CHEMOSYSTEMATICS OF *THALICTRUM MINUS* COMPLEX[1, 2]

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ABSTRACT.—Twenty-eight native Bulgarian populations of *Thalictrum minus* complex (Ranunculaceae) show a clear correlation between the cytotype and the type of dimer isoquinoline alkaloids (2n = 42 with BBI and 2n = 70 with ABI alkaloids). A similar correlation is evident also in the genus *Thalictrum* L. There are probably different evolutionary lines: in one the biogenesis reaches to the BBI types and in the other to the ABI types.

With some 120 species, *Thalictrum* L. is one of the largest genera of the Ranunculaceae. The species are widespread in the Northern Hemisphere (1). In Europe there are thirteen species, four of them being endemic in the continent (2) and some are species complexes (or polymorphic species). In the Balkan peninsula nine *Thalictrum* species are known, and in Bulgaria six species are to be found (four subspecies have been also reported) (3). Of great taxonomic, evolutionary and phytochemical interest is the complex *Thalictrum minus*. It is wide spread in most of Europe, the Caucasus, Siberia and Southwestern Asia. The cytological investigations during the last fifty years proved its cytologic as well as its morphologic variability. Several cytotypes have been found: diploid (2n = 14) was reported from Italy (4), hexaploids (2n = 42) from many localities and by a number of authors from 1927 onwards (5, 6, 7). Decaploid cytodeme (2n = 70) was reported for a population of the species in Kamtchatka (8) and dodecaploids (2n = 84) for plants from the European part of the USSR (9). Some other chromosome numbers are also known in the complex—a pentaploid (2n = 35) (9) and an aneoploid (2n = 40) (9).

In all native Bulgarian populations studied (7), two cytotypes were found—hexaploid, more common in the lowland and mountain foothills from sea level up to an altitude of 700–1200 m and decaploid, rarer, restricted to some localities in the mountains from 600–1200 up to 2200 m (see Map 1).

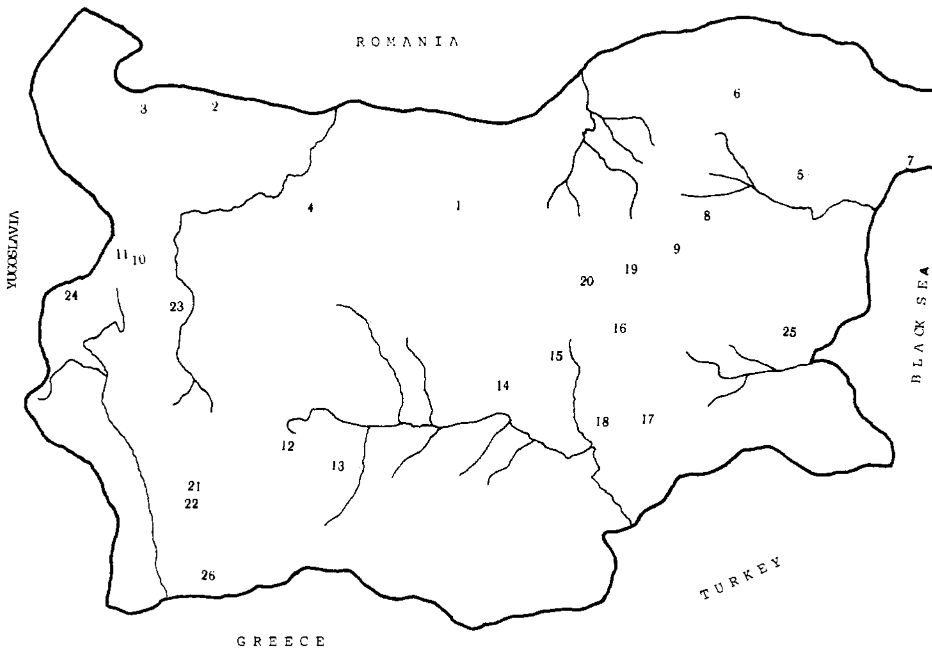
From cytological data in Bulgaria and the reference data for other parts of Europe and Asia, one may assume that hexaploids are probably the most common in the complex; while decaploids are rarer, diploids and dodecaploids being the rarest at present. Tetraploids up to now are not recorded. The cytogeographical pattern of the complex at present is not clear. One may connect the decaploid and dodecaploid cytotypes with more extreme ecological niches. On the other hand there is not a clear correlation between the known cytotypes and morphotypes or subspecies. The origin of polyploid and the putative parents involved are still to be discovered. It is not known whether hexaploids, decaploids and dodecaploids are of monotopic origin or have originated at different times and in several places. Until further cytologic investigations are made in the complex in its large geographic area, data from the phytochemical investigations may be accepted as an important contribution to the understanding of the evolutionary pattern and the systematics of the complex. The pattern of the alkaloids found in species of *Thalictrum* till now is not complete at all, but still it could be used for understanding of the taxonomy and the evolution of the group.

The investigation of *Thalictrum* alkaloids has a long history. In 1880 a sub-

[1]To the memory of Professor S. Morris Kupchan, the outstanding research worker in the field of plant tumor inhibitors.

