , H-4)

46. DEOXYVASICINONE* [227 f]



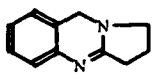
Adhatoda beddomei [42], Arundo donax [59], Galega officinalis [52], Linaria transiliensis [51], Mackinlaya macrosciadia [60], Nitraria komarovii [56], N. sibirica [53], Peganum harmala [54], P. nigellastrum [55]

47. DEOXYPEGANIDINE* [227 g]



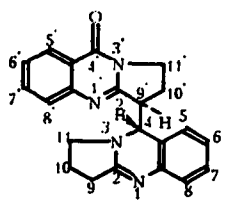
Peganum harmala [61]

48. DEOXYPEGANINE* [227 h]



Adhatoda vasica [62], Galega officinalis [52], Nitraria komarovii [56], Peganum harmala [62], P. nigellastrum [63]

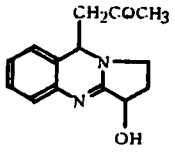
49. DIPEGINE* [227 i]



Peganum harmala [64]

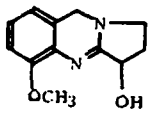
PMR: 1.91 (2H, H-10); 2.10 (1H, J=13.4, 9.0, 8.9, 8.2, H-10'a); 2.20 (1H, J=13.4, 8.9, 8.2, 4.3, H-10'e); 2.61 (1H, J=16.5, 6.5, 6.5, H-9e); 2.70 (1H, J=16.5, 9.5, 9.5, H-9a); 2.89 (1H, J=10.1, 7.8, 7.8, H-11a); 3.22 (1H, J=10.1, 5.9, 5.9, H-11e); 3.55 (1H, J=8.9, 8.9, 2.1, H-9'); 3.96 (1H, J=12.4, 8.2, 8.2, H-11'a); 4.19 (1H, J=12.4, 9.0, 4.3, H-11'e); 5.74 (1H, J=2.1, H-4); 7.08 (1H, J=8.0, 1.5, H-5); 7.10 (1H, J=7.9, 6.9, 1.5, H-7); 7.16 (1H, J=7.9, 1.8, H-8); 7.24 (1H, J=8.0, 6.9, 1.8, H-6); 7.51 (1H, J=8.0, 6.7, 1.6, H-6'); 7.74 (1H, J=8.2, 1.6, 0.6, H-8'); 7.80 (1H, J=8.2, 6.7, 1.4, H-7'); 8.30 (1H, J=8.0, 1.4, 0.6, H-5') [117]
Abs. conf. 4R, 9'S [117]

50. ISOPEGANIDINE* [227 j]



Peganum harmala [64]

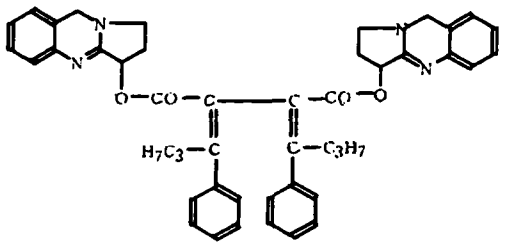
51. 8-METHOXYPEGANINE



Adhatoda vasica [65]
$C_{12}H_{14}N_2O_2$: 218.2540
mp .: 224–225°
$[\alpha]_D \pm 0°$
UV : 307 (3.85)

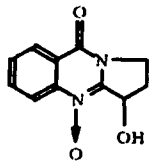
IR : 3470, 1630, 1605, 1500, 1250, 845
Mass: 218 (M^+), 217, 203, 199
PMR: 2.18 (2H, m, H-10); 3.21 (2H, m, H-11); 3.80 (3H, s, OCH_3); 4.50 (2H, s, H-4); 4.71 (1H, t, H-9); 6.60–7.00 (3H, m, H-5, H-6, H-7)

52. NORDINE



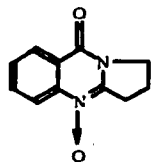
Daemonorops draco [87]
$C_{46}H_{46}N_4O_4$: 718.8922
mp .: 292°

53. VASICINONE N-OXIDE* [227 k]



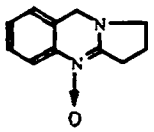
Nitraria komarovii [78]

54. DEOXYVASICINONE N-OXIDE* [227 *l*]



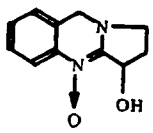
Nitraria komarovii [78]

55. DEOXYPEGANINE N-OXIDE* [227 m]



Nitraria komarovii [79]

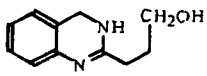
56. PEGANINE N-OXIDE



Nitraria komarovii [80]
$C_{11}H_{12}N_2O_2$: 204.2272
mp .: 207–208° (alc.-ac.)
$[\alpha]_D \pm 0°$

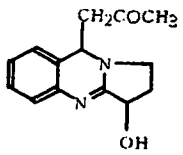
UV: 207, 220 sh., 225, 232 sh., 302 (4.16, 4.21, 4.27, 4.18, 4.06)
UV (H^+): 213, 220, 225 sh., 282
IR: 3150, 2940, 2860, 2840, 1630, 1585, 1510, 1465, 1270, 1230, 770.
Mass: 204(M^+, 3), 203 (4), 188(8), 187 (12), 186 (10), 171 (9), 155 (26), 140 (100), 123 (24), 122 (14), 98 (64), 84 (65), 83 (77).
PMR: 2.25, 2.66 (2H,m, H-10); 3.68 (2H, m, H-11); 4.75 (2H, s, H-4); 5.38 (1H, t, H-9); 6.15 (1H, br.sOH); 6.96 (1H,m, H-5); 7.16 (3H,m, H-6, H-7, H-8)

57. PEGAMINE* [227 n]



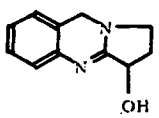
Peganum harmala [75]

58. PEGANIDINE* [227 o]



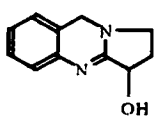
Peganum harmala [62]

59. (−)-PEGANINE [227 p]



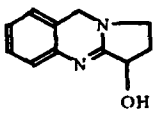
Adhatoda beddomei [42], A.vasica [66], Nitraria komarovii [56], Peganum harmala [67]

60. (±)-PEGANINE* [227 r]



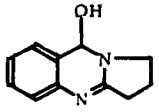
Adhatoda vasica [68], Anisotes sessiliflorus [69], Galega orientalis [70], Linaria alpina, L.anticaria, L.avenaria, L.pseudolaxiflora, L.repens, L.triornithophora [71], L.dalmatica, L.genistifolia [72], L.purpurea, L.ventricosa [73], L.popovii, L.transiliensis, L.vulgariformis [51], L.vulgaris [74], Peganum harmala [75], P.nigellastrum [55], Sida acuta, S.humilis, S. rhombifolia, S.spinosa [44], S.cordifolia [45]

61. (+)-PEGANINE



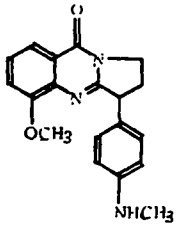
Galega officinalis [76].
$C_{11}H_{12}N_2O$: 188.2282
mp.: 170–173°
$[\alpha]_D$+163°

62. PEGANOL* [227 s]



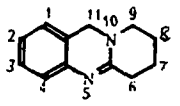
Peganum harmala [77]

63. SESSIFLORINE



Anisotes sessiliflorus [69]
$C_{19}H_{19}N_3O_2$ 321.3772
mp.: 195–197° (meth.)
UV: 212, 239, 286, 315, 327 (34700, 30300, 9200, 8800, 6600)
UV (H^+): 212, 239, 286, 315, 327 (30100, 19400, 7000, 6900, 5900)
IR: 6.05μ
Mass 321 (M^+), 306, 303, 277, 215, 191, 144
PMR (τ-scale): 2.11 (dd, J=8.1, H-8); 2.40–2.80 (m, H-3', H-5'); 3.21 (bd, J=6, H-2'); 3.21 (bd J=6, H-6'); 5.20–5.85 (3H,m, H-3, H-5); 6.06 (s, OCH_3); 7.05 (s, NCH_3), 7.10–7.60 (m H-4)

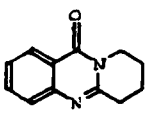
64. 6,7,8,9-TETRAHYDRO-11H-PYRIDO-[2,1-b]-QUINAZOLINE



Mackinlaya klossii [60]. M.macrosciadia, M.subulata [85]
$C_{12}H_{14}N_2$: 186.2560

mp.: 85–87° (eth.)
[sulf.: 285° (alc.) picr.: 217°]
UV: 242, 294 (3.78, 3.36)
IR (CCl_4): 3500, 3380, 3270, 1627 [60]
Mass: 186 (85), 185 (100), 144 (13), 89 (13), 77 (25), 51 (29)
PMR: 1.65–1.93 (4H, H-7, H-8), 2.28–2.73 (2H,m, H-6); 2.80–3.17 (2H,m, H-9); 4.33 (2H, s, H-11); 6.67–7.13 (4H,m, H-1, H-2, H-3, H-4) [200]

65. 6,7,8,9-TETRAHYDROPYRIDO-[2,1-b]-QUINAZOLIN-11-ONE



Mackinlaya klossii [60]. M. macrosciadia, M.subulata [85]
$C_{12}H_{12}N_2O$: 200.2392
mp.: 98.5–99.5° (hx.)

Mass: 200 (M^+, 100), 199 (85), 185(54), 130(13), 116(21), 90(27), 89(21), 77(25), 76(28) [200]
PMR: 2.00 (t, H-7, H-8), 2.80–3.15 (2H, t, H-6); 3.90–4.20 (2H, t, H-9); 7.42–7.63 (H-2, H-3, H-4); 8.12–8.33 (1H,m, J=8.2, H-1)

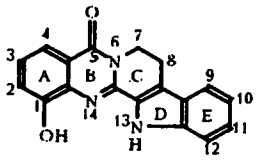
III. Quinazolinocarbolines

The quinazolinocarboline alkaloids form a very specific group of compounds found only in tropical representatives of the family Rutaceae (the genera *Araliopsis, Euxylophora, Evodia, Hortia, Tetradium, Vepris,* and *Zanthoxylum*). At the present time they number 27 compounds. The richest sources of them are *Euxylophora paraensis* (12 alkaloids) and *Evodia rutaecarpa* (10 alkaloids). As is known, in plants of the Rutaceae family the quinazolinocarbolines are present together with other classes of alkaloids — in particular, those of the furanoquinoline, acridone, and quinoline types. They all have a common anthranilic acid mechanism of biosynthesis. A special investigation has been devoted to questions of the distribution of alkaloid-bearing plants in this family [91]. Within this group, individual genera and species are characterized by the types of alkaloids that they contain. This is shown particularly clearly for species of the genera *Fagara* and *Zanthoxylum*, where the presence of certain bases is not a bad auxiliary taxonomic index. In light of these results and also of information on the distribution of quinazolinocarboline alkaloids over the genera in the Rutaceae family, the possibilities of the chemotaxonomy of this family (particularly the *Evodia* and *Euxylophora* genera) appear to us to be extremely promising.

The quinazolinocarbolines represent a chemical combination of two types of heterocyclic systems: indole and quinazoline. Among them are found representatives with cleavage of ring *B* or *C* and also with the cleavage of rings *B* and *C* simultaneously.

In a number of cases, moreover, ring *C* is dehydrogenated at the C_7–C_8 bond. Substituents may be present in rings *A* (hydroxyl, methoxyl, methylenedioxy) and *E* (methoxyl). The alkaloid paraensine is distinguished by an original structure, which includes an additional partially dehydrogenated pyran ring.

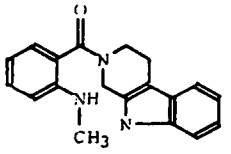
66. 1-HYDROXYRUTECARPINE



Euxylophora paraensis [92], Tetradium grabrifolium [94], Vepris louisii [93]
$C_{18}H_{13}N_3O_2$: 303.3188
mp.: 316–318° (meth.)
h-chl. 326–328° (meth.-chlf.)

UV (meth+NaOH): 309, 393 [92]
UV: 286, 293, 332, 348, 361, 279 (3.78, 3.83, 4.34, 4.45. 4.53, 4.42)
IR: 3340. 3275, 1660, 1630, 1607, 1570, 1533, 1500, 1440, 1394, 1322, 720 [93]
Mass: 303 (M^+, 100), 302 (72), 169 (3.8), 168 (9.4)
PMR: 3.31 (2H, t, J=7, H-8); 4.57 (2H, t, J=7, H-7); 7.12 (1H, dt, J=8.1, H-11); 7.21 (1H, dd, J=8.1, H-2); 7.32 (1H, t, J=8, H-3); 7.33 (1H, dt, J=8.1, H-10); 7.53 (1H, dd, J=8.1, H-12); 7.66 (1H, dd, J=8.1, H-4); 7.72 (1H, dd, J=8.1, H-9); 8.51 (1H, s, OH) [94]

67. GOSUIAMIDE I

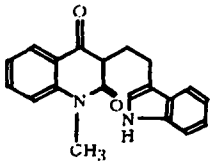


Evodia rutaecarpa [115]
$C_{19}H_{18}N_3O$: 304.3703
mp.: 178–180° (bz.-ac.)
UV: 225, 253, 281.5, 290, 313 (4.65, 4.04, 3.90, 3.84, 3.47)
IR: 3400, 3280, 2900, 1620, 1500, 1350, 1300, 1020, 990, 890, 740

Mass: 305 (M^+)
PMR (Py-d_5): 2.69 (3H, d, J=5.1, $NHCH_3$); 2.84 (2H, m, H-6); 3.85 (2H, m, H-6); 4.99–5.08 (2H, m, H-3); 6.08 (1H, q, J=5.1, H-14); 6.75 (1H, d, J=8.1, H-16); 6.80 (1H, t, J=7.3, H-18); 7.25–7.33 (2H, m, H-10, H-11); 7.36–7.40 (1H, m, H-17); 7.37 (1H, d, J=7.3, H-19); 7.57 (1H, d, J=8.1, H-12); 7.56 (1H, d, J=7.3, H-9)
^{13}C NMR (Py-d_5):

C-2	131.4 (s)	C-10	119.4 (d)	C-17	131.3 (d)
3	44.8 (t)	11	121.6 (d)	18	115.8 (d)
5	42.3 (t)	12	111.7 (d)	19	128.1 (d)
6	22.1 (t)	13	137.4 (s)	20	120.7 (s)
7	108.0 (s)	15	148.2 (s)	21	171.0 (s)
8	127.7 (s)	16	111.1 (d)	$NHCH_3$	30.0 (q)
9	118.3 (d)				

68. GOSUIAMIDE II



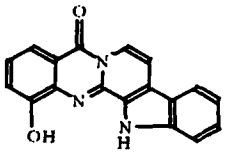
Evodia rutaecarpa [115]
$C_{19}H_{17}N_3O_2$: 319.3614
mp .: 216–218° (alc.)
IR 3330, 1690, 1650, 1610, 1490, 1430, 1400, 1360, 860, 840
Mass: 319 (M^+)

PMR (Py-d_5): 3.46 (2H, t, J=8.1, H-6); 3.49 (3H, s, NCH_3); 4.65 (2H, t, J=8.1, H-5); 7.13 (1H, d, J=8.8, H-16); 7.21 (1H, dd, J=8.1, 6.3, H-18); 7.30 (2H, m, H-9, H-11); 7.38 (1H, d, J=2.2, H-2); 7.60 (2H, m, H-12, H-17); 8.33 (1H, m, H-10); 8.40 (1H, dd, J=8.1, 1.5, H-19); 11.85 (1H, d, J=2.2, H-1)

^{13}C NMR (Py-d_5):

C-2	123.5 (d)	C-10	119.5 (d)	C-17	135.0 (d)
3	161.7 (s)	11	121.9 (d)	18	122.7 (d)
5	42.9 (t)	12	112.0 (d)	19	128.6 (d)
6	24.5 (t)	13	140.9 (s)	20	116.0 (s)
7	112.5 (s)	15	150.9 (s)	21	161.7 (s)
8	137.7 (s)	16	114.2 (d)	NCH_3	30.5 (q)
9	119.3 (d)				

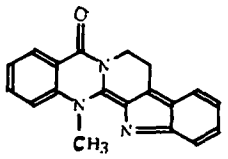
69. 1-HYDROXY-7,8-DEHYDRORUTECARPINE



Vepris louisii [93]
$C_{18}H_{11}N_3O_2$: 301.3030
mp .: >340° (meth.)
UV : 230, 258, 294, 312, 363, 381, 402 (4.70, 4.69, 4.44, 4.30, 4.44, 4.64, 4.68)
IR : 3360, 3270, 1690, 1670, 1640, 1610, 1580, 1550, 1490, 1380, 1330, 1245, 1145, 720

Mass 301 (M^+, 100), 300 (4), 272(4), 244 (10), 169 (7), 168 (46), 167 (7), 140 (13).
PMR (DMSO-d_6): 7.20–7.80 (6H, m, H-Ar); 7.85 (1H, d, J=7.5, H-8); 8.18 (1H, dd, J=8, 2, H-4); 8.55 (1H, d, J=7.5, H-7); 9.36 (1H, br.s, OH); 12.36 (1H, br.s, NH)

70. DEHYDROEVODIAMINE



Evodia meliaefolia [95], E.rutaecarpa [109]
$C_{19}H_{15}N_3O$: 301.3466
mp .: 189–190°
{h-chl. 215–218°}
UV : 246, 313, 365 (4.51, 4.02, 4.71)
IR : 3440, 1700, 1610, 1550, 1430, 1380, 1280, 1260, 1235, 1210, 1105, 760, 750, 735

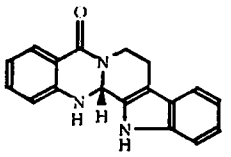
Mass: 301, 287, 286, 165, 156, 144.
PMR (DMSO-d_6): 3.33(2H, t, J=6.7, H-6), 4.40 (3H, s, CH_3), 4.47 (2H, t, J=6.7, H-5); 7.27 (1H, t, J=8.5, H-10); 7.52 (1H, dt, J=1.2, 8.5, H-11); 7.72 (1H, d, J=8.5, H-12); 7.80 (1H, dt, J=1.2, 8.5, H-18); 7.88 (1H, d, J=8.5, H-8); 8.13 (1H, dt, J=1.2, 8.5, H-17); 8.19 (1H, d, J=8.5, H-16); 8.35 (1H, dd, J=1.2, 8.5, H-19); 12.70 (1H, s, H-1)

^{13}C NMR (DMSO-d_6): [148]

C-21	158.2 (s)	C-18	128.6 (d)	C-20	118.7 (s)
3	149.9 (s)	19	127.7 (d)	16	118.4 (d)
13	141.4 (s)	8	123.3 (s)	12	113.5 (d)
15	139.6 (s)	10	121.6 (d)	5	42.0 (t)
17	136.7 (d)	9	121.5 (d)	22	40.8 (q)
7	130.4 (s)	2	120.0 (s)	6	18.5 (t)
11	128.8 (d)				

Pharm: hypotensive and negative chronotropic effects [203]
Uterine activity [204]. Vasodilator activity [223]

71. 13,14-DIHYDRORUTECARPINE

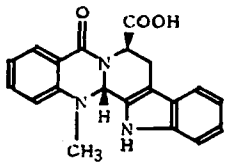


Evodia rutaecarpa [111]
$C_{18}H_{15}N_3O$: 289.3356
mp.: 214–216° (e-a) [111]: 226–228° [201]
$[\alpha]_D$–564° (DMF)
UV (meth.): 281, 290 (4.03, 3.91)

IR: 3330, 3280, 1633, 1618, 1609, 1425, 760, 750, 735
Mass: 289 (M^+), 159, 143 (100), 130 [206]
PMR (DMSO-d_6, TMS): 2.65–3.40 (4H, m); 4.83 (1H, dt, J=13.3); 6.06 (1H, s); 6.70–7.60 (7H, m); 7.80 (1H, dd, J=8.2); 10.90 (1H, br.s)
^{13}C NMR [201]

C-21	163.5	C-8	126.5	C-16	115.0
15	147.1	18	125.7	12	111.5
13	136.0	11	121.7	7	109.1
17	133.2	9	119.8	3	63.7
2	130.6	10	118.9	5	40.5
19	127.9	20	115.8	6	19.9

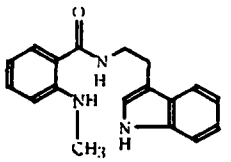
72. 7-CARBOXYEVODIAMINE



Evodia rutaecarpa [112]
$C_{20}H_{17}N_3O_3$: 347.3714
mp: amorph.
$[\alpha]_D$+441° (chlf.)
UV (acetonitrile): 268, 281, 289, 330
IR (chlf.): 3475, 1745, 1665

Mass: 302, 300, 229, 201, 134
PMR {$COOCH_3$}: 2.46 (s, NCH_3); 3.22 (J=16, 6, ABX); 3.55 (J=16, 1.5, ABX); 5.76 (J=6, 1.5, H-7, H-8); 6.22 (brs $W_{1/2}$=3, H-13b); 3.59 (s, $COOCH_3$); 7.10–7.70 (7H, H-Ar); 8.16 (1H, dd, J=8, 1.5, H-Ar); 8.41 (NH)
Abs. conf.: 7S, 13b S

73. N-(2-METHYLAMINOBENZOYL)TRYPTAMINE

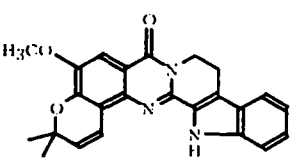


Evodia rutaecarpa [118]
$C_{18}H_{19}N_3O$: 293.1528
mp: 114–117° (bz.) [118]: 126–127° (toluene) [201]
UV: 223, 259, 284, 292, 346 (4.40, 3.93, 3.47, 3.45, 3.55)

IR 3450, 3272, 1633, 1583, 1519, 1280, 1220, 1170, 744, 733
Mass: 293 (M^+)
PMR (Py-d_5): 2.73 (3H, d, J=4.9, $NHCH_3$); 3.34 (2H, t, J=7.3, H-6); 4.00 (2H, q, J=7.3, H-5); 6.62 (1H, t, J=7.3, H-18); 6.71 (1H, d, J=8.5, H-16); 7.23 (1H, t, J=7.3, H-10); 7.29 (1H, dd, J=8.6, 7.3, H-11); 7.34 (1H, s, H-2); 7.36 (1H, dd, J=8.5, 7.3, H-17); 7.57 (1H, d, J=8.6, H-12); 7.90 (1H, d, J=7.3, H-19); 7.91 (1H, d, J=7.3, H-9); 8.32 (1H, bq, J=4.9, H-14); 9.01 (1H, br.t J=7.3, H-4); 11.75 (1H, s, H-1) [118]
^{13}C NMR (Py-d_5): [118]

C-2	123.4	C-10	119.2	C-17	132.7
5	41.2	11	121.8	18	114.6
6	26.4	12	111.2	19	128.7
7	113.3	13	137.7	20	116.7
8	128.5	15	151.2	21	170.7
9	119.3	16	111.2	$NHCH_3$	29.6

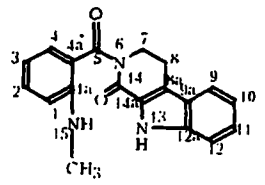
74. PARAENSINE



Euxylophora paraensis [119]
$C_{24}H_{21}N_3O_3$: 399.4470
mp.: 281–282° (bz.)
UV (meth): 342, 358, 376 (4.32, 4.42, 4.29)
IR (Nujol): 3310, 1650, 1640, 1600, 1550
Mass: 399(M^+), 384, 369, 358, 128, 115

PMR 1.48 (6H, s, 2xCH_3); 3.42 (2H, t J=7, CH_2CH_2N); 3.89 (3H, s, OCH_3); 4.51 (2H, t, J=7, CH_2CH_2N); 5.63 (d, J=10, H-olefin); 7.20–7.70 (H-Ar, H-olefin, NH); 7.53 (s, H-4)
PMR (Py-d_5): 1.48, 3.10; 3.76; 4.62; 5.56; 7.05–7.85; 7.88

75. RHETSININE

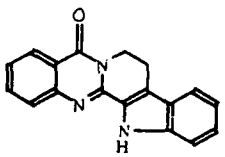


Araliopsis tabouensis [114], Zanthoxylum budrunga [116], Z.oxyphyllum [117], Z.rhetsa [113]
$C_{19}H_{17}N_3O_2$: 319.3614
mp .: 185–187° (alc.-eth.,dec.)
{h-chl. 258° (dec)}
UV: 314
UV (alc. +$NaBH_4$): 283, 292 [114]
IR: 3400, 3250, 1690, 1675
Mass: 319 (M^+) [116]; 186, 184, 157, 129, 105 [114]
PMR: 3.32 (2H, t, J=6, NCH_2CH_2); 4.40 (3H, bs, NCH_3); 4.48 (2H, t, J=6, NCH_2CH_2); 7.28 (1H, t, J=10, H-3); 7.53 (1H, dt, J=10.2, H-2); 7.71 (1H, br.d J=10, H-1); 7.81 (1H, dt, J=10.2, H-10); 7.89 (1H, bd, J=10, H-12); 8.14 (1H, dt, J=10.2, H-11); 8.20 (1H, bd, J=10, H-9); 8.36 (1H, dd, J=10.2, H-4); 12.60 (1H, s, NH)
^{13}C NMR: [116]

C-1	127.6	C-7	42.0	C-11	121.5
1a	141.3	8	18.5	12	113.4
2	136.6	8a	118.7	12a	130.2
3	128.6	9	118.5	14	150.0
4	128.7	9a	123.2	14a	139.6
4a	120.0	10	121.5	NCH_3	40.8
5	158.2				

HPLC: [202]

76. RUTECARPINE

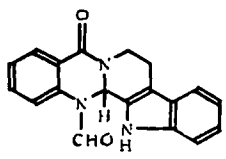


Evodia meliaefolia [95], E.rutaecarpa [96], Hortia arborea [97], H.badinii [98], H.regia [99], Zanthoxylum budrunga [100], Z.limonella [101], Z.pluviatile [102]
$C_{18}H_{13}N_3O$: 287.1060
mp .: 259° (bz.-pet.eth.) [100]; 265–266° (chlf.-meth.) [102]
UV (meth) 276, 288, 330, 344, 361 [205]
IR: 3325, 1655
Mass: 287 (M^+, 100), 286, 259, 258, 231, 229, 143.5, 143, 129 [206]
PMR: 3.23 (2H, t, J=7, $ArCH_2$); 4.60 (2H, t, J=7, CH_2N); 7.30–7.80 (8H, m, H–Ar); 8.30 (1H, s, NH) [207]
^{13}C NMR [201]

C-21	159.9	C-19	125.9	C-9	119.3
15	146.8	18	125.9	10	119.3
3	143.6	16	125.3	7	117.3
13	138.1	8	124.1	12	112.1
17	133.7	11	124.1	5	40.5
2	126.4	20	120.2	6	18.8

HPLC: [202]
Pharm: vasodilator effect [223]