[2]Part of this work was reported on the 12th Symposium of IUPAC on Chemistry of Natural Products, September, 1980 in Tenerife.

stance with basic properties was recorded for the first time in *T. macrocarpum* (10), and in 1891 berberine was isolated from *T. flavum* (11). Later alkaloids were found in *T. angustifolium* Jaq., *T. minus* L., *T. simplex* L. and *T. petaloideum* L. (12). Gradually the phytochemical studies expanded to several *Thalictrum* species. In 1950 five new alkaloids were recorded from *T. minus*, and an attempt was made to establish their structures (13). In the last 30 years scientists, mainly from Bulgaria, Japan, USA and USSR, have studied different taxa of *Thalictrum*. Some 27 species have been investigated (mainly rhizomes) until the present. In 1970–1976 there were around 60 alkaloids (14–16) known. By May, 1981, 160 alkaloids had been isolated and their structures determined. A great number of the alkaloids proved to have well expressed biological activity (mainly hypotensive, antimicrobial and antitumor) (17–22).



MAP 1. Cytogeography of *Thalictrum minus* complex in Bulgaria.

A–2n=42: 1. Gorna Studena; 2. Cibar; 3. Lom; 4. Pleven; 5. Aleksandrija; 6. Tervel; 7. Taukliman-Balcik; 8. Targoviste; 9. Omurtag; 10. Beledie-han; 11. Ponor; 12. Glavinica; 13. Cervena Stena; 14. Cirpan; 15. Stara Zagora; 16. Mogila; 17. Topolovgrad; 18. Kamena reka; 25. Burgas.

B–2n=70: 19. Kotel; 20. Sliven; 21. Pirim Javorov; 22. Pirin-Banderica; 23. Ljulin; 24. Tran; 26. Slavjanka-Paril.

All alkaloids in *Thalictrum* are isoquinolines: simple isoquinolines, benzyltetrahydroisoquinolines, pavines, isopavines, aporphines, phenanthrenes, protoberberines, protopines, bisbenzylisoquinolines (BBI) and aporphine-benzylisoquinolines (ABI). They could be divided into two major groups: monomers and dimers (see table 2). Of the monomers, 77 individual alkaloids belong to 11 subgroups. In two species (*T. hernandezii* and *T. sultanbadaense*) monomers have not been isolated to date.

Rather characteristic for the species investigated is the subgroup of the protoberberines; one or another alkaloid appears in almost all of the species. In seven species only one protoberberine has been isolated: in *T. dasycarpum*, *T. longipedunculatum*, *T. tubiferum*, *T. foetidum*, *T. simplex* and *T. pedunculatum* it is berberine and in *T. actaefolium* it is the the closely related canadine (tetrahydroberberine). Berberine seems to be characteristic for most of the species but it

TABLE 1. List of alkaloids found in *Thalictrum* species.

SIMPLE ISOQUINOLINES
(1) O-Methylcotypalline, **(2)** noroxyhydrastinine, **(3)** corypalline, **(4)** *N*-methyl-6,7-dimethoxyisoquinolinium chloride, **(5)** *N*-methyl-6,7-dimethoxyisoquinolone, **(6)** thalifoline, **(7)** *N*-methylcorydaldine, **(8)** thalactamine, **(9)** 1,2-dihydro-6,7-methylendioxyisoquinolone, **(9a)** thalflavine.

BENZYLTETRAHYDROISOQUINOLINES
(10) thalmeline, **(11)** thalifendlerine, **(12)** (+)-reticuline, **(13)** *N*-methyl-palaudiniumchloride, **(14)** (−)-*N*-methylcoclaurine, **(15)** armepavine, **(16)** takatonine, **(17)** (+)-laudanidine.

PAVINES AND ISOPAVINES
(18) (−)-talidine, **(19)** thalisopavine, **(20)** (−)-argemonine, **(21)** (−)-norargemonine, **(22)** (−)-bisnorargemonine, **(23)** argemonine methochloride, **(24)** isonorargenomine, **(25)** eschscholzidine, **(26)** platycerine, **(27)** eschscholzidine methochloride,

APORPHINES
(28) thalicmine (ocoteine), **(29)** thaliporphine (thalicmidine), **(30)** glaucine, **(31)** preocoteine, **(32)** (+)-magnoflorine (thalictrine), **(33)** (+)-thalphenine, **(34)** (+)-bisnorthalphenine, **(35)** (+)-nanthenine methochloride **(36)** (+)-corydine **(37)** (+)-*N*-methyllaurotetanine, **(38)** *N*-demethylthalphenine, **(39)** isocorydine, **(40)** isoboldine, **(41)** *O*-methylisoboldine, **(42)** thalicminine, **(43)** thalicsimidine, **(44)** *O*-methylcassiffiline (northalicmine), **(44a)** thalisopinine.

PHENANTHRENES
(45) thaliglucinone, **(46)** thaliglucinone metho salt, **(47)** thaliglucine, **(48)** thaliglucine metho salt, **(49)** thalflavidine, **(50)** thalictuberine, **(50a)** thalphenine-methine.