77. 14-FORMYLDIHYDRORUTECARPINE

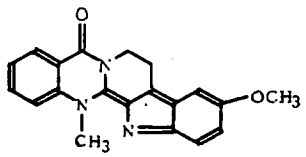


Evodia rutaecarpa [111]
$C_{19}H_{15}N_3O_2$: 317.3456
mp .: 280–281° (meth.-DMF)
$[\alpha]_D$+260° (DMF)
UV (meth.): 283, 291 (3.98, 3.91)
IR: 3342, 2918, 1690, 1608, 1493, 1472, 1413, 1378, 1327, 1318, 1302, 1282, 1240, 868, 771, 761, 747, 702
Mass: 318 (4), 317 (M^+, 16), 289 (11), 288 (52), 287 (100), 286 (53), 170 (22), 169 (62), 148 (11), 147 (9), 146 (18), 143 (13)
PMR (DMSO-d_6, TMS): 2.60–3.70 (3H, m); 4.72 (1H, dd, J=12.5, 5); 6.80–7.70 (8H, m), 7.92 (1H, d, J=8); 9.10 (1H, s); 11.05 (1H, br.s)

^{13}C NMR [201]

C-15	163.2	C-18	126.0	C-10	117.8
21	163.1	8	125.8	12	111.4
NCHO	162.0	20	119.8	7	110.8
13	136.8	11	119.5	3	61.8
17	133.0	16	119.2	5	43.6
2	131.2	9	118.0	6	19.0
19	126.8				

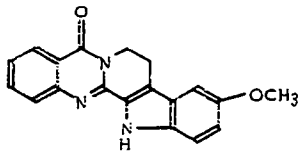
78. HORTIAMINE



Hortia arborea [103], H.braziliana [110]
$C_{20}H_{17}N_3O_2$: 331.1744
mp . 208° (bz .)
{h-chl. 243° (alc.water, dec.) m-i. 209° (alc.-water, dec.)}

UV (acetonitrile) : 411 (47300) [97]
Pharm: hypotensive action [110]

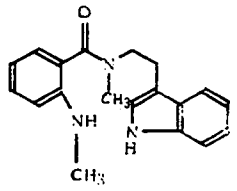
79. HORTIACINE



Hortia arborea [103], H.badini [98], H.longifolia [104]
$C_{19}H_{15}N_3O_2$: 317.3456
mp .: 252° (e-a)
IR: 3338, 1648, 1611, 1491, 1461, 1394, 1213, 1162, 1098, 1026, 798, 761 [201]

Mass: 318 (19), 317 (M^+, 100), 302 (23), 284 (22) [201]

80. EVODIAMIDE



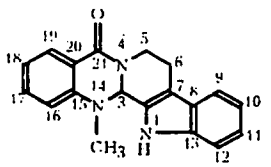
Evodia rutaecarpa [115]
$C_{19}H_{21}N_3O$: 307.3940
mp .: 208–209° (bz.)
UV: 221, 250, 284, 291, 311
IR: 3350, 3200, 1620, 1600, 1580, 1518, 1285, 1235, 1120, 750
Mass: 307 (M^+)

PMR: 2.66 (3H, d, J=4.4 $NHCH_3$); 3.00 (3H, br.s. NCH_3); 3.21 (2H, m, H-6); 3.86 (2H, m, H-5); 5.71 (1H, m, 14–NH); 6.71 (1H, d, J=8.8, H-9); 6.75 (1H, d, J=7.3, H-18); 7.24–7.36 (6H, m, H-2, H-10, H-11, H-12, H-17, H-19); 7.58 (1H, d, J=7.3, H-9); 11.86 (1H, s, 1–NH)

^{13}C NMR

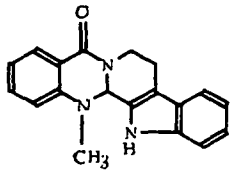
C-2	123.4	C-11	121.8	C-17	130.6
6	24.1	12	112.0	18	115.8
8	128.3	13	137.6	19	128.0
9	119.1	15	147.6	21	171.0
10	119.2	16	110.9	$NHCH_3$	30.0

81. (±)-EVODIAMINE



Zanthoxylum rhetsa [113]
$C_{19}H_{17}N_3O$: 303.3624
mp .: 277°
HPLC : [223]

82. (+)-EVODIAMINE

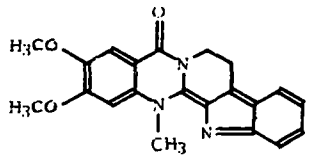


Araliopsis tabouensis [114], Evodia meliaefolia [95], E.rutaecarpa [96], Zanthoxylum rhetsa [113]
$C_{19}H_{17}N_3O$: 303.3624
mp .. 278°
$[\alpha]_D$+352°
UV : 314;
UV (alc.-$NaBH_4$): 283, 292
IR: 3400, 3250, 1690, 1675
Mass : 303(M^+, 100), 302, 274, 170, 169, 151.5, 143, 134 [206]
PMR : 2.53 (3H, s, NCH_3); 5.90 (1H, s, H-3); 7.30–7.80 (8H, m, H–Ar); 8.20 (1H, s, NH) [207]
^{13}C NMR [201]

C-21	164.1	C-8	125.8	C-12	111.5
15	148.7	11	121.8	7	111.4
13	136.3	9	120.2	3	69.7
17	133.3	20	119.2	5	39.5
2	130.3	10	118.8	NCH_3	36.4
18	127.4	16	118.1	6	19.4
19	127.3				

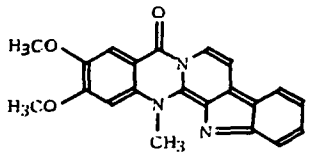
HPLC : [202, 203]
Pharm: vasodilator effect [223]. Antianoxic effect [224]

83. EUXYLOPHORINE A



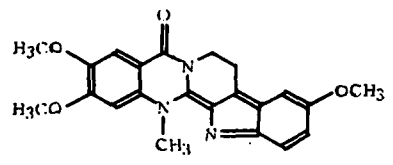
Euxylophora paraensis [105]
$C_{21}H_{19}N_3O_3$: 361.3982
mp .: 227–230° (bz.)
UV (acetonitrile) : 253, 402 (4.44, 4.60)
IR (Nujol) 1670, 1656, 1618, 1603, 1545
PMR (Py-d_5): 3.30 (2H, t); 3.90 (s, OCH_3); 3.96 (s, OCH_3); 4.75 (2H, t); 5.23 (s, NCH_3); 7.20–8.20 (6H, m, H–Ar)

84. EUXYLOPHORINE B



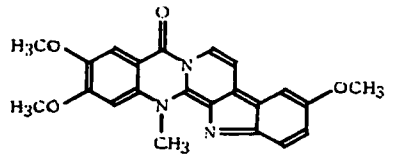
Euxylophora paraensis [106]
$C_{21}H_{17}N_3O_3$: 359.3824
mp .: 268–271° (chlf., dec.)
{h-chl. 270–280° (meth., dec.)
UV (acetonitrile) 278, 352 (4.47, 4.70)
UV (h-chl., acetonitrile): 297, 335, 346, 405 (4.28, 4.18, 3.43, 3.85)
IR (Nujol) 1690, 1618, 1605, 1555, 1510
IR {h-chl., Nujol} : 3320, 1710, 1615, 1580
Mass: 359 (M^+)
PMR(CD_3COOD+ chlf.): 4.22 (3H, s, OCH_3); 4.30 (3H, s, OCH_3); 4.81 (3H, br.s, NCH_3); 7.37 (1H, s, H-1); 8.05 (1H, s, H-4); 7.40–8.30 (4H, m, H–Ar); 8.32 (1H, d, J=9, H-8); 9.34 (1H, d, J=9, H-7); 11.70 (1H, br.s , NH).

85. EUXYLOPHORINE C



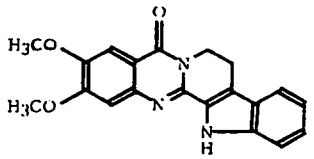
Euxylophora paraensis [107]
$C_{22}H_{21}N_3O_4$: 391.4240
mp .: 207–209° (bz., dec.)
UV (acetonitrile) 303, 408 (4.14, 4.40).
IR : 1665, 1620, 1555
Mass 391 (M^+)
PMR: 3.40 (2H, t, J=7, H-6); 4.02 (3H, s, OCH_3); 4.12 (3H, s, OCH_3); 4.15 (3H, s, OCH_3); 4.50 (3H, br.s $W_{1/2}$=3, NCH_3); 4.75 (2H, t, J=7, H-7); 7.20–7.60 (4H,m, H–Ar); 7.85 (1H, s, H-4); 10.10 (1H, br.s , NH)

86. EUXYLOPHORINE D



Euxylophora paraensis [107]
$C_{22}H_{19}N_3O_4$: 389.4082
mp .: 256–260° (bz., dec.)
UV.(acetonitrile) 277, 360 (4.33, 4.65)
Mass : 389 (M^+)

87. EUXYLOPHORICINE A



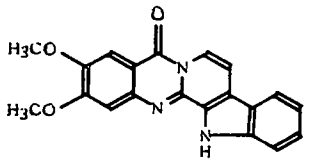
Euxylophora paraensis [105]
$C_{20}H_{17}N_3O_3$: 347.3714
mp .: 295–298° (chlf.-meth) [105]; 294–295° [201]
UV (meth.)255, 337, 353, 360 (4.50, 4.49, 4.54, 4.43)
IR (Nujol): 3300–3200, 1650, 1615, 1590

PMR : 3.10 (t) ; 3.80 (s, OCH_3); 3.85 (s, OCH_3); 4.60 (t); 7.20–7.90(m, NH, H–Ar)

^{13}C NMR [201]

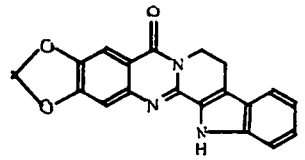
159.7 (s)	127.3 (s)	112.4 (d)
154.5 (s)	125.0 (s)	107.1 (d)
148.2 (s)	124.3 (d)	106.0 (d)
144.0 (s)	119.7 (2d)	55.8 (2q)
143.2 (s)	116.8 (s)	37.6 (t)
138.5 (s)	113.7 (s)	18.9 (t)

88. EUXYLOPHORICINE B



Euxylophora paraensis [105]
$C_{20}H_{15}N_3O_3$: 345.3556
mp .: 310–312° (chlf.-meth.)
UV: 256, 294, 304, 330, 353, 372, 392 (4.54, 4.40, 4.53, 4.37, 4.27, 4.45, 4.51)
IR (Nujol) 3350, 1656, 1634, 1600, 1575
PMR(CD_3COOD): 8.20, 9.13 (J=7, H-7, H-8)

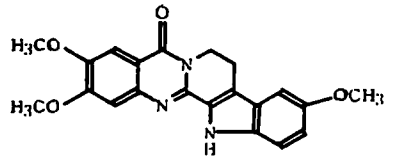
89. EUXYLOPHORICINE C



Euxylophora paraensis [106]
$C_{19}H_{13}N_3O_3$: 331.3288
mp .: 310–312° (sp.)
UV (acetonitrile): 252, 337, 350, 368 (4.55, 4.50, 4.53, 4.36)

IR (Nujol): 3350, 1655, 1630, 1600, 1550, 940 [106]
IR: 3345, 1653, 1631, 1598, 1471, 1331, 1228, 1131, 729 [201]
Mass 331 (M^+)
PMR(CD_3COOD+chlf.): 3.58 (2H, t, J=7, H-8); 4.82 (2H, t, J=7, H-7); 6.28 (2H, s, OCH_2O); 7.28 (s, H-1); 7.72 (1H, s, H-4); 7.20–7.80 (4H,m, H–Ar); 10.60 (1H, br.s, NH)

90. EUXYLOPHORICINE D



Euxylophora paraensis [107]
$C_{21}H_{19}N_3O_4$: 377.3972
mp .: 293–295° (chlf.) [107]; 291–292° [201]
UV (acetonitrile) 252, 341, 356, 374 (4.44, 4.45, 4.48, 4.32)

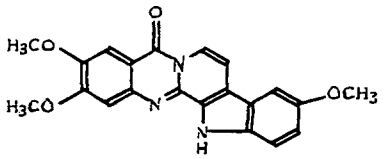
IR: 3450, 1670, 1620, 1600 [107]
IR: 3365, 1652, 1612, 1492, 1460, 1292, 1230, 1097, 818
Mass 377 (M^+)

PMR : 3.43 (2H, τ, J=7, H-8); 4.03 (3H, s, OCH_3); 4.10 (6H, s, 2xOCH_3); 4.78 (2H, t, J=7, H-7); 7.20–7.60 (4H,m, H-Ar); 7.78 (1H, s, H-4); 7.95 (1H, br.s, NH)

^{13}C NMR: [201]

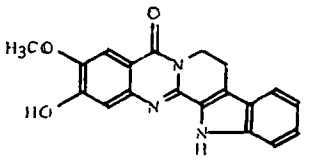
159.7 (s)	133.6 (s)	113.2 (d)
154.4 (s)	127.5 (s)	105.8 (d)
153.6 (s)	125.0 (s)	100.3 (d)
148.0 (s)	116.3 (s)	55.6 (2q)
144.0 (s)	115.4 (d)	38.0 (d)
143.2 (s)	113.5 (s)	18.9 (t)

91. EUXYLOPHORICINE E



Euxylophora paraensis [107]
$C_{21}H_{17}N_3O_4$: 375.3814
mp .: 290° (chlf.)
UV(chlf.) 255, 289, 292, 307, 355, 376, 398 (4.65, 4.55, 4.48, 4.54, 4.57, 4.62, 4.64)
Mass 375 (M^+)

92. EUXYLOPHORICINE F



Euxylophora paraensis [108]
$C_{19}H_{15}N_3O_3$: 333.3446
mp .: 226° (bz.-pet.eth.)
UV (meth.) 247, 337, 347, 364 (4.50, 4.48, 4.51, 4.43)
UV (meth. +NaOH): 304
UV (meth .+HCl): 372

IR : 3300
Mass: 333 (M^+, 100), 332 (22), 318(15), 303.6, 264.4, 166.5 (13)
PMR (CD_3COOD-chlf.): 3.53 (t, CH_2CH_2N); 4.90 (t, J=7.0, CH_2CH_2N); 4.20 (s, OCH_3); 7.20–7.80 (5H,m, H-Ar); 7.92 (1H, s, H-4)

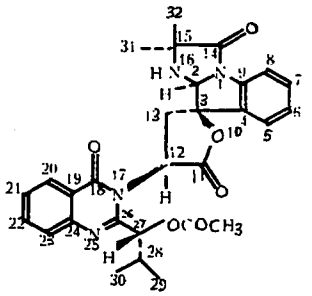
IV. Tryptoquivalines

Tryptoquivaline and its analogs are products of the vital activity of three species of ascomycetous fungi (Ascomycetes): *Aspergillus clavatus, Aspergillus fumigatus*, and *Corynascus setosus*. Up to the present time, two groups of workers, from the USA and Japan, have isolated 19 substances of this nature.

They are all fairly complex heterocyclic systems consisting of six rings, one of which is a spiro-γ-lactone. The latter is attached to the indole part of the molecule in position 3. The indole component, in its turn, is linked with a saturated imidazole ring by an N_1–C_2 bond. The quinazoline unit is bound to the spiro-γ-lactone ring by an N_{17}–C_{12} bond. In all these structures, the presence of three carbonyl functions at carbon atoms 11, 14, and 18 is obligatory. The N_{16} nitrogen may have the following substituents: hydrogen, hydroxyl, methoxycarbonyl. The quinazoline part of the molecule frequently contains a grouping of one of three types: CH(OH)-$CH(CH_3)_2$, CH(OAc)-$CH(CH_3)_2$, CO-$CH(CH_3)_2$. Finally, in position 15 there are one or two methyl groups. In addition to the complex structure, which was revealed mainly by the XSA method, the tryptoquivalines possess four or five asymmetric centers. These are the C_2, C_3, C_{12}, C_{15}, and C_{27} carbon atoms. The absolute configurations of these centers were also determined for nortryptoquivaline by the XSA method [124].

It is interesting to note that in the microorganism *Aspergillus fumigatus* tryptoquivalines are produced together with other quinazoline derivatives — fumiquinazolines A, B, and C, which are discussed below.

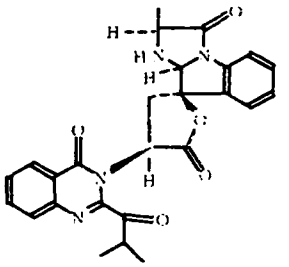
93. DEOXYNORTRYPTOQUIVALINE



Aspergillus clavatus [120]
$C_{28}H_{28}N_4O_6$: 516.2009
mp: 158–160° (eth.)
$[\alpha]_D$ +70° (chlf.)
UV 228, 233, 254, 268, 278, 305, 317 (43900, 40100, 15600, 11700, 10500, 4100, 3300)
IR (chlf.) : 3360, 2975, 2935, 2880, 1790, 1724, 1676, 1607, 1483
Mass 516 (M^+, 100)

PMR 1.00 (3H, d, J=7); 1.15 (3H, d, J=7); 1.55 (3H, d, J=7); 2.16 (3H, s); 2.58 (1H, m); 2.87 (1H, dd, J=10,13); 3.07 (1H, dd, J=10,13); 4.12 (1H, q, J=7); 5.22 (1H, s); 5.55 (1H, d, J=9); 5.65 (1H, t, J=10); 7.02–7.74 (7H, m); 8.14 (1H, m)

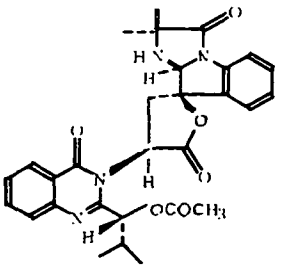
94. DEOXYNORTRYPTQUIVALONE



Aspergillus clavatus [120]
$C_{28}H_{24}N_4O_5$: 472.1747
mp: 192–193° (eth.)
$[\alpha]_D$ +171° (chlf.)
UV 232, 288, 320 (32400, 9250, 6250)
IR (chlf.) : 3360, 2980, 2935, 2880, 1790, 1705, 1680, 1610, 1588, 1484, 1469
Mass 472 (M^+)

PMR: 1.26 (3H, d, J=7); 1.30 (3H, d, J=7); 1.56 (3H, d, J=7); 3.02 (1H, dd, J=10, 13); 3.32 (1H, dd, J=10, 13); 4.08 (1H, m, J=7); 4.12 (1H, q, J=7); 5.36 (1H, s); 5.48 (1H, t, J=10); 7.04–7.84 (7H, m); 8.24 (1H, m)
HPLC

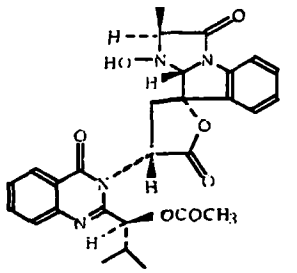
95. DEOXYTRYPTOQUIVALINE



Aspergillus clavatus [120]
$C_{29}H_{30}N_4O_6$: 530.5768
mp: 150–152° (meth.chl.-hx.)
$[\alpha]_D$ -57° (chlf.)
UV 227, 232, 252, 267, 278, 304, 318 (44500, 41900, 18500, 12000, 10300, 3300, 2700)
IR (chlf.) : 3360, 3310, 2980, 2935, 2875, 1790, 1720, 1676, 1604, 1483, 1469.
Mass 530 (M^+, 100)

PMR: 1.04 (3H, d, J=7); 1.20 (3H, d, J=7); 1.53 (6H, s); 2.16 (3H, s); 2.54 (1H, m); 3.06 (2H, d, J=10); 5.24 (1H, s); 5.52 (1H, d, J=9); 5.65 (1H, t, J=10); 7.11–7.74 (7H, m); 8.20 (1H, m)
HPLC

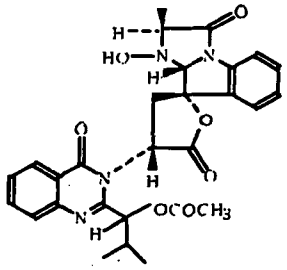
96. NORTRYPTOQUIVALINE



Aspergillus clavatus [120], A.fumigatus [124]
$C_{28}H_{28}N_4O_7$: 532.1958
mp: 256–258° (meth. chlf.-hx.)
$[\alpha]_D$ +170° (chlf.)
UV 228, 233, 254, 267, 279, 306, 319 (43600, 42000, 18700, 11900, 10200, 4500, 3500)
IR (chlf.) : 3490, 2980, 2940, 2880, 1790, 1728, 1670, 1610, 1485, 1471, 1410.
Mass 532 (M^+)

PMR 1.02 (3H, d, J=7), 1.16 (3H, d, J=7); 1.58 (3H, d, J=7); 2.16 (3H, s); 2.57 (1H, m); 2.94 (1H, dd, J=10, 13); 3.18 (1H, dd, J=10, 13); 4.28 (1H, q, J=7); 5.10 (1H, s); 5.54 (1H, d, J=9); 5.65 (1H, t, J=10); 7.01–7.79 (7H, m); 8.12 (1H, m)
XSA: [124]
Abs. conf. 2S, 3S, 12R, 15S, 27S [124]
HPLC
Pharm: antibacterial activator

97. CS-B



Corynascus setosus [208]
$C_{28}H_{29}N_4O_7$: 533.2023
mp t.: 236–238° (meth.)
$[\alpha]_D$ +196° (chlf.)
UV (meth.) 209, 290, 307, 318 (4.64, 3.80, 3.53, 3.43)
IR (chlf.) : 3500, 3000, 1780, 1720, 1660, 1600
Mass 533.2023 (M^+)

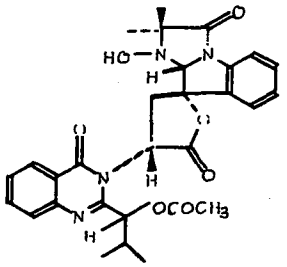
PMR 5.23 (s, H-2); 7.41 (bd, J=7.6, H-5); 7.28 (td, J=7.6, 1.1, H-6); 7.49 (td, J=7.6, 1.1, H-7); 7.63 (br.d J=7.6, H-8); 5.87 (t, J=10.1, H-12); 3.09 (dd J=13.3, 9.5, H-13); 3.15 (dd J=13.3, 10.7, H-13); 4.35 (q, J=7.2, H-15); 7.16 (s, 16-OH); 8.22 (dd, J=8.4, 1.5, H-20); 7.55 (td, J=8.4, 1.3, H-21); 7.84 (td, J=8.4, 1.5, H-22); 7.79 (br.d J=8.4, H-23); 5.66 (d, J=9.8, H-27); 2.68 (m H-28); 0.98 (3H, d J=6.6, H-29); 1.16 (3H, d, J=6.6, H-30); 2.21 (3H, s, H-33); 1.59 (3H, d, J=7.2, H-34)

^{13}C NMR

C-2	89.9 (d)	C-13	34.1 (t)	C-24	146.5 (s)
3	83.9 (s)	14	169.2 (s)	26	151.5 (s)
4	133.7 (s)	15	67.9 (d)	27	79.0 (d)
5	123.7 (d)	18	161.8 (s)	28	31.8 (d)
6	125.7 (d)	19	120.3 (s)	29	19.0 (q)
7	131.9 (d)	20	126.7 (d)	30	18.9 (q)
8	116.1 (d)	21	128.3 (d)	32	170.5 (s)
9	137.8 (s)	22	135.5 (d)	33	20.8 (q)
11	169.3 (s)	23	128.0 (d)	34	11.0 (q)
12	54.6 (d)				

Abs. conf. 27R

98. CS-C



Corynascus setosus [208]
$C_{29}H_{31}N_4O_7$: 547.2183
mp t.: 225–227° (meth.)
$[\alpha]_D$ −138° (chlf.)
UV (meth.) 209, 289, 306, 318 (4.67, 3.83, 3.54, 3.44)
IR (chlf.) 3500, 3000, 1790, 1735, 1675, 1610
Mass 547.2183 (M^+)

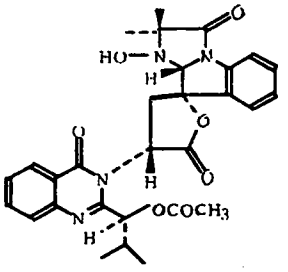
PMR 5.05 (s H-2), 7.41 (br.d J=7.6, H-5); 7.28 (td J=7.6, 1.1, H-6); 7.48 (td J=7.6, 1.1, H-7); 7.64 br.d J=7.6, H-8), 5.88 (t, J=10.0, H-12); 3.12 (dd J=13.5, 9.7, H-13); 3.14 (dd J=13.5, 10.1, H-13); 6.99 (s, 16-OH); 8.25 (dd J=7.2, 1.3, H-20); 7.55 (td, J=7.2, 1.2, H-21); 7.84 (td J=7.2, 1.3, H-22); 7.79 (br.d J=7.2, H-23); 5.65 (d 10.1, H-27); 2.69 (m H-28); 1.06 (3H, d J=6.8, H-29); 1.17 (3H, d, J=6.8, H-30); 2.22 (3H, s, H-33); 1.49 (3H, s, H-34); 1.50 (3H, s, H-35)

^{13}C NMR

C-2	87.6 (d)	C-13	34.6 (t)	C-26	151.5 (s)
3	83.9 (s)	14	169.4 (s)	27	78.9 (d)
4	133.7 (s)	15	71.4 (s)	28	31.8 (d)
5	123.7 (d)	18	161.7 (s)	29	18.9 (q)
6	125.6 (d)	19	120.3 (s)	30	18.9 (q)
7	131.9 (d)	20	126.8 (d)	32	170.6 (s)
8	116.1 (d)	21	128.2 (d)	33	20.8 (q)
9	138.1 (s)	22	135.5 (d)	34	16.9 (q)
11	169.4 (s)	23	128.0 (d)	35	22.8 (q)
12	54.7 (d)	24	146.5 (s)		

Abs. conf. 27R

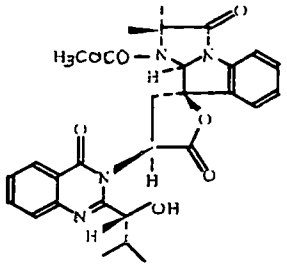
99. TRYPTOQUIVALINE



Aspergillus clavatus [125], A.fumigatus [121]
$C_{29}H_{30}N_4O_7$: 546.2114
mp : 153–155°
$[\alpha]_D$–142° (chlf.)
UV 228, 275, 305, 317 (37000, 8550, 3800, 3040)
IR (chlf.), 3520, 1790, 1735, 1680, 1615
Mass 546 (M^+)

PMR 1.03 (3H, d, J=7); 1.17 (3H, d, J=7); 1.50 (3H, s); 1.52 (3H, s); 2.19 (3H, s); 2.63 (1H, m); 3.10 (1H, d, J=10); 3.15 (1H, d, J=10); 3.63 (1H); 4.04 (1H); 5.00 (1H, c); 5.61 (1H, d J=9); 5.70 (1H, t J=10); 7.12–7.90 (7H,m); 8.22 (1H, d, J=8) [125]
XSA {p-bromophenylurethane deriv.} [125]
Abs. conf: 27S [208]
HPLC [120]
Pharm: anticonvulsive activity

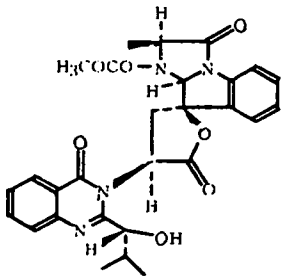
100. TRYPTOQUIVALINE C



Aspergillus fumigatus [121]
$C_{29}H_{30}N_4O_7$: 546.5758
mp : 215–217° (meth., dec.)
$[\alpha]_D$–168° (chlf.)
UV (meth.) 228, 233, 255, 280, 307, 320 (39800, 38000, 21100, 14200, 4200, 2700)
IR: 3490, 1760, 1745, 1665, 1600
Mass 546 (M^+)