PROTOBERBERINES
(51) berberine (thalsine), **(52)** (+)-canadine (tetrahydroberberine), **(53)** palmatine, **(54)** jatrorrhizine, **(55)** thalifendine, **(56)** thalidastine, **(57)** deoxythalidastine, **(58)** columbamine, **(59)** oxyberberine (berlambine), **(60)** palmatrubine, **(61)** berberrubine, **(62)** (−)-isocorypalmine, **(63)** *N*-methylcanadine-hydroxide (canadine-β-methochloride, **(63a)** thalifaurine, **(63b)** dehydrodiscretine.

PROTOPINES
(64) β-Allocryptopine (thalictrimine), **(65)** cryptopine (thalisopyrine), **(66)** protopine, **(67)** thalictrisine, **(68)** protothalipine.

GLYCOSIDE-BENZYLISOQUINOLINES
(69) (−)-veronamine.

MORPHINAN–DIENONES
(70) (−)-palladine.

HERNANDALINE TYPE
(71) (+)-hernandaline, **(72)** thaliadine.

OXOBENZYLISOQUINOLINES
(73) Rugosinone.

BISBENZYLISOQUINOLINES (BBI)
I. *One ether bridge*—11-12': **(74)** thalistyline, **(75)** *N*-desmethylthalistyline, **(76)** methothalistyline, **(77)** thalibrine, **(78)** neothalibrine, **(79)** thalirabine, **(80)** thaliracebine, **(81)** thalistine, **(82)** *O*-methylthalibrine, **(83)** thalirugidine, **(84)** thalirugine, **(85)** thaliruginine, **(86)** northalibrine.
II. *Two ether bridges*—7-8'; 11-12': **(87)** homoaromoline (homothalicrine), **(88)** aromoline (thalicrine), **(89)** thalrugosamine, **(90)** oxyacanthine, **(91)** obaberine.
III. *Two ether bridges*—8-7'; 11-12': **(92)** hernandezine (thalicsimine), **(93)** thalidezine, **(94)** isothalidezine, **(95)** *N*-desmethylthalidezine, **(96)** obamegine, **(97)** thalrugosine, **(98)** berbamine, **(99)** isotetrandrine (*O*-methylberbamine), **(100)** thalsimine, **(101)** *N*-norhernandezine, **(102)** thalibrunine, **(103)** *N*-northalibrunine, **(104)** thalibrunimine, **(105)** oxothalibrunimine, **(106)** thalictrinine, **(107)** dihydrothalictrinine, **(108)** thalisamine, **(109)** thalsimidine.
IV. *Two ether bridges*—8-6'; 11-12': **(110)** *O*-methylthalicberine (Thalmidine), **(111)** *O*-methylthalmethine, **(112)** thalicberine, **(113)** thalmethine.
V. *Two ether bridges*—8-5'; 11-12': **(114)** thalidasine, **(115)** thalfoetidine (thalictrinine), **(116)** thalpindione, **(117)** *N*-methylthalrugosidine, **(118)** thalrugosidine, **(119)** thalrugosinone.
VI. *Two ether bridges*—5-8'; 11-12': **(120)** thalfine, **(121)** thalfinine, **(122)** thalmirabine.
VII. *Two ether bridges*—5-7'; 12-13': **(123)** thalbadaensine, **(124)** thalictine.
VIII. *Two ether bridges*—5-8'; 12-13': **(125)** thalmine, **(126)** thaligosidine.
IX. *Two ether bridges*—8-7'; 12-13': **(127)** thalrugosaminine, **(128)** thalisopine, **(129)** thalisopidine, **(130)** *O*-methylthalisopine, **(131)** thaligosinine, **(132)** thaligosine.

APORPHINE–BENZYLISOQUINOLINES
(133) thalicarpine, **(134)** thalmelatine, **(135)** thalictropine, **(136)** (+)-thalictrogamine, **(137)** (+)-pennsylvanine, **(138)** thalipine, **(139)** pennsylvanamine, **(140)** dehydrothalicarpine, **(141)** thalidoxine**, **(142)** northalicarpine, **(143)** revolutopine, **(144)** thalirevoline, **(145)** thalilutidine, **(146)** thalilutine, **(147)** thalirevolutine, **(148)** foetidine (fetidine), **(149)** adiantifoline **(150)** *O*-desmethyldiantifoline, **(151)** dehydrothalmelatine, **(152)** thaliadanine, **(153)** thalmelatidine, **(154)** thalmineline.

OTHER DIMERS NOT MENTIONED IN THE TABLE
(155) pennsylpavine, **(156)** pennsylpavoline (130), **(157)** revolutinone (47).

TABLE 2. Types and distributional pattern of isoquinoline alkaloids in *Thalictrum* species.