PMR 1.04 (3H, d, J=6), 1.14 (3H, d, J=6); 1.48 (3H,s.); 1.50 (3H, s); 2.17 (3H, s); 3.03 (1H, dd, J=14, 10); 3.20 (1H, dd J=14, 10); 2.67 (1H,m); 4.99 (1H, s); 5.59 (1H, d, J=9); 5.67 (1H, t, J=10); 7.08 (1H, s); 7.33–7.93 (7H,m); 8.22 (1H, d, J=8)

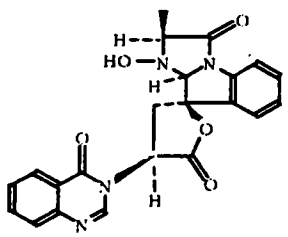
101. TRYPTOQUIVALINE D



Aspergillus fumigatus [121]
$C_{28}H_{28}N_4O_7$: 532.5490
mp.: 224–225° (meth., dec.)
$[\alpha]_D$–115° (chlf.)
UV (meth.) 227, 233, 257, 277, 305, 319 (48100, 45200, 21500, 14500, 4800, 3300)
IR 3430, 1778, 1732, 1660, 1610
Mass 532 (M^+)

PMR: 0.97 (3H, d, J=7); 1.09 (3H, d, J=7); 1.56 (3H, d, J=7); 2.14 (3H, s); 2.57 (1H, m); 2.93 (1H, dd, J=14.9); 3.19 (1H, dd, J=14.9); 4.32 (1H, q, J=7); 5.10 (1H, s); 5.61 (1H, d J=8); 5.74 (1H, t J=9); 7.26 (1H, s); 7.11–7.99 (7H,m); 8.24 (1H, d, J=8)

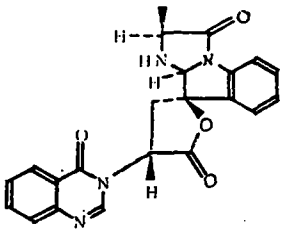
102. TRYPTOQUIVALINE E



Aspergillus fumigatus [122]
$C_{22}H_{18}N_4O_5$: 418.1277
mp : 257° (ac., dec.)
$[\alpha]_D$–257° (chlf.)
UV (meth.)225.5, 232, 254, 265.5, 275.5, 291, 303, 315 (32300, 29800, 16000, 11700, 8400, 3500, 3000, 2600)
IR 3430, 1780, 1740, 1732, 1677, 1658, 1614
Mass 418 (M^+, 100), 402 (94), 356 (22), 254 (37), 215 (86)

PMR (Py-d_5): 1.63 (d, J=7, CH_3); 3.38, 3.56 (dd, J=13, 10, CH_2); 4.26 (q J=7, CH); 5.42 (s, CH); 6.48 (t, J=10, CH); 6.83–7.80 (7H,m, H–Ar); 8.17 (1H, d, J=8, =CH-); 8.59, 8.66 (1H, s, =CH-); 10.42 (br.s NOH)

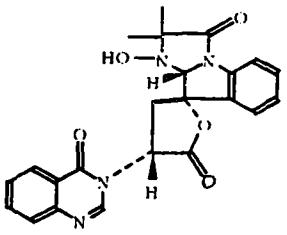
103. TRYPTOQUIVALINE F



Aspergillus fumigatus [122]
$C_{22}H_{18}N_4O_4$: 402.1328
mp: 277° (meth., dec.)
$[\alpha]_D$-109° (chlf.)
UV (meth.) 226, 232, 255, 265, 276, 290, 303, 315 (33400, 31200, 12400, 11100, 8100, 3100, 2800, 2200)
IR: 3365, 1775, 1725, 1664, 1606
Mass 402 (M^+, 50), 374 (22), 215 (47), 146 (100)

PMR (Ac.): 1.68 (d, J=7, 31-CH_3, 32-CH_3); 2.15 (s, Ac); 3.19, 3.33 (dd, J=13.9, 13-CH_2); 4.44 (q, J=7, 15-CH); 5.40 (t, J=9, 12-CH); 5.65 (s, 2-CH); 7.12–8.07 (7H, m, H-Ar); 8.04 (1H, s, H-26); 8.21 (1H, d, J=7, H-20)

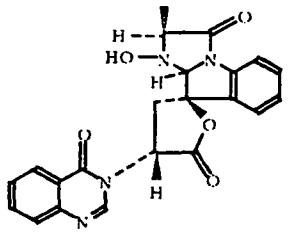
104. TRYPTOQUIVALINE G



Aspergillus fumigatus [122]
$C_{23}H_{20}N_4O_5$: 432.1433
mp: 240–241.5° (ac., dec.)
$[\alpha]_D$-215° (ac.)
UV (meth.) 226, 232, 253, 265, 275, 291, 302, 315 (34300, 31700, 17400, 11800, 8200, 3700, 3000, 2500
IR: 3470, 1778, 1738, 1662, 1610.
Mass 432 (M^+, 53); 414 (12), 386 (16), 242 (68), 229 (100), 228 (65)

PMR (Py-d_5): 1.50 (s, 31-CH_3); 1.62 (s, 32-CH_3); 3.43, 3.64 (dd, J=14, 10, 13-CH_2); 5.30 (s, 2-CH); 6.56 (t, J=10, 12-CH); 6.96–7.96 (7H, m, H–Ar); 8.23 (1H, d, J=8, H-20); 8.66 (1H, s, H-26); 10.64 (bs, NOH)

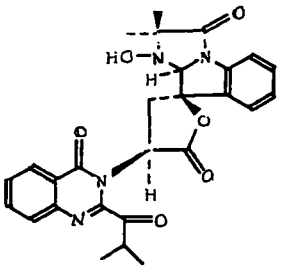
105. TRYPTOQUIVALINE H



Aspergillus fumigatus [122]
$C_{22}H_{18}N_4O_5$: 418.1277
mp 274° (meth., decomp.)
$[\alpha]_D$-155° (ac.)
UV (meth.) 226, 232, 255, 266, 276, 291, 303, 315 (33100, 30900, 16600, 11300, 8500, 3600, 3100, 2500)
IR: 3430, 1780, 1742, 1734, 1667, 1609
Mass 418 (M^+, 20), 400 (7), 215 (47), 146 (100)

PMR (Py-d_5): 1.45 (d, J=8, 31-CH_3, 32-CH_3); 2.96, 3.60 (dd, J=13, 10, 13-CH_2); 3.98 (q, J=8, 15-CH); 5.25 (s, 2-CH); 5.76 (t, J=10, 12-CH); 6.68–7.88 (7H, m, H–Ar); 8.11 (1H, d, J=8, H-20); 8.38, 8.41 (1H, s, H-26); 10.60 (br.s NOH)

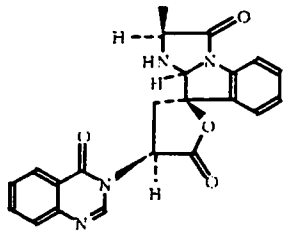
106. TRYPTOQUIVALINE I



Aspergillus fumigatus [122]
$C_{27}H_{26}N_4O_6$: 502.1852
mp: 232–235.5° (meth. chl.-meth, dec.)
$[\alpha]_D$+239° (chlf.)
UV (meth.) 235, 250, 292, 321 (31700, 21400, 9600, 6100)
IR: 3480, 1780, 1732, 1710, 1675, 1609.
Mass 502 (M^+, 28), 486 (19), 252 (20), 242 (32), 229 (100)

PMR 1.22 (d J=7, 29-CH_3); 1.28 (d, J=7, 30-CH_3); 1.49 (6H, s, 31-CH_3, 32-CH_3); 3.06, 3.39 (dd, J=14, 10, 13-CH_2); 4.07 (q, J=7, 28-CH); 4.99 (s, 2-CH); 5.47 (t, J=10, 12-CH); 7.00–7.94 (7H, m, H–Ar); 8.24 (1H, d, J=7, H-20); 7.01 (s, NOH)

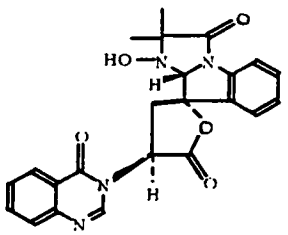
107. TRYPTOQUIVALINE J



Aspergillus fumigatus [122]
$C_{22}H_{18}N_4O_4$: 402.1328
mp.: 254–258° (ac.-meth., water)
$[\alpha]_D$+135° (chlf.)
UV (meth.): 225.5, 231, 253, 264, 275, 290, 302, 310 (41100, 38000, 16200, 12800, 9700, 4200, 3900, 3100)
IR: 3375, 1780, 1713, 1670, 1610
Mass: 402 (M^+, 59), 215 (24), 202 (23), 174 (71), 44 (100)

PMR(DMSO-d_6): 1.41 (d, J=7, 31-CH_3, 32-CH_3); 3.08, 3.10 (d, J=10, 13-CH_2); 3.87 (q, J=7, 15-CH); 5.41 (bd, J=6, 2-CH); 6.01 (t, J=10, 12-CH); 7.20–8.02 (7H, m, H–Ar); 8.17 (1H, d, J=8, H-20); 8.49 (1H, s, H-26); 3.76 (NH)

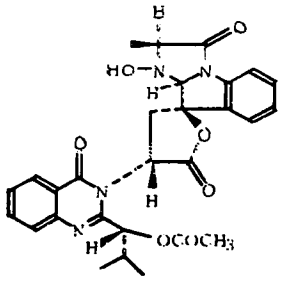
108. TRYPTOQUIVALINE L



Aspergillus fumigatus [123]
$C_{23}H_{20}N_4O_5$: 432.1457
mp.: 265–268° (ac.)
$[\alpha]_D$–229° (DMSO)
UV (meth.): 216, 226, 231, 252, 264, 274, 290, 302, 315 (33900, 33000, 30800, 17400, 12300, 8400, 3700, 3000, 2400)
IR: 3230, 1784, 1749, 1670, 1616, 1485, 1260, 1200

Mass:: 432 (M^+, 76), 286 (13), 269 (15), 256 (16), 242 (28), 229 (100); 199 (16), 188 (27), 173 (13), 147 (39), 130 (26)
PMR(DMSO-d_6): 1.26 (3H, s); 1.36 (3H, s); 3.03 (1H, dd, J=13, 10); 3.43 (1H, dd, J=13, 10); 5.21 (1H, s); 5.57 (1H, t, J=10); 7.24–8.00 (7H, m); 8.23 (H, d, J=8); 8.53 (1H, s); 8.74 (1H, s)

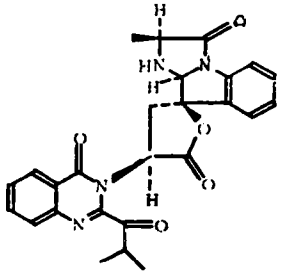
109. TRYPTOQUIVALINE M



Aspergillus fumigatus [123]
$C_{26}H_{28}N_4O_7$: 532.1932
mp.: 157–164° (meth.-water)
$[\alpha]_D$–154° (chlf.)
UV (meth.):228, 232, 255, 278, 305, 317 (32700, 30700, 15400, 9300, 2900, 2700)
IR: 3400, 1788, 1725, 1678, 1600, 1480, 1464, 1210
Mass: 532 (M^+, 100), 261 (33), 255 (23), 215 (50), 214 (22), 201 (56), 130 (19)

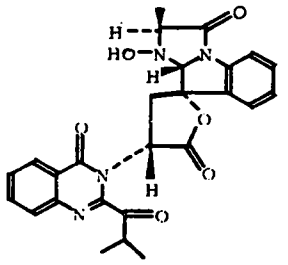
PMR: 0.92 (3H, d, J=6); 1.04 (3H, d, J=6); 1.55 (3H, d, J=7), 2.16 (3H, s); 2.68 (1H, dd, J=11, 10), 2.74 (1H, m); 3.65 (1H, dd, J=11, 10); 4.15 (1H, q, J=7); 5.22 (1H, s); 5.54 (1H, d J=10); 5.87 (1H, t, J=10); 6.86 (1H, br.s); 7.12–7.88 (7H, m); 8.24 (1H, d, J=8)

110. TRYPTOQUIVALINE N



Aspergillus fumigatus [123]
$C_{26}H_{24}N_4O_5$: 472.1770
mp.: 193–197° (meth.)
$[\alpha]_D$+127° (DMSO)
UV (meth.): 232, 251, 291, 320 (32300, 17900, 9000, 6100)
IR: 3360, 1780, 1722, 1705, 1680, 1607, 1481, 1250
Mass: 472 (M^+, 100), 444 (22), 256 (40), 243 (17), 228(48), 217 (44), 199 (17), 186 (20), 174 (44), 158 (24), 146 (38), 130 (35)

PMR: 1.26 (3H, d, J=7); 1.30 (3H, d, J=7); 1.55 (3H, d, J=7); 3.03 (1H, dd, J=13.10); 3.05 (1H); 3.31 (1H, dd, J=13.10); 4.08 (1H, m); 4.12 (1H, q, J=7); 5.34 (1H, s); 5.46 (1H, t, J=10); 7.04–7.80 (7H, m); 8.24 (1H, d, J=8)