MONOMERS

Type of alkaloids Taxa	Simple isoquinolines (1–9)	Benzyltetahydro-isoquinolines (10–17)	Pavines and isopavines (18–27)	Aporphines (28–44)	Phenanthrenes (45–50a)	Protoberberines (51–63)	Protopines (64–68)	Glycosidic benzyliso-quinolines (69)	Morphinandienones (70)	Hernandaline type (71,72)	Oxybenzyliso-quinolines (73)	Total monomers in the species
1. Sect. Macrogynes Lec.												
1.1 Subsect. Anomalo-carpes Lec.												
T. hernandezii Tausch...												—
T. fendleri Engelm......		11(24)		28,30, 32(25), 29,31 (26)		51,54 (25) 55,56 (24,25)		69(27)				11
T. macrocarpum L......						51(10)						1
T. longistylum DC......				32(29)	45(29)	51,53–55,58, 59(29)						8
T. podocarpum Humb...				32(30)	45(30)	51,53–55,58, 59(30)						8
1.2. Subsect. Homalocarpes Lec.												
T. polygamum Muhl....	1,2(31)	12(31) 13(32)	18(31)	32(32, 33) 33(34), 34(35), 35(36)	45(33) 46,48 (35), 50a (34) 47(34)	51(32, 33) 55(33), 57(31, 33), 60(31), 61(33)			70(31)	71(37)		21
T. dasycarpum Fisch et Lall.................	3(39)	17(39)	19,21, 22(39)	32(40)		51(40)						7
T. longipedunculatum Steud............				32(46)	51(46)							2
T. dioicum L............	1(45)	14(45)		36,37 (45)		51,55, 61,62 (45)			70(45)			9
T. revolutum DC........	4(47)	12(18), 14(18, 47),15 (47), 17(18)	20,25 (47,48), 23,26, 27(47), 24(18), 26(18, 47)	32,33 (49), 34(48), 37(18, 50),38 (47,48)	45(49) 49(50)	51,53–55,57, 58(49)	64(47, 48)					26
2. Sect. Microgynes Lec.												
2.1. Subsect. Longistamines Lec.												
T. aquilegifolium L......				39(53)								1
T. tubiferum Maxim.....						51(54)						1
T. sultanbadaense Stapf.................												—
T. actaefolium Sieb. et Zucc.................						52(56)						1
T. alpinum L...........	2,5(57)			32,40, 41(57)		51,53–55,58, 59(57)						11

TABLE 2. Types and distributional pattern of isoquinoline alkaloids in *Thalictrum* species.

DIMERS

Bisbenzylisoquinolines Type of ether bridges I 74–86	II 87–91	III 92–109	IV 110–113	V 114–119	VI 120–122	VII 123,124	VIII 125,126	IX 127–132	Total BBI in the species/group	Aporphine-benzylisoquinolines 133–154	Total ABI in the species	Total alkaloids in the species/group	Origin of the plant material investigated
		92(23)							1		—	1	Mexico
		92(25, 28), **93**(26)							2	**133**(25)	1	14	Tabiona, Utah, USA
												1	
74–77 (29)									4			12	Colombia
74–76 (30)		**92–95** (30)							7			15	Colombia
										133(33), **134**(37), **135**(37, 38),**136** (38),**137**, **139**(31, 37),**138** (31)	7	28	Pennsylvania, USA
				114(41)					1	**133**(17, 43,44), **140**(42)	2	10	Wisconsin, USA
				114(143) **115**(46)					2		—	4	UzSSR
									—	**133–137**+ (141)(45)	5	14	Pennsylvania, USA
78(47)			**110**(47, 49) **111**(49)	**114**(49)				**127**(49)	5	**133**,**134** (47,48, 49),**136**–**138**,**143**, **144**,(18), **137**(49), **138**,**143**, **144**(47), **142**(50), **144–147** (52),**138**, **143**(48a)	11	42	Ohio, USA
									—		—	1	Bulgaria
									—		—	1	Korea
	92(55)					**123**(55)			2		—	2	UzSSR
									—		—	1	Japan
78(57)	**92**(58)			**114**,**116**–**118**(57)				**127**(57)	7	**133**(57)	1	19	UzSSR Finland (seeds) Ohio, USA (living plants)

+Recorded but not confirmed.

TABLE 2.—*Continued*

MONOMERS

Type of alkaloids Taxa	Simple isoquinolines (1–9)	Benzyltetrahydro-isoquinolines (10–17)	Pavines and isopavines (18–27)	Aporphines (28–44)	Phenanthrenes (45–50a)	Protoberberines (51–63)	Protopines (64–68)	Glycosidic benzyliso-quinolines (69)	Morphinandienones (70)	Hernandaline type (71,72)	Oxybenzyliso-quinolines (73)	Total monomers in the species
T. flavum L.	9a(62)			32(59)	49(60)	51(11, 59,62), 52(61)	65(59, 62)					6
T. foetidum L.				32(46)		51(46)						2
T. foliolosum DC.	2(68)			32(66)		51,53, 54(67), 59(68)						6
T. isopyroides C.A.M.				28(69), 32(46), 42(69)			65(69)					4
T. lucidum L.				32(71)	45(71)	51,53–55,58, 59(71)						8
T. minus complex[a] (incl. *T. thunbergii* DC., *T. foetidum* auct. bulg., non L.)	2,6,7,8	10,12, 16	20,25	28,29, 30,32, 33,42	45	51,54, 55,58, 63	64			72		23
T. rugosum Poar. (*T. glaucum* Desf.)	2,3,9 (110)			32(86, 111), 33(112)	45 (112) 47(53) 50(110)	51(86, 111), 54 (111), 55,57 (112), 58 (111, 112), 59(110)	66(110) 68(112)				73(110)	17
T. rochebrunianum Franc. et Sav.				32(114)	45(33)	51,54 (114)						4
T. simplex L.				32(117) 42(120) 43(84, 85,117)		51(118)	64(117) 67(120)					6
T. strictum Ledeb.			20(126)	28,42, 44(126)								4
2.2. Subsect. Brevistamines Lec.												
T. pedunculatum Engew.						51(127)						1
T. fauriei Hayata[b]				32(129)		63a, 63b (129)						3

[a]References see table 3.
[b]Systematic position undetermined.

TABLE 2.—*Continued*

DIMERS

Bisbenzylisoquinolines, Type of ether bridges: I 74–86	II 87–91	III 92–109	IV 110–113	V 114–119	VI 120–122	VII 123,124	VIII 125,126	IX 127–132	Total BBI in the species/group	Aporphine-benzylisoquinolines 133–154	Total ABI in the species	Total alkaloids in the species/group	Origin of the plant material investigated
	92(61)								1	**133**(62)	1	8	KirgSSR
				120,**121** (63)					2	**133**(64) **148**(64, 65)	2	6	KirgSSR
83(68)				**118**(68)				**127**,**128** (68)	4		—	10	Himalaya, India
			110(70)					**128**–**130** (69),**128** (70)	4		—	8	UzSSR
	87,**90**, **91**(71)	**96**,**97** (71)	**110**(71)	**114**(71)					7		—	15	Yuggoslavia, FRG (seeds), Ohio, USA (living plants)
78,**80**, **81**,**82**	**87**,**88**,**91**	**97**,**98**,**99**	**110**,**111**, **112**,**113**	**114**,**115**	**120**,**121**, **122**	**124**	**125**	**127**	22	**133**,**134**, **138**,**140**, **149**,**150**, **151**,**152**, **153**,**154**	10	56	See tables 2 and 3
78 (110), **83**–**85** (113)	**88**,**91** (110) **89** (110a)	**100**(53)		**114**(53), **119** (110)			**126** (113)	**127** (112) **131**,**132** (113)	14		—	31	Poland, Ohio, USA
77,**86** (115)		**92**(114) **101**–**107** (116)							10		—	14	Japan
		93(122), **92**(118, 121,122), **100**(123, 124,122), **108**(122), **109**(124, 125)		**115** (119)					6		—	12	Bulgaria, UzSSR KirgSSR
									—		—	4	Far East, USSR
									—		—	1	India
									—		—	3	Taiwan

has not been found in *T. strictum*, *T. aquilegifolium*, *T. isopyroides*, *T. sultanbadaense* and *T. hernandezii*.

The aporphines are the second characteristic group of monomeric alkaloids, the most common of the aporphines being magnoflorine. The alkaloids of the subgroup "simple" and "benzyltetrahydroisoquinolines" are quite rare in the Homalocarpes (128) with *T. minus* being an exception. Species of subsection Anomalocarpes and Longistamines (*T. minus* is an exception) are intermediate, while those of subsection Homalocarpes are very rich in monomer alkaloids (*T. longistamines* being an exception). In Longistamines the two subgroups (claviforms and filiforms according to Lecoyer, 128) seem to be quite different. In the claviforms three monomeric alkaloids have been isolated from only three species. In the filiforms *T. minus* appears to be a very rich species—24 different subgroup of alkaloids have been found.

Eighty-one dimeric alkaloids have been isolated from the genus. These could be subdivided mainly into two groups: bisbenzylisoquinoline (BBI)–59 alkaloids and aporphine-benzylisoquinoline (ABI)–22 alkaloids (and three other kinds of dimers). In the BBI alkaloids, nine subgroups are differentiated; alkaloids built up with one ether bridge are the most numerous (13 alkaloids) and then those with two ether linkages of type III (18 alkaloids). Only 3 alkaloids of type VI have been isolated to date and were found in *T. foetidum* and *T. minus*. Alkaloids ot types VII and VIII are very few and were found in *T. sultanbadaense*, *T. minus* and *T. rugosum*.

All ABI alkaloids are of the same type of ether linkage between the benzylisoquinoline and the aporphine. It is characteristic that thalicarpine (Nr. 133) was isolated from all species which have ABI alkaloids.

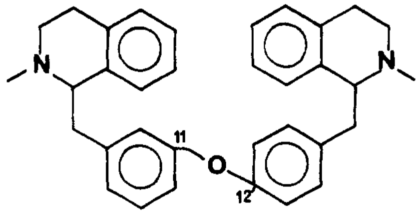
In the species of the subsection Anomalocarpes (128), a single ABI (thalicarpine) was found in *T. fendleri*. Subsection Homalocarpes has quite an interesting alkaloid pattern; being rather poor in BBI, it is very rich in ABI in all but one species (*T. longipedunculatum*). In the species of the subsection Longistamines, the first subgroup (claviforms) not only has no ABI but in three species the BBI are also absent. The complex *T. minus* appears very rich in dimers—with 22 BBI and 10 ABI.