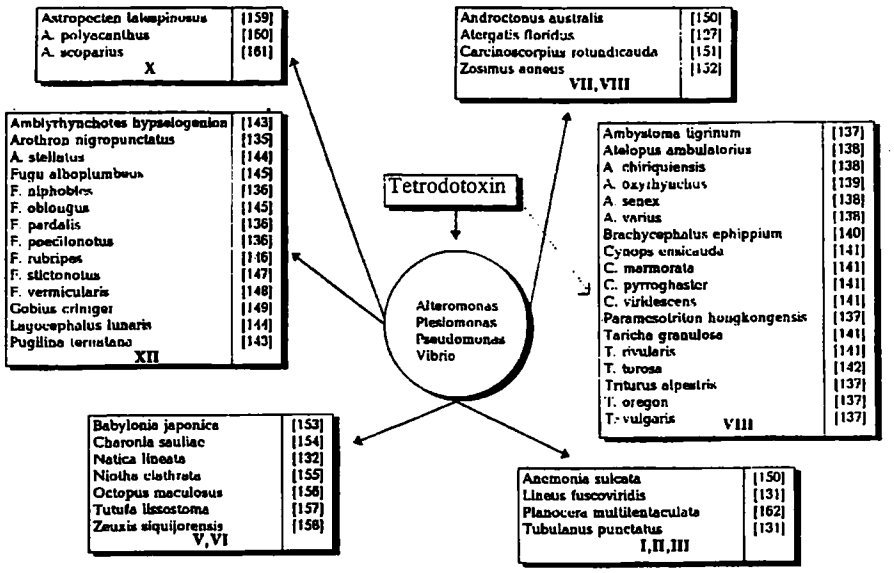
Aspergillus clavatus [125]
$C_{26}H_{24}N_4O_6$: 488.1696
mp.: 202–204°
$[\alpha]_D$ –254° (chlf.)
UV: 234, 292, 320 (34950, 9550, 6300)
IR (chlf.): 3525, 1790, 1735, 1715, 1680
Mass: 488 (M^+)
PMR: 1.24 (3H, d, J=7); 1.31 (3H, d, J=7); 1.59 (3H, d, J=7); 3.09 (1H, dd, J=10,14); 3.47 (1H, dd., J=11.14); 4.12 (1H, quintet, J=7); 4.36 (1H, q, J=7); 5.24 (1H, s); 5.51 (1H, t, J=10); 7.12–7.94 (7H, m); 8.28 (1H, d, J=8)

HPLC: [120]
Pharm: anticonvulsive activity

V. Tetrodotoxins

A distinguishing feature of the distribution of alkaloids of the tetrodotoxin group is their wide representation in marine animals of the most diverse classes and also in amphibia inhabiting bodies of fresh water. In particular, tetrodotoxin and its analogs are found in nemertines (Nemertini: *Lineus, Tubulanus*), gastropod mollusks (Gastropoda: *Babylonia, Charonia, Natica, Niotha, Tutufa, Zeuxis*), a cephalopod mollusk — the blue spotted octopus (Cephalopoda: *Octopus maculosus*), marine crustacea (Crustaceae: *Atergatis, Zosimus*), globe fishes (Tetraodontidae: *Amblyrhynchotes, Arothron, Fugu, Lagocephalus, Pugilina*), amphibian families of salamandrian animals (Ambystomatidae: *Ambystoma*) and true salamanders (Salamandridae: *Cynops, Paramesotriton, Taricha, Triturus*).

Above all, tetrodotoxin is found in corals (Anthozoa: *Anemonia*), turbellarian worms (Turbellaria: *Planocera*), Merostomata (*Androctonus, Carcinoscorpius*), starfish (Asteroidea: *Astropecten*), gobies (Gobiidae: *Gobius criniger*), and amphibians of toad families (Brachycephalidae: *Atelopus, Brachycephalus*) (see Scheme 1).



Scheme 1. Distribution of tetrodotoxin in Nature: 1) Anthozoa (corals); II) Turbellaria; III) Nemertini; V) Gastropoda; VI) Cephalopoda; VII) Crustacea; VIII) Merostomata; X) Asteroidea (starfish); XII) Pisces (fishes); XIII) Amphibia.

According to modern ideas, which have been confirmed experimentally, tetrodotoxin and some of its derivatives are produced by a number of bacteria living on the sea bottom (*Pseudomonas, Alteromonas, Bacillus, Plesiomonas, Vibrio*) and are then accumulated by the above-mentioned salt-water dwellers [163, 164]. It is interesting to note that no alkaloids of the

tetrodotoxin group have been detected hitherto either in algae or in higher plants. At the present time, 13 toxins of this type have been described.

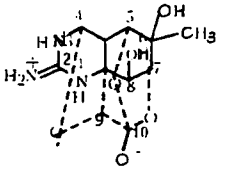
Tetrodotoxin was one of the first quinazoline alkaloids. It was isolated in 1909 from the fish *Fugu rubripes*. However, only after 40 years was tetrodotoxin obtained in crystalline form, while its chemical structure was established by the 1960's and was then confirmed by synthesis [165, 166]. From the chemical point of view, tetrodotoxin is a combination of an aminoperhydroquinazoline with a guanidine group, and it can exist in two forms: hemilactal and lactone [126].

As a rule, these compounds contain hydroxy groups in positions 6 and 8, and sometimes in positions 4 and 9, as well. Other substituents at carbon atom 6 may be hydroxyl, hydrogen, dihydroxymethyl, and methyl. Anhydro bases are known among the tetrodotoxins, and also compounds with extremely original structure, such as 1-hydroxy-5,11-dideoxytetrodotoxin (hydroxyl at a nitrogen atom), tetrodonic acid, and chiriquitoxin.

The group of animal toxins under consideration is known, above all, thanks to their unique biological properties. In very low concentrations (10^{-7} M) tetrodotoxin and its analogs block the transmission of nervous impulses in excitable tissues (nerve and muscle tissues). A large number of original and review papers have been devoted to this question. In spite of the fact that tetrodotoxin possesses a very high toxicity and, from this index, may be assigned to the group of so-called ultratoxins [167], the organisms elaborating them are, as a rule, extremely resistant to them. In view of this, the role of tetrodotoxin and its analogs as powerful agents of chemical protection seems obvious.

As investigations of recent years have shown, tetrodotoxin is present in considerable concentrations in sea-bed deposits [168]. As in many marine animals, the accumulation of this toxin in bottom deposits is the result of the activity of a whole series of tetrodotoxin-producing bacteria — in particular, *Vibrio alginolyticus* [133, 163, 169]. It is assumed that this toxin is a stable component of these deposits and is capable of remaining in an active state for a long time. There is no doubt that tetrodotoxin and its derivatives must exert a definite physiological action on benthic animals feeding on detritus, some of which are apparently capable of accumulating the poison. Thus, the wide distribution of toxins of this type in marine organisms of the most diverse classes has a secondary character.

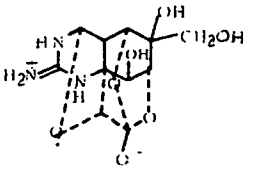
112. 4,9-ANHYDRO-11-DEOXYTETRODOTOXIN



Cynops ensicauda [126]
$C_{11}H_{15}N_3O_6$: 285.2536
Amorph.
Mass (SIMS): 286 $(M+H)^+$

PMR ($CD_3COOD+D_2O$ TMS): 1.61 (s, H-11); 2.95 (d, J=3.0, H-4a); 4.01 (t, J=2.0, 2.0, H-7); 4.15 (dd, J=3.0, 2.0, H-5); 4.56 (s, H-9); 4.63 (d, J=2.0, H-8); 5.51 (s, H-4)

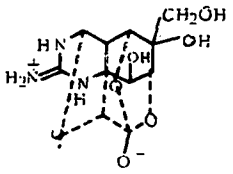
113. 4,9-ANHYDROTETRODOTOXIN



Arergatis floridus [127], Charonia sauliae [128], Cynops ensicauda [126], Fugu pardalis, F.poecilonotus, F.rubripes [129], F.vermicularis [130], Lineus fuscoviridis [131], Natica lineata [132], Octopus maculosus [133], Tubulanus punctatus [131]
$C_{11}H_{15}N_3O_7$: 301.2526

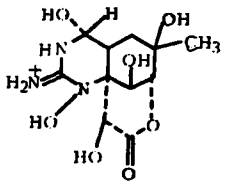
Amorph.
Mass (glycerol): 315, 302 $(M+H)^+$, 277 (100) [129]
PMR ($CD_3COOD-D_2O$, TMS): 3.06 (d, J=4.1, H-4a); 4.03 (d, J=13.3, 11-CH_2); 4.11 (d, J=13.3, 11-CH_2); 4.27 (q, J=3.5, 1.1, H-7); 4.47 (q, J=4.1, 1.1, H-5); 4.70 (s, H-9); 4.74 (d, J=3.5, H-8); 5.64 (s, H-4)
HPLC: [147]
Pharm: LD_{50}-92 Mu/mg (s/c, mice) [129]

114. 4,9-ANHYDRO-6-EPITETRODOTOXIN



Cynops ensicauda [126]
$C_{11}H_{15}N_3O_7$: 301.2526
$[\alpha]_D$+10° (AcOH)
Mass: 302 $(M+H)^+$
PMR: 2.87 (d, J=2.3, H-4a); 3.65, 3.67 (d, J=12.7, 11-CH_2), 4.20 (t, J=2.0, H-7); 4.33 (dd, J=2.3, 2.0, H-5); 4.41 (d, J=2.0, H-8); 4.61 (s, H-9); 5.54 (s, H-4)

115. 1-HYDROXY-5,11-DIDEOXYTETRODOTOXIN



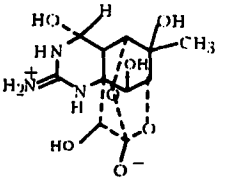
Taricha granulosa [134]
$C_{11}H_{18}N_3O_7$: 304.2763
Amorph
$[\alpha]_D$+14.47° (AcOH)
Mass: 304.1141 (M^+)

PMR: 1.35 (s, H-11); 1.38 (dd, J=15.7, 13.3, H-5β); 2.14 (ddd, J=15.6, 3.7, 1.4, H-5α); 2.77 (ddd, J=13.2, 9.3, 3.9, H-4a); 4.46 (dd, J=3.9, 1.4, H-7); 4.58 (d, J=3.9, H-8); 4.80 (s, H-9); 5.14 (d, J=9.4, H-4)
^{13}C NMR:

C-2	158.9	C-6	69.8	C-9	69.9
4	77.5	7	81.2	10	176.6
4a	38.8	8	67.5	11	27.9
5	34.3	8a	74.1		

HPLC

116. 11-DEOXYTETRODOTOXIN



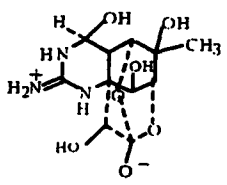
Arothron nigropunctatus [135], Cynops ensicauda [126], C.pyrrhogaster, Taricha granulosa, Triturus alpestris, T.oregon [137], Feugu niphobles, F.pardalis, F.poecilonotus [136]
$C_{11}H_{17}N_3O_7$: 303.2684
mp.: 202° (AcOH-water, dec.)
$[\alpha]_D$+5° (AcOH)

Mass: 304 $(M-H)^+$
PMR (CD_3COOD+D_2O, TMS): 164 (s, H-11); 2.37 (d, J=9.4, H-4a); 3.91 (t, J=1.6, H-7); 3.94 (s, H-9); 4.08 (br.s H-5); 4.30 (d, J=1.6, H-8); 5.49 (d, J=9.4, H-4).
^{13}C NMR (CD_3COOD): [126]

C-2	156.4	C-6	69.1	C-9	70.8
4	75.0	7	83.6	10	110.6
4a	40.5	8	72.6	11	25.1
5	77.5	8a	59.1		

HPLC: [209]
Pharm: LD_{50} 71 mg/kg (i/p, mice)

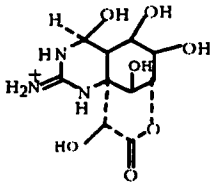
117. 11-DEOXY-4-EPITETRODOTOXIN



Cynops ensicauda [126]
$C_{11}H_{17}N_3O_7$: 303.2684
Amorph.
Mass(SIMS): 304 $(M+H)^+$

PMR: 1.64 (s, H-11); 2.87 (d, J=5.0, H-4a); 3.91 (t, J=1.5, 1.5, H-7); 3.96 (s, H-9); 4.13 (d, J=1.5, H-5); 4.29 (d, J=1.5, H-8); 5.13 (d, J=4.9, H-4)

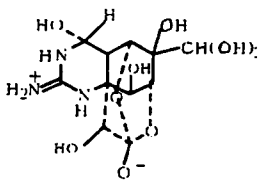
118. 11-NORTETRODOTOXIN-6(R)-OL



Arothron nigropunctatus [135], Fugu niphobles, F. pardalis, F.poecilonotus [136]
$C_{10}H_{16}N_3O_7$: 290.2495
Amorph.
Mass:: 290 (M^+)

PMR (CD_3COOD-D_2O, TMS): 2.00 (d, J=9.8, H-4a); 3.94 (br.s H-6); 4.15 (d, J=1.4, H-8); 4.32 (br.s H-5); 4.56 (s, H-9); 4.72 (br.s H-7); 5.55 (d, J=9.3, H-4)
HPLC.
Pharm {Ac.}: LD_{99}-70 mg/kg

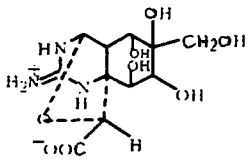
119. 11-OXOTETRODOTOXIN



Arothron nigropunctatus [135]
$C_{11}H_{17}N_3O_9$: 335.2664
Amorph.
Mass:: 336 $(M+H)^+$

PMR (CD_3COOD+D_2O, TMS): 2.31 (br.dJ=9.5, H-4a); 3.98 (H-9); 4.19 (H-7); 4.27 (H-8); 4.37 (H-5); 5.51 (d, J=9.5, H-4); 5.74 (s, H-11)
HPLC. [209]
Pharm {Ac.}: LD_{50} 120 mg/kg (i/p, mice)

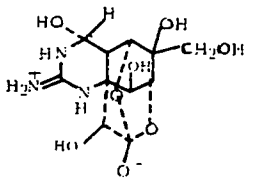
120. TETRODONIC ACID



Feugu pardalis, F.poecilonotus, F.rubripes [129]
$C_{11}H_{17}N_3O_8$: 319.2674
Amorph.
Mass (glycerol): 320 $(M+H)^+$, 299, 277 (100)