Table 1 shows the great variety of isoquinoline alkaloids in the genus *Thalictrum*. What is interesting here is the fact that in the species of *Thalictrum* both monomers and the two types of dimers are biosynthesized. With some exceptions, the ABI indicate a significant quality of a species. In some species the monomers prevail: in the section Macrogynes, in Anomalocarpes there are 15 monomers, while there are 8 BBI, and the ABI (with one exception) could not be found at all. In Homalocarpes another pecularity is observed: the species are rich in alkaloid types—42 monomers, 6 BBI and 14 ABI.

In Microgynes the Longistamines are radically different from Brevistamines, in which only one species has been studied and alkaloids found.

In the subsection Longistamines the systematic subdivision (claviforms and filiforms) does not show a clear correlation with the alkaloid pattern. The species *T. aquilegifolium*, *T. tubiferum*, *T. sultanbadaense*, *T. strictum* and *T. actaefolium* are extremely poor in alkaloids. All other species can be subdivided into two groups: species from *T. alpinum* to *T. isopyroides* have almost equal monomers and BBI; of the ABI only thalicarpine, found in three species, and fetidine (Nr. 148), found in one species, are observed. On the other hand, in the species from *T. lucidum* to *T. simplex*, there are alkaloids of all types. It is very characteristic here that all ABI are recorded only from the *T. minus* complex.

In this light the systematic order of Lecoyer (128) seems to need some alteration. In the section Macrogynes, the Anomalocarpes and Homalocarpes are clearly separated by their alkaloid content which correlates to their morphologic



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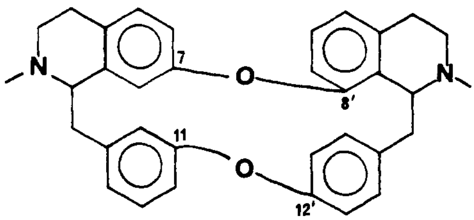

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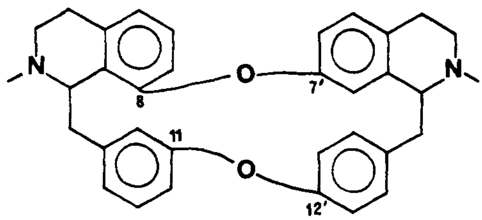
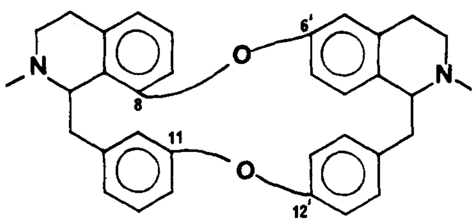
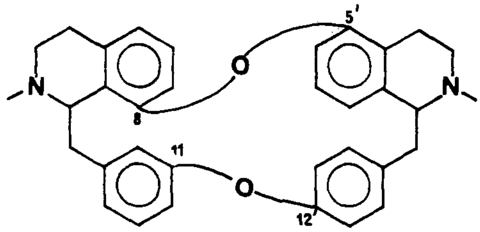


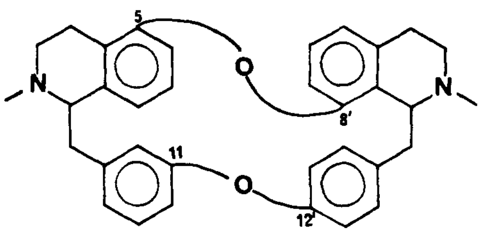
III



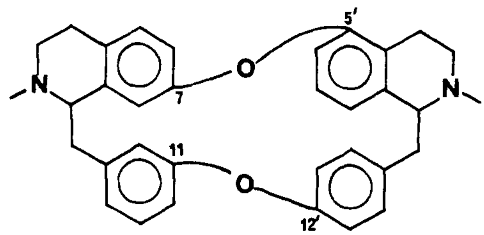
IV



V



VI



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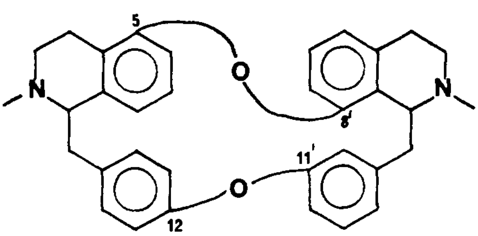
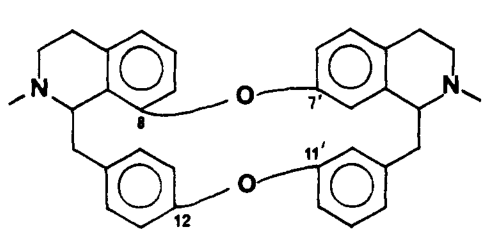


VIII



IX

characteristics. In the section Mycrogynes this is not the case. Data for the Brevistamines are almost nil. In the subsection Longistamines, one can see two lines: the first is of species *T. aquilegifolium* to *T. actaefolium,* and the second includes all species from *T. alpinum* to *T. strictum* (table 1). This does not correspond to the subdivisions of Lecoyer (128). In respect to the alkaloid content of the species this subsection needs better systematic treatment.

T. minus complex has been intensively studied in Bulgaria during the last 20

TABLE 3. Alkaloids in *Thalictrum minus* complex.