PMR(CD_3COOD-D_2O, TMS): 2.86 (d, J=4.7, H-4a); 3.79 (s, 11-CH_2); 3.90 (q, J=4.1, 1.1, H-7), 4.03 (q, J=4.1, 1.1, H-5); 4.29 (d, J=4.1, H-8); 5.30 (s, H-9); 5.39 (s, H-4)
HPLC

121. TETRODOTOXIN



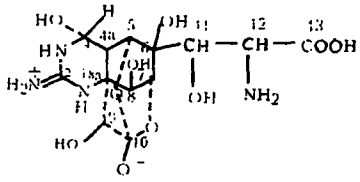
See scheme No. 1
$C_{11}H_{17}N_3O_8$: 319.2674
mp: 220°
Mass(glycerol): 320[$(M+H)^+$, 100], 302, 277 [129]

PMR(CD_3COOD-D_2O, TMS): 2.35 (d, J=9.5, H-4a); 3.96 (s, H-9); 4.02 (d, J=12.6, H-11); 4.04 (d, J=12.6, H-11); 4.08 (t, J=1.8, H-7); 4.25 (br.s, H-5); 5.50 (d, J=9.4, H-4)
^{13}C NMR (CD_3COOD): [126]

C-2	156.6	C-6	71.5	C-9	70.9
4	75.1	7	79.7	10	110.8
4a	40.7	8	72.8	11	65.5
5	73.8	8a	59.7		

HPLC: [147]
Pharm.: neurotropic activity, vasodilator action. A series of drugs based on tetrodotoxin has been proposed for infiltration and cerebrospinal anesthesias [210].
LD_{50} 332, 10 mg/kg (oral, i/v mice) [219]

122. CHIRIQUITOXIN



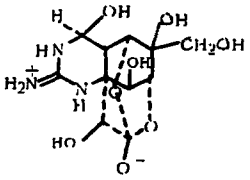
Atelopus chiriquiensis [138]
$C_{13}H_{20}N_4O_{10}$: 392.3178
Amorph.
$[\alpha]_D$-17° (AcOH)
IR: 1800, 1741, 1667 [211]
Mass: 393 $(M+H)^+$

PMR (CD_3COOD+D_2O, TMS): 2.31 (d, J=9.4, H-4a); 4.00 (s, H-9); 4.27 (d, J=1.8, H-12); 4.39 (br.t H-7); 4.40 (br.s H-5); 4.40 (br.s H-8); 4.90 (d, J=1.8, H-11); 5.51 (d, J=9.4, H-4) [211]
^{13}C NMR (CD_3COOD): [138]

C-2	156.6	C-7	81.1	C-10	111.0
4	75.2	8	72.7	11	70.3
4a	40.5	8a	59.3	12	58.1
5	73.5	9	70.9	13	174.1
6	72.1				

Abs. conf. 11R, 12S [211]
HPLC: [209]
Pharm: {Ac.}: LD_{50} 14 mg/kg (i/p, mice). Blocks conduction of sodium channels [212]

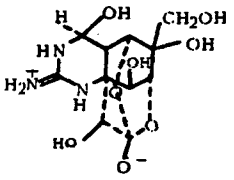
123. 4-EPITETRODOTOXIN



Arothron nigropunctatus [135], Charonia sauliae [128], Cynops ensicauda [126], Fugu pardalis, F.poecilonotus, F.rubripes [129]; Lineus fuscoviridis [131], Octopus maculosus [133]
$C_{11}H_{17}N_3O_8$: 319.2674

Amorph.
Mass (glycerol): 412, 369, 320 $(M+H)^+$, 302, 277 (100)
PMR (CD_3COOD+D_2O, TMS): 2.73 (d, J=5.3, H-4a); 3.85 (vc, H-5); 3.91 (s, 11-CH_2); 3.98 (br.s H-7); 4.07 (br.s H-8); 4.17 (br.s H-9); 5.04 (d, J=5.3, H-4) [129]
HPLC: [147]
Pharm: LD_{50} 710 mu/mg (s/c, mice) [129]

124. 6-EPITETRODOTOXIN



Ambystoma tigrinum, Cynops pyrrhogaster, Triturus alpestris, - T.vulgaris [137], Arothron nigropunctatus [135], Cynops ensicauda [126], Fugu niphobles, F.pardalis, F.poecilonotus [136]
$C_{11}H_{17}N_3O_8$: 319.2674

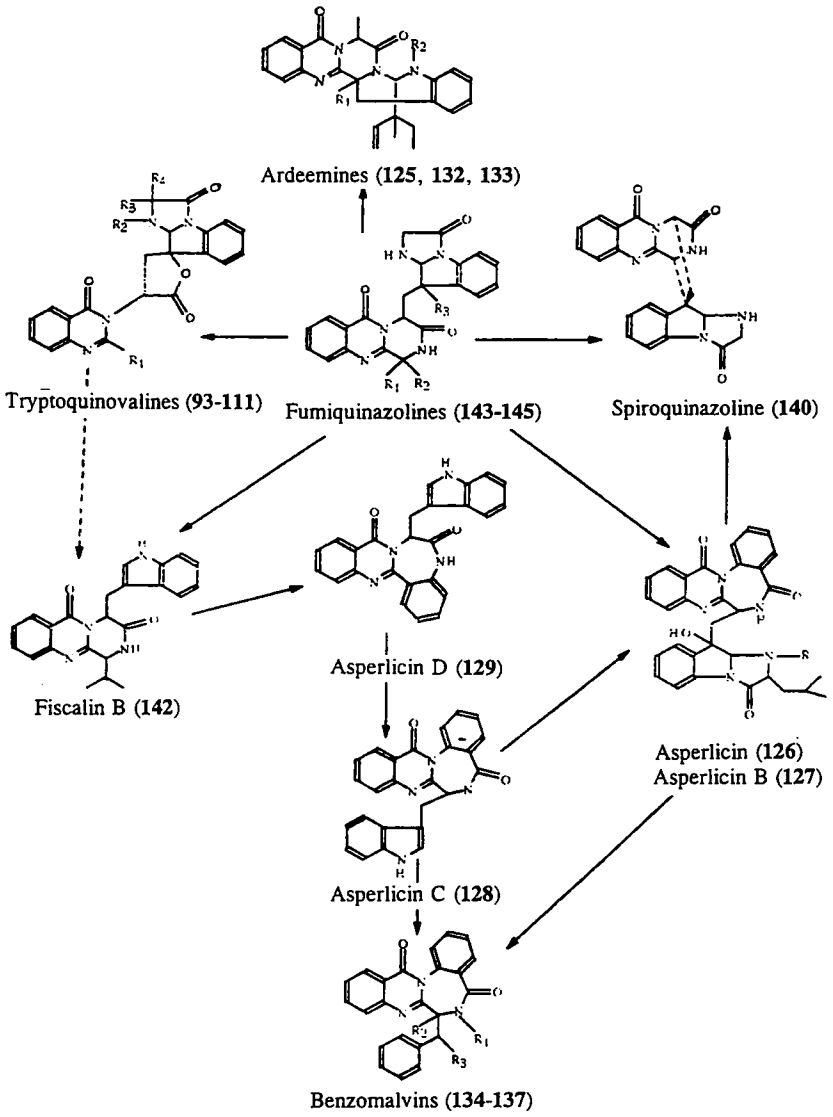
Amorph.
$[\alpha]_D$-5° (AcOH)
Mass:: 320 $(M+H)^+$
PMR (CD_3COOD+D_2O, TMS): 2.01 (d, J=9.0, H-4a); 3.74 (s, H-11); 4.00 (s, H-9); 4.08 (br.s H-7); 4.17 (br.s, H-8); 4.30 (d, J=1.6, H-5); 5.55 (d, J=9.4, H-4)
^{13}C NMR: (CD_3COOD):

C-2	156.5	C-6	72.8	C-9	70.8
4	75.1	7	82.0	10	110.7
4a	41.8	8	72.9	11	65.1
5	75.4	8a	59.6		

Pharm: LD_{50} 60 mg/kg (i/p, mice)

VI. Quinazoline Alkaloids with Various Structures

In this group we have placed alkaloids differing both in chemical structure and in sources of isolation. Their producing agents are bacteria (*Candida*), ascomycetous fungi (*Apergillus, Penicillium, Corynascus, Neosartorya*), higher plants of the families Polygonaceae (*Polygonum*), Brassicaceae (*Isatis*), Lecythidaceae (*Couroupita*), Acanthaceae (*Strobilanthes*), and marine animals (Bryoza: *Hincksinoflustra*). So far, 21 such alkaloids are known, and we have arbitrarily combined them into one group.



Scheme 2. Quinazoline alkaloids of ascomycetous fungus (Ascomycetes)

In spite of the obvious structural differences between the alkaloids under consideration, it appears completely possible to distinguish among them a group of compounds closely related both in chemical structure and in natural origin. These are the asperlicins (5 alkaloids), the fumiquinazolines (3 alkaloids), the benzomalvins (4 alkaloids), and the ardeemines (3 alkaloids). The latter have been obtained synthetically quite recently [225]. Fiscalin B and spiroquinazoline must be added to this series. They are all products of the vital activity of the fungi Ascomycetes. In addition to their common origin, the substances mentioned have similar structural elements. Thus, for example, the fumiquinazolines, which represent a combination of pyrazinoquinazoline and imidazoindole heterocyclic systems, are extremely similar to the tryptoquinazolines described in the preceding section. In contrast to the latter, they contain no γ-lactone ring.

The simultaneous presence of fumiquinazolines and tryptoquivalines in *A. fumigatus* probably gives grounds for assuming their biogenetic relationship. On the other hand, in their pyrazinoquinazoline moiety, the fumiquinazolines very

greatly resemble the ardeemines, similarity being observed not only in the structure of the heterocyclic skeleton but also in the positions of the carbonyl groups. Furthermore, in the ardeemines the quinazoline constituent is attached by a C–N bond to a pyrroloindole system. Finally, the fumiquinazolines have an imidazoindole component in common with asperlicin and asperlicin B. However, in the latter it is linked by a methylene bridge with a quinazolinobenzodiazepine fragment. In their turn, with respect to this characteristic, asperlicin and asperlicin B are similar to asperlicins C and D, on the one hand, and to the benzomalvins, on the other hand. Their structural difference consists in the fact that in position 19 asperlicins C and D have an indole grouping and the benzomalvins an unsubstituted aromatic ring.

A recently isolated alkaloid with an original structure — spiroquinazoline — may be considered as a combination of the pyrazinoquinazoline components of the fumiquinazolines and the imidazoindole components of the asperlicins. All these structural features suggest that mutual transitions exist between the tryptoquivalines, fumiquinazolines, benzomalvins, ardeemines, and asperlicins (see Scheme 2). These can quite possibly take place under the conditions of the biocatalytic processes occurring in ascomycetous fungi. This hypothesis is supported by the simultaneous presence of tryptoquinovalines and fumiquinazolines in *A. fumigatus* (as mentioned above) and also of tryptoquinovalines and fiscalin B in *C. setosus*.

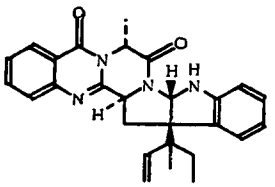
Unfortunately, in view of the clear deficiency of experimental facts, the proposed scheme must be regarded as extremely provisional. It is believed that a further deeper and all-sided study of the biochemistry of the Ascomycetes and, in particular, the genus *Aspergillus* will permit conclusions to be drawn on the biogenesis of this group of alkaloids.

The following two alkaloids — kingdaione (candidine) and tryptanthrine (couroupitine A) are produced both by bacteria and by flowering plants (*Isatis, Strobilanthes, Couroupita, Polygonum*). Both of them are antimicrobial agents [184].

Finally, the last quinazolines with an original structure known at the present time are auranthine from the culture *Penicillium aurantiogriseum* and hinckdentine A from the marine organism *Hincksinoflustra denticulata*. Hinckdentine A is the second representative of the quinazoline alkaloids containing a bromine atom in its molecule.

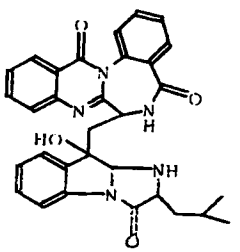
Since practically all quinazoline bases of the group under consideration were isolated comparatively recently (with the exception of tryptanthrin, discovered in 1971), information on their biosynthesis is either completely lacking or has a fragmentary nature. For example, so far as concerns asperlicins C and E, the opinion has been expressed that they originate from tryptophan and anthranilic acid [185]. The recently described synthesis of hinckdentine A from indolo[1,2-c]quinazoline permits the assumption of a similar mechanism for their biosynthesis [186].

125. (–)-ARDEEMINE



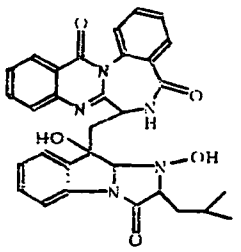
Aspergillus fischeri [213]
Pharm.: [214]

126. ASPERLICIN



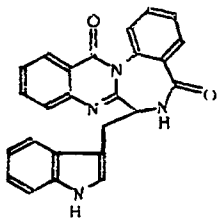
Aspergillus alliaceus [170]
$C_{31}H_{29}N_5O_4$: 535.5996
XSA:
Pharm: antagonist of the peptide hormone cholecystokinin [171]

127. ASPERLICIN B



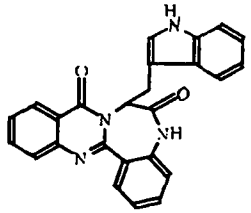
Aspergillus alliaceus [171]
$C_{31}H_{29}N_5O_5$: 551.5986
Abs. conf..: 2S, 9R*
Pharm: antagonist of cholecystokinin (cck), selectively affecting peripheral cck receptors.

128. ASPERLICIN C



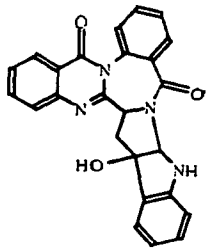
Aspergillus alliaceus [172]
$C_{25}H_{17}N_4O_2$: 405.4341
XSA. [185]
Pharm: antagonist of the peptide hormone cholecystokinin [171]

129. ASPERLICIN D



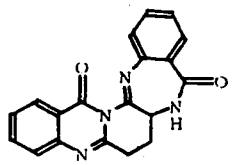
Aspergillus alliaceus [172]
$C_{25}H_{18}N_4O_2$: 406.4420

130. ASPERLICIN E



Aspergillus alliaceus [172]
$C_{25}H_{18}N_4O_3$: 422.4410
XSA: [185]
Pharm: antagonist of the peptide hormone cholecystokinin

131. AURANTHINE



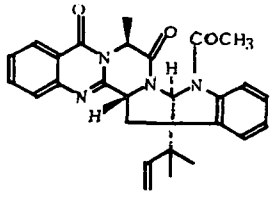
Penicillium aurantiogriseum [174]
$C_{19}H_{14}N_4O_2$: 330.3444
$[\alpha]_D$-164°
{ h-chl.>300°}
UV: 228, 268, 280, 310, 322
IR : 3450, 3175, 1675, 1615, 1595, 1450, 1380, 1250

Mass: 330 (M^+), 277, 249 (100), 248, 234, 220, 192, 132, 130, 124, 119, 102
^{13}C NMR:

169.7	130.6	126.9
160.7	129.9	121.1
153.6	129.0	118.6
145.4	128.7	53.2
134.1	127.1	25.4
133.6	127.06	13.6
131.3		

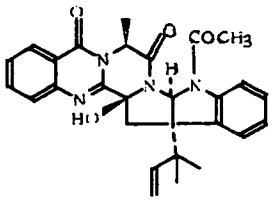
HPLC.

132. (−)-5-N-ACETYLARDEEMINE



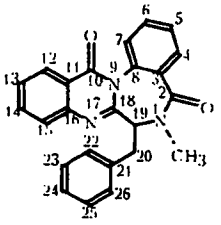
Aspergillus fischeri [213]
$C_{28}H_{25}N_4O_3$: 465.5293
XSA
Pharm: agent for suppressing the resistance of cancer cells to drugs [225]

133. (−)-15β-HYDROXY-5-N-ACETYLARDEEMINE



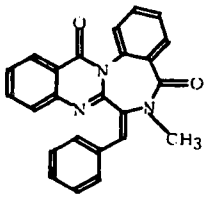
Aspergillus fischeri [213]
$C_{28}H_{28}N_4O_4$: 484.5520

134. BENZOMALVIN A



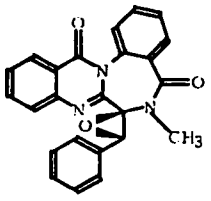
Penicillium sp. [182]
$C_{24}H_{19}N_3O_2$: 381.4322
PMR: 3.03 (H-27); 3.42, 3.79 (H-20); 4.87 (H-19) [183]
^{13}C NMR: 167.6 (C-2); 153.7 (C-18); 59.3 (C-19); 33.7 (C-20); 27.9 (C-27) [183]
HPLC.
Pharm: P-substance inhibitor

135. BENZOMALVIN B



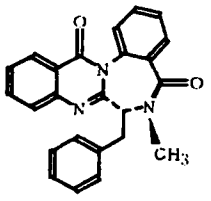
Penicillium sp. [182]
$C_{24}H_{17}N_3O_2$: 379.4164
PMR: 3.45 (H-27); 6.72 (H-20) [183]
^{13}C NMR: 165.8 (C-2); 151.1 (C-18); 128.9 (C-19); 132.8 (C-20); 36.1 (C-27) [183]
HPLC
Pharm: P-substance inhibitor

136. BENZOMALVIN C



Penicillium sp. [182]
$C_{24}H_{17}N_3O_3$: 395.4154
HPLC
Pharm: P-substance inhibitor

137. BENZOMALVIN D



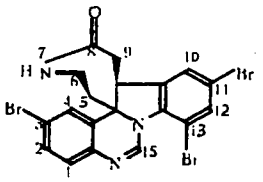
Penicillium sp.: [183]
$[\alpha]_D$+48°
PMR: 2.33 (1H, dd, J=13.8, 11.3); 2.74 (1H, dd, J=13.8, 5.9); 2.91 (3H, s); 4.75 (1H, dd, J=11.3, 5.9); 6.96 (2H, dd, J=7.6, 1.5); 7.20–7.28 (3H, m); 7.53 (1H, td, J=7.6, 1.5); 7.59–7.67 (4H, m); 7.79 (1H, td, J=7.6, 1.5); 8.01 (1H, dd, J=7.6, 1.5); 8.32 (1H, dd, J=7.6, 1.5)

^{13}C NMR:

35.9 (t)	127.7 (d)	133.0 (s)
38.3 (q)	128.1 (d)	135.0 (d)
70.3 (d)	128.8 (d, 3C)	135.9 (s)
121.4 (s)	129.0 (d)	146.3 (s)
127.3 (d)	130.7 (d)	153.7 (s)
127.4 (d)	131.1 (d)	161.5 (s)
127.5 (d)	132.1 (s)	165.4 (s)

Abs. conf.: 19S
HPLC

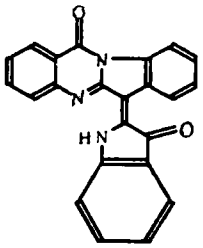
138. HINCKDENTINE A



Hincksinoflustra denticulata [175]
$C_{19}H_{14}Br_3N_3O$: 540.0507
mp.: 196–197°
$[\alpha]_D$ −274°
UV: 239, 303, 337, 344, 357
IR: 3400, 1671, 1600, 1576, 1449, 1337, 1300
Mass: 537 (539 (541 543 (M^+)

PMR: 1.87 (ddd, J=14.9, 8.8, 1.5, H-5a); 2.17 (ddd, J=14.9, 8.8, 1.5, H-5b); 2.98 (dddd, J=14.9, 8.8, 4.4, 1.5, H-6a); 3.15 (dddd, J=14.9, 5.0, 1.5, 1.5, H-6b); 3.32 (ddd, J=16.1, 6.2, 1.6, H-9a); 3.48 (dd, J=16.1, 3.0, H-9b); 4.07 (dddd, J=6.2, 3.0, 1.4, 1.1, H-9a); 6.58 (br.t 4.4, 1.6, NH); 7.23 (d, J=8.5, H-1), 7.42 (d, J=2.2, H-4); 7.46 (dd, J=1.9, 1.4, H-10); 7.48 (dd, J=8.5, 2.2, H-2); 7.59 (dd, J=1.9, 1.1, H-12); 9.09 (s, H-15)
XSA
HPLC

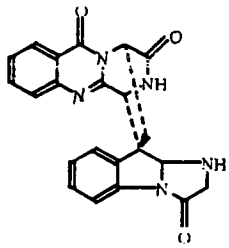
139. KINGDAINONE



Candida lipolytica [176], Isatis tinctoria, Strobilanthes cusia [177]
$C_{23}H_{13}N_3O_2$: 363.3738
mp.: 269–270°
UV (chlf.): 244, 250, 282, 538, 573 (4.34, 4.36, 4.21, 3.95, 4.11) [215]
IR: 3210, 2730, 1690, 1650, 1625, 1600, 1460, 1355, 1315, 740

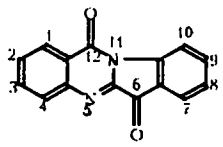
Mass: 364 (23), 363 (100), 335 (37), 259 (10), 258 (11), 242 (9)
PMR: 7.05 (1H, t, J=7.5, H-5'); 7.09 (1H, d, J=7.8, H-7'); 7.39 (1H, td, J=7.5, 1.2, H-8); 7.48 (1H, td, J=8.0, 1.4, H-9); 7.52 (1H, t, J=7.5, H-2); 7.54 (1H, d, J=8.0, H-6'); 7.75 (1H, dd, J=7.5, 1.0, H-4'); 7.79 (1H, t, J=7.0, H-3); 7.83 (1H, d, J=7.5, H-4); 8.42 (1H, dd J=7.9, 1.4, H-1); 8.66 (1H, d, J=7.4, H-10); 9.22 (1H, d, J=7.8, H-7); 11.75 (1H, s, NH) [216]

140. SPIROQUINAZOLINE



Aspergillus flavipes [217]

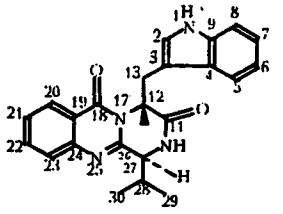
141. TRYPTANTHRIN



Candida lipolytica [178], Couroupita guianensis [179], Isatis tinctoria, Polygonum tinctorium [180], Strobilanthes cusia [181]
$C_{15}H_8N_2O_2$: 248.2396
mp.: 267–268°

UV: 248, 252, 277, 311, 328, 387 (3.36, 3.72, 0.595, 0.729, 0.670, 0.550)
IR (chlf.): 1722, 1684, 1596 [181]
Mass: 248 (M^+, 100), 220 (32), 192 (13.7)
PMR: 7.30–8.70 (8H, H–Ar)
XSA: [220]
Pharm: fungicidal activity [181]

142. FISCALIN B (CS-D)



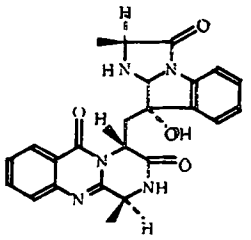
Corynascus setosus [208], Neosartorya fischeri [218]
$C_{23}H_{22}N_4O_2$: 386.4516
mp : 164.5–170.5° (chlf. meth.)
$[\alpha]_D$–124° (meth.)
UV (meth.): 220, 273, 290, 305, 318 (4.65, 4.06, 3.90, 3.60, 3.47)
IR: 3258, 1680, 1600, 1460

PMR: 0.57 (3H, d, J=7.0, H-29); 0.59 (3H, d, J=7.0, H-30); 2.57 (m, H-28); 2.67 (d, J=2.4, H-27); 3.56 (dd, J=14.8, 5.5, H-13); 3.65 (dd, J=14.8, 2.8, H-13); 5.59 (dd, J=5.5, 2.8, H-12); 6.10 (br.s, H-10); 6.53 (d, J=2.1, H-2); 6.84 (td, J=7.8, 1.0, H-6); 7.04 (td, J=7.8, 1.0, H-7); 7.21 (br.d, J=7.8, H-8); 7.35 (br.d, J=7.8, H-5); 7.45 (td, J=7.9, 1.1, H-21); 7.48 (br.d, J=7.9, H-23); 7.69 (td, J=7.9, 1.5, H-22); 8.21 (br.s, H-1); 8.29 (dd, J=7.9, 1.5, H-20)

^{13}C NMR:

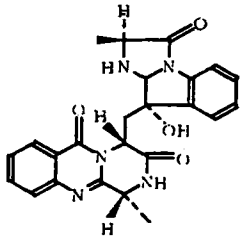
C-2	122.6 (d)	C-11	168.5 (s)	C-23	126.1 (d)
3	108.2 (s)	12	55.7 (d)	24	146.0 (s)
4	126.2 (s)	13	26.3 (t)	26	149.2 (s)
5	117.6 (d)	18	159.9 (s)	27	57.1 (d)
6	118.9 (d)	19	119.1 (s)	28	28.5 (d)
7	121.5 (d)	20	125.9 (d)	29	13.7 (q)
8	110.0 (d)	21	126.0 (d)	30	17.7 (q)
9	135.0 (s)	22	133.6 (d)		

143. FUMIQUINAZOLINE A



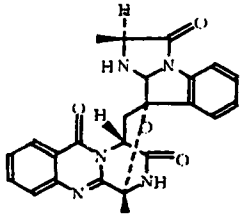
Aspergillus fumigatus [173]
$C_{24}H_{23}N_5O_4$: 445.4752
Pharm: cytotoxic activity

144. FUMIQUINAZOLINE B



Aspergillus fumigatus [173]
$C_{24}H_{23}N_5O_4$: 445.4752
Pharm: cytotoxic activity

145. FUMIQUINAZOLINE C



Aspergillus fumigatus [173]
$C_{24}H_{21}N_5O_4$: 443.4594
XSA
Pharm: cytotoxic activity

If we consider the problem of the distribution of the quinazoline alkaloids in Nature as a whole, attention is immediately attracted by the circumstance that compounds of this class are found in representatives of all three kingdoms of living Nature — microorganisms, plants, and animals. At the same time, their sources are frequently taxons that are phylogenetically very remote and in no way connected with one another. This suggests that at least some of the quinazoline

alkaloids, especially those of the simplest structure, play the role of protoalkaloids — i.e., substances directly connected with amino acids and found in the most diverse families of plants and animals [90].

At the same time, it is impossible to deny the fact that many quinazolines and some groups of them (for example, the quinazolinocarbolines and tryptoquivalines) are distributed within a single family, genus, or even species. This undoubtedly indicates that they are narrowly specialized and highly organized products of secondary metabolism.

From the aspect of structural chemistry, it appears interesting to us that although the quinazoline alkaloids are a fairly small class of natural compounds, their structures are very diverse. This is shown not only in the methods of constructing the main heterocyclic skeleton but also in the nature of the substituting functional groups, among which are sometimes present such substituents rarely found among alkaloids as bromine, free carboxyl, and others.

In conclusion, it would be desirable to mention that we have scarcely touched upon aspects of structural investigations, stereochemistry, chemical transformations, methods of analysis, pharmacological activity, and many others. Such an urgent problem as the biogenesis of the various types of quinazoline alkaloids has hardly been considered, either. A whole series of reviews and original papers have been devoted to this most important question.

The continuously increasing stream of publications on this subject permits the hope that even in the foreseeable future an answer must be found to the general philosophical question of the place and role in living Nature of alkaloids in general and of the quinazoline alkaloids in particular.

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