Type of alkaloids		Bulgaria	Japan	USA	USSR
Simple isoquinolines	Noroxyhxdrastinine **2** (74,75,76)	+		+	
	Thalifoline **6** (74,76)			+	
	N-methylcorydaldine **7** (51)			+	
	Thalactamine **8** (77,78)	+			
Benzyltetrahydroisoquinolines	Thalmeline **10** (75)	+			
	(+)-Reticuline **12** (79)			+	
	Takatonine **16** (80,91)		+		
Pavines and isopavines	Argemonine **20** (81)	+			
	Eschscholzidine **25** (81)	+			
Aporphines	Thalicmine **28** (13,82,83,84,85,144)				+
	Thaliporphine (Thalicmidine) **29** (13,82,83,84,85,144)				+
	Glaucine **30** (81,82)	+			+
	Magnoflorine **32** (46,76,91)		+	+	+
	(+)-Thalphenine 33 (51)			+	
	Thalicminine **42** (82,87,144)				+
Phenanthrenes	Thaliglucinone **45** (79)			+	
	Thalictuberine **50** (88)		+		
Protoberberines	Berberine **51** (46,76,78,81,86,[a]89,90,91)	+	+	+	+
	Jatrorrhizine **54** (51)			+	
	Thalifendine **55** (51,76)			+	
	Columbamine **58** (51)			+	
	N-methylcanadine-hydroxide **63** (81,92)	+			+
Protopines	β-Allocryptopine **64** (82,93)				+
Hernandaline type	Thaliadine **72** (94)			+	
Bisbenzylisoquinolines	Thalirabine **79** (79)			+	
	Thaliracebine **80** (79)			+	
	Thalistine **81** (51)			+	
	O-methylthalibrine **82** (51)			+	
	Homoaromoline **87** (95,96)		+		
	Aromoline **88** (95,96)		+		
	Obaberine **91** (79)			+	
	Thalrugosine **97** (51)			+	
	Berbamine **98** (97,98)	+			
	Isotetrandrine (*O*-methylberbamine) **99** (97,98)	+			
	O-methylthalicberine **110** (53,76,78,81,99,100)	+	+	+	+

TABLE 3. *Continued.*

Type of alkaloids		Bulgaria	Japan	USA	USSR
	O-methylthalmethine	+			
	111(78,81,101,106)				
	Thalicberine	+	+		
	112(78,81,99,100)				
	Thalmethine	+		+	
	113(78,81,101,106,138)				
	Thalidasine	+		+	
	114(53,79)				
	Thalfoetidine	+			
	115(98)				
	Thalfine			+	
	120(79)				
	Thalfinine			+	
	121(79)				
	Thalmirabine			+	
	122(51)				
	Thalictine		+		
	124(72)				
	Thalmine			+	+
	125(13,102)				
	Thalrugosaminine			+	
	127(79)				
Aporphine-benzyl-	Thalicarpine	+			
isoquinolines	**133**(103)				
	Thalmelatine	+			
	134(103,104)				
	Thalipine	+			
	138(81)				
	Dehydrothalicarpine	+			
	140(105)				
	Adiantifoline	+		+	
	149(73,75,76)				
	O-desmethyladiantifoline	+		+	
	150(75,94)				
	Dehydrothalmelatine	+			
	151(107)				
	Thaliadine			+	
	152(94)				
	Thalmelatidine	+			
	153(75,108)				
	Thalmineline[b]				
	154(109)				

[a]Romania
[b]Poland, FRG.

years. The first investigated population from Sliven (in 1963) showed a new isoquinoline alkaloid type, the ABI alkaloids, thalicarpine and thalmelatine. Soon after that in specimens from Lozen (Map 1 and table 2) another alkaloid type appeared, the BBI alkaloids, thalmethine and *O*-methylthalmethine. Gradually more and more populations were studied, and a characteristic pattern of individual alkaloids became evident (table 2). From the accumulated data, it was evident that all 27 native Bulgarian populations of the *T. minus* complex fall into two groups: in the first group (table 2, populations number 11–18 and 25, 27) the biosynthesis of the isoquinoline alkaloids favors the BBI types, while in the second group (table 2, populations number 19–27) the ABI alkaloids are favored, but the BBI types are deviated.

The populations studied showed a geographical pattern—those with BBI alkaloids are mostly found in lowlands, while those with ABI are found primarily in mountainous areas. This made us look for more general regularities in the complex pattern and for the possible chemosystematic correlations. A clear correlation between the different cytotypes and chemotypes was found. All hexaploids are characterized by the BBI having the ether bridge of types II, III, IV,

TABLE 4. Geographical pattern of the different types of alkaloids of *Thalictrum minus* complex in Bulgaria.

Population studied	2n=nx	Type of alkaloids	Monomers	Dimers
1. Gorna Studena	6x	Total alkaloids below 0.018%[c]		
2. Cibar	6x	"		
3. Lom	6x	"		
4. Pleven	6x	"		
5. Alexandrija	6x	"		
6. Tervel	6x	"		
7. Taukliman-Balcim	6x		Thalactamine Berberine	Thalmethine *O*-Methylthalmethine Thalicberine *O*-Methylthalicberine
8. Targoviste	6x	Total alkaloids below 0.018%[c]		
9. Omurtag	6x	"		
10. Beledie-han	6x	"		
11. Ponor	6x	"		
12. Glavinica	6x	"		
13. Cervena Stena (Backovo)	6x			Thalfoetidine Berbamine Isotetrandrine (*O*-Methylberbamine)
14. Cirpan[a]	6x		Berberine	Thalmethine *O*-Methylthalmethine
15. Stara Zagora	6x			
16. Mogila	6x			
17. Topolovgrad	6x		N-Methylcanadine hydroxide Berberine Argemonine Eschscolzidine Glaucine	Thalmethine *O*-Methylthalmethine Thalicberine *O*-Methylthalicberine
18. Kamena reka[a]	6x		N-Methylcanadine hydroxide Argemonine Eschscholzidine Glaucine Berberine	Thalmethine *O*-Methylthalmethine Thalicberine *O*-Methylthalicberine
25. Burgas	6x			Thalidasine *O*-Methylthalicberine
27. Lozen[b]			Berberine	Thalmethine *O*-Methylthalmenthine
19. Kotel[c]	10x			Thalicarpine
20. Sliven	10x		Berberine Glaucine Thalmeline Noroxyhxdrastinine	Thalicarpine Thalmelatine Dehydrothalicarpine Dehydrothalmelatine Adiantifoline *O*-Desmethyladiantifoline Thalmelatidine
21. Pirin-Javorov[a]	10x			Thalmelatine
22. Prim-Banderica	10x			Thalmelatine
23. Ljulin[c]	10x			Thalmelatine
24. Tran	10x			
26. Slavjanka-Paril[b]			Berberine Glaucine	Thalmelatine Thalipine

[a]Alkaloids for this population not published yet.
[b]Chromosome number not yet recorded.
[c]Unpublished tlc data (L. Evstatieva, Institute of Botany, Bulg. Academy of Sciences).

and V, while in all decaploids the ABI alkaloids are predominant. This was found also when we compared the alkaloids recorded for the *T. minus* complex in USSR, USA, and Japan (table 3). There is no data for the origin of the material examined and the chromosome number of the respective specimens, but, considering the alkaloid contents most probably the Soviet and American species were decaploid or hexaploid while the Japanese species were diploid or hexaploid.

Finally we may find some correlations between the alkaloid pattern of the *T. minus* complex and the genus as a whole. The evolutionary pattern of the complex is evidently connected with adaptive irradiation, hybridization and polyploidy, and at present diploids and dodecaploids appear the least widespread in occurrence. Decaploids are the more frequent and more dispersed in different parts of the species area, and the hexaploids are probably the most common. The evolutionary development to different polyploidy levels is very likely related to different stages of the biosynthesis of the alkaloids. The biogenesis of the alkaloids in hexaploids reaches the BBI types, but in decaploids there is a genetically preferred biogenetic route to ABI and a small number of BBI type. One may assume these differences are due to different genoms and to the involvement of different putative parents in the process of hybridization and polyploidlization which has produced allopolyploids at different levels 6x, 10x, 12x.

Similarly in the genus *Thalictrum* there are several evolutionary lines (probably independent). In some of them the development has reached the stage where there are very few dimers (almost exclusively of BBI type), while in others it has led to a higher level where the dimers are not only prevailing but are mostly of the ABI type (table 5).

TABLE 5. Total monomers and dimers in the studied species of *Thalictrum* of the respective sections and subsections in the genus.

Taxa	Alkaloids			Total
	Monomers	Dimers		
		BBI	ABI	
Macrogynes				
Anomalocarpes	15	8	1	24
Homalocarpes	44	6	14	64
Total	59	14	15	88
Microgynes				
Longistamines	42	54	11	109
Brevistamines	1	—	—	1
Total	43	54	11	110
Grand total	102	68	26	198

Isoquinoline alkaloids are the major and most common type of alkaloids (along with diterpene alkaloids in *Aconitum* and *Delphinium*) in the whole family of Ranunculaceae (131). In the tribe Thalictreae itself aporphine and protoberberine alkaloids have been established only in a few species of *Aquilegia* and *Isopyrum*. This is in contrast to the *Thalictrum* species where a great variety of isoquinoline alkaloids are biosynthesized (132–137).

ADDENDUM

Six additional species have been studied and the following alkaloids were described:

1. *T. isopyroides*—dehydrothalicmine (aporphine) .... Ref. 139
2. *T. strictum*—(−)-2,3-methylendioxy-4,8,9-trimethoxypavinane (pavine) .... Ref. 140
3. *T. polygamum*—thalignine (BBI, type III) .... Ref. 141
4. *T. dioicum*—(−)-thalidine (pavine) .... Ref. 142
5. *T. longipedunculatum*—thalicsine (phenanthrene) .... Ref. 143
6. *T. minus*—thalicmidine N-oxide (aporphine) .... Ref. 144
7. *T. minus*—preocoteine N-oxide (aporphine) .... Ref. 144

After this addition the total number of *Thalictrum* alkaloids increases to 167.

